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Interventions to reduce or prevent obesity in pregnant women: a systematic review

S Thangaratinam,[1,2]* E Rogozińska,[1,3] K Jolly,[4] S Glinkowski,[3] W Duda,[3] E Borowiack,[3] T Roseboom,[5] J Tomlinson,[2] J Walczak,[3] R Kunz,[6] BW Mol,[7] A Coomarasamy[2] and KS Khan[1]

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The research reported in this issue of the journal was commissioned by the HTA programme as project number 09/27/06. The contractual start date was in May 2010. The draft report began editorial review in June 2011 and was accepted for publication in November 2011. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design.The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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Abstract

Interventions to reduce or prevent obesity in pregnant women: a systematic review

S Thangaratinam,[1,2]* E Rogozińska,[1,3] K Jolly,[4] S Glinkowski,[3] W Duda,[3] E Borowiack,[3] T Roseboom,[5] J Tomlinson,[2] J Walczak,[3] R Kunz,[6] BW Mol,[7] A Coomarasamy[2] and KS Khan[1]

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Background: Around 50% of women of childbearing age are either overweight [body mass index (BMI) 25–29.9 kg/m^2] or obese (BMI ≥ 30 kg/m^2). The antenatal period provides an opportunity to manage weight in pregnancy. This has the potential to reduce maternal and fetal complications associated with excess weight gain and obesity.
Objectives: To evaluate the effectiveness of dietary and lifestyle interventions in reducing or preventing obesity in pregnancy and to assess the beneficial and adverse effects of the interventions on obstetric, fetal and neonatal outcomes.
Data sources: Major electronic databases including MEDLINE, EMBASE, BIOSIS and Science Citation Index were searched (1950 until March 2011) to identify relevant citations. Language restrictions were not applied.
Review methods: Systematic reviews of the effectiveness and harm of the interventions were carried out using a methodology in line with current recommendations. Studies that evaluated any dietary, physical activity or mixed approach intervention with the potential to influence weight change in pregnancy were included. The quality of the studies was assessed using accepted contemporary standards. Results were summarised as pooled relative risks (RRs) with 95% confidence intervals (CIs) for dichotomous data. Continuous data were summarised as mean difference (MD) with standard deviation. The quality of the overall evidence synthesised for each outcome was summarised using GRADE (Grading of Recommendations Assessment, Development, and Evaluation) methodology and reported graphically as a two-dimensional chart.
Results: A total of 88 studies (40 randomised and 48 non-randomised and observational studies, involving 182,139 women) evaluated the effect of weight management interventions in pregnancy on maternal and fetal outcomes. Twenty-six studies involving 468,858 women reported the adverse effect of the interventions. Meta-analysis of 30 RCTs (4503 women) showed a reduction in weight gain in the intervention group of 0.97 kg compared with the control group (95% CI –1.60 kg to –0.34 kg; $p = 0.003$). Weight

management interventions overall in pregnancy resulted in a significant reduction in the incidence of pre-eclampsia (RR 0.74, 95% CI 0.59 to 0.92; $p = 0.008$) and shoulder dystocia (RR 0.39, 95% CI 0.22 to 0.70; $p = 0.02$). Dietary interventions in pregnancy resulted in a significant decrease in the risk of pre-eclampsia (RR 0.67, 95% CI 0.53 to 0.85; $p = 0.0009$), gestational hypertension (RR 0.30, 95% CI 0.10 to 0.88; $p = 0.03$) and preterm birth (RR 0.68, 95% CI 0.48 to 0.96; $p = 0.03$) and showed a trend in reducing the incidence of gestational diabetes (RR 0.52, 95% CI 0.27 to 1.03). There were no differences in the incidence of small-for-gestational-age infants between the groups (RR 0.99, 95% CI 0.76 to 1.29). There were no significant maternal or fetal adverse effects observed for the interventions in the included trials. The overall strength of evidence for weight gain in pregnancy and birthweight was moderate for all interventions considered together. There was high-quality evidence for small-for-gestational-age infants as an outcome. The quality of evidence for all interventions on pregnancy outcomes was very low to moderate. The quality of evidence for all adverse outcomes was very low.

Limitations: The included studies varied in the reporting of population, intensity, type and frequency of intervention and patient complience, limiting the interpretation of the findings. There was significant heterogeneity for the beneficial effect of diet on gestational weight gain.

Conclusions: Interventions in pregnancy to manage weight result in a significant reduction in weight gain in pregnancy (evidence quality was moderate). Dietary interventions are the most effective type of intervention in pregnancy in reducing gestational weight gain and the risks of pre-eclampsia, gestational hypertension and shoulder dystocia. There is no evidence of harm as a result of the dietary and physical activity-based interventions in pregnancy. Individual patient data meta-analysis is needed to provide robust evidence on the differential effect of intervention in various groups based on BMI, age, parity, socioeconomic status and medical conditions in pregnancy.

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Contents

List of abbreviations

ACOG	American Congress of Obstetricians and Gynaecologists
BMI	body mass index
CEMACH	Confidential Enquiry into Maternal and Child Health
CENTRAL	Cochrane Central Register of Controlled Trials
CI	confidence interval
CMACE	Centre for Maternal and Child Enquiries
GDM	gestational diabetes mellitus
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HDU	high-dependency unit
HR	hazard ratio
HTA	Health Technology Assessment
IGT	impaired glucose tolerance
IOM	Institute of Medicine
IQR	interquartile range
ITU	intensive therapy unit
LGA	large for gestational age
LILACS	Latin American and Caribbean Health Sciences Literature
MD	mean difference
NICE	National Institute for Health and Clinical Excellence
NICU	neonatal intensive care unit
NOS	Newcastle–Ottawa Scale
NRS	non-randomised study
NTD	neural tube defect
OR	odds ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	randomised controlled trial
RR	relative risk
SGA	small for gestational age

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

Executive summary

Background

The increasing prevalence of obesity is a major health problem: a recent Health Survey for England found that one-quarter of both men (23.6%) and women (23.8%) are obese, with a body mass index (BMI) of ≥ 30 kg/m^2. In total, 50% of women of childbearing age are either overweight (BMI 25–29.9 kg/m^2) or obese, with 18% starting pregnancy as obese. Currently, 20–40% of women gain more than the recommended weight during pregnancy, resulting in an increased risk of maternal and fetal complications. More than half of women who die during pregnancy, childbirth or the puerperium are either obese or overweight. The maternal complications associated with obesity include miscarriage, hypertensive disorders such as pre-eclampsia, gestational diabetes mellitus, infection, thromboembolism, caesarean section, instrumental and traumatic deliveries, wound infection and endometritis. The fetal risks associated with obesity include stillbirths and neonatal deaths, macrosomia, neonatal unit admission, preterm births, congenital abnormalities and childhood obesity with associated long-term risks. Excessive weight gain in pregnancy is also associated with persistent retention of the weight gained beyond pregnancy in the mother and an increase in obesity in children at 2–4 years. The health risks to the mother and baby of obesity and excessive weight gain pose significant demands on the health-care system, with an increased need for additional care and resources in both primary and secondary care settings.

The antenatal period provides a window of opportunity to deliver weight management interventions as pregnant women are motivated to make changes and there are opportunities for regular contact with health professionals. Although reduction in weight gain or weight loss may be of benefit, there is a potential for harm to the mother or baby as a result of the weight loss itself or as a result of the interventions. The Institute of Medicine (IOM) guidelines describe the optimum weight gain in pregnancy for American women based on their BMI. The guidelines recommend a gestational weight gain of 11.5–16.0 kg in women with normal BMI (BMI 18.5–24.9 kg/m^2), of 7.0–11.5 kg in overweight women (BMI 25–29.9 kg/m^2) and of 5–9 kg in obese women (BMI ≥ 30 kg/m^2). Current recommendations provide limited information on the magnitude of the benefits and adverse outcomes resulting from weight management in pregnancy.

Objectives

This health technology assessment (HTA) project was undertaken to evaluate the evidence on dietary and lifestyle interventions to reduce weight or prevent weight gain in pregnancy. The objectives were to:

- determine the effectiveness of various dietary and lifestyle interventions in pregnancy that prevent or treat obesity for maternal and fetal weight (primary objective)
- determine the effectiveness of various dietary and lifestyle interventions that prevent or treat obesity for obstetric antenatal, intrapartum and postnatal outcomes
- evaluate the benefit of the dietary and lifestyle weight management interventions in pregnancy for fetal and neonatal morbidity and mortality

- study the potential short- and long-term adverse effects in mother and baby due to dietry and lifestyle in pregnancy.
- assess the overall strength of evidence across outcomes for effectiveness and harm of interventions.

Methods

Systematic reviews of the effectiveness and harm of interventions were carried out using a methodology in line with current recommendations. The following databases were searched (1950 until March 2011) to identify relevant studies: MEDLINE, EMBASE, BIOSIS, Latin American and Caribbean Health Sciences Literature (LILACS), Science Citation Index, Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE), HTA database and PsycINFO. Relevant unpublished studies and those reported in the grey literature were searched for in databases including Inside Conferences, Systems for Information in Grey Literature (SIGLE), Dissertation Abstracts and ClinicalTrials.gov. Language restrictions were not applied. The search strategy was developed by including search terms related to 'pregnancy' and 'weight'. The search was limited by filters for 'human studies' and 'study type' (randomised clinical trials and observational trials exclusive of case series and case reports). We designed a separate search strategy in the databases previously described to identify studies on harm by including adverse effects text words and indexing terms to ensure that they were not missed. Study selection was performed by two independent reviewers. First, the electronic searches were scrutinised and full manuscripts of all citations that were likely to meet the predefined selection criteria were obtained. Studies that met the predefined and explicit criteria regarding population, interventions, outcomes and study design were selected for inclusion in the review.

Studies that evaluated any dietary, physical activity or behavioural counselling intervention with the potential to influence weight change in pregnant women were included. Pregnant women who were underweight (BMI < 18.5 kg/m^2) were excluded. Both randomised controlled trials and observational studies were included. For evaluation of adverse effects, in addition to these, case series were included. The quality of the selected randomised controlled trials and observational studies was assessed based on accepted contemporary standards. The risk of bias of the individual randomised studies was assessed in six domains: sequence generation, allocation sequence concealment, blinding, incomplete outcome data, selective outcome reporting and other potential sources of bias. Results were summarised as pooled relative risks (RRs) with 95% confidence intervals (CIs) for dichotomous data. Continuous data were summarised as mean difference (MD) with 95% CIs. Separate analyses were performed on randomised and non-randomised data. For meta-analysis of the data in the effectiveness review, non-randomised and observational data were considered only if there was a paucity of randomised trial evidence for interpretation. The chi-squared and I^2 statistics were used to assess statistical heterogeneity between trials. If substantial heterogeneity was detected ($I^2 > 50\%$), possible causes were explored and subgroup analyses for the main outcomes performed. Subgroups defined a priori were BMI of the women, type of intervention, responders, publication year (last 20 years), study quality and setting. Heterogeneity that was not explained by subgroup analyses was modelled using random-effects analysis, where appropriate. Publication bias was assessed by funnel plots of the log-odds ratios. All analysis was carried out using RevMan 5.0 statistical software (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark).

The relevant obstetric and neonatal outcomes considered to be important to decision-making were identified by a two-round Delphi survey of clinicians. Gestational diabetes, pre-eclampsia,

thromboembolism and maternal admission to the high-dependency unit (HDU) or intensive care were considered to be the critically important clinical outcomes in the evaluation of interventions to prevent or reduce obesity in pregnancy. The critically important fetal outcomes were small-for-gestational-age fetuses, shoulder dystocia, intrauterine death, long-term neurological sequelae and admission to the neonatal intensive care unit. The quality of the overall evidence synthesised for each outcome was summarised using GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology and reported graphically as a two-dimensional chart.

Results

Effectiveness of interventions

Study selection and identification

From 19,583 citations, 88 full papers were selected for assessment of eligibility. A total of 56 experimental studies (40 randomised and 16 non-randomised controlled studies; involving 8842 women) and 32 observational studies (26 cohort and six case–control studies; involving 173,297 women) evaluated the effectiveness of dietary, physical activity and other lifestyle interventions in pregnancy for maternal and fetal outcomes.

Quality of the included studies

There was a low risk of bias for blinding for objective outcome assessments (38/40, 95%) and freedom from selective reporting (31/40, 77.5%). Four of the 40 randomised studies (10%) were blinded for subjective outcomes. Half of the studies adequately addressed the issue of incomplete outcome data (19/40). Sequence generation and allocation concealment were adequate in 40% (16/40) and 7.5% (3/40) of studies, respectively, and unclear in the others.

The quality of the included non-randomised studies varied from moderate to low. None of the 16 studies used blinding. More than 70% of the included cohort studies were adequate for representativeness, selection of the cohort, outcome assessment and follow-up. Of the case–control studies, case definition, representativeness, comparability and ascertainment of outcome were adequate in > 70%.

Effect of interventions on weight-related outcomes

A total of 30 randomised studies reported the effect of interventions on maternal weight and 28 the effect of interventions on fetal weight-related outcomes. Meta-analysis of the 30 studies (involving 4503 women) showed a overall reduction in weight gain in the intervention group of 0.97 kg compared with the control group (95% CI –1.60 kg to –0.34 kg; $p = 0.003$). This reduction in gestational weight gain was largest in the dietary intervention group, with a MD of –3.36 kg (95% CI –4.73 kg to –1.99 kg; $p < 0.00001$). There was a reduction trend in the number of women in the intervention group exceeding the IOM recommendations for weight gain in pregnancy (RR 0.77, 95% CI 0.42 to 1.42) and BMI at delivery (MD –0.23, 95% CI –1.4 to 0.94) for all interventions.

Meta-analysis of the 28 RCTs including 4573 babies showed a significant reduction in the pooled birthweight estimate of the infants in the intervention group, with a MD of –0.07 kg (95% CI –0.14 kg to –0.01 kg; $p = 0.03$) for all interventions. There was a 27% reduction (RR 0.73, 95% CI 0.54 to 0.99; $p = 0.05$) in the pooled estimate for the risk of large-for-gestational-age newborn (12 RCTs, involving 3021 newborns). There was no difference in the incidence of low-birthweight or small-for-gestational-age infants between the two groups, with a RR of 0.99 (95% CI 0.76 to 1.29). The studies were homogeneous. The effect was consistently observed with all interventions.

Effect of interventions on obstetric outcomes

A total of 29 randomised trials evaluated the effect of interventions in pregnancy on obstetric outcomes. Weight management interventions in pregnancy resulted in a significant overall reduction in the incidence of pre-eclampsia (RR 0.74, 95% CI 0.59 to 0.92; $p = 0.008$) and shoulder dystocia (RR 0.39, 95% CI 0.22 to 0.70; $p = 0.02$). The largest effect was observed with dietary interventions, with a significant decrease in pre-eclampsia (RR 0.67, 95% CI 0.53 to 0.85; $p = 0.0009$) and gestational hypertension (RR 0.30, 95% CI 0.10 to 0.88; $p = 0.03$). Dietary interventions in pregnancy also resulted in a significant reduction in preterm births (RR 0.68, 95% CI 0.48 to 0.96; $p = 0.03$) and a trend towards a reduction in the incidence of gestational diabetes (RR 0.52, 95% CI 0.27 to 1.03). There were no overall differences in the rates of caesarean section (RR 0.93, 95% CI 0.85 to 1.03) or induction of labour (RR 1.12, 95% CI 1.00 to 1.26) between the groups for the interventions.

The mean gestational age of delivery was slightly reduced in the pooled estimate of all interventions, but was not statistically significant (MD –0.03 weeks, 95% CI –0.13 weeks to 0.07 weeks).

Effect of interventions on fetal and neonatal morbidity and mortality

Ten randomised studies (3375 babies) evaluated fetal and neonatal morbidity and mortality. There were no differences in the rates of admission to the neonatal intensive care unit, respiratory distress syndrome, neonatal hypoglycaemia, stillbirths and neonatal deaths or in Apgar scores at 1 minute and 5 minutes after delivery for all interventions. No differences were observed for stillbirths or perinatal deaths in the included non-randomised trials.

Adverse effects of interventions

A total of 26 studies involving 468,858 women were selected from 14,832 citations to evaluate the adverse effects of interventions. They included two randomised controlled trials and 24 observational studies (19 cohort and five case–control design).

Most of the data on adverse effects from dietary interventions were derived from studies on extreme diet and famine. There was an increase in the rate of neural tube defects and cleft lip and palate in pregnant women practising extreme forms of dieting and on high-glycaemic index diets. Starvation in pregnancy was associated with an increased incidence of metabolic syndrome, dyslipidaemia, coronary artery disease and hypertension. No significant maternal or fetal adverse effects of physical activity in pregnancy, such as cord abnormalities, threatened miscarriage, meconium-stained liquor, abnormal fetal heart rate pattern, maternal sepsis or chorioamnionitis, were observed.

Conclusions

Dietary and physical activity interventions in pregnancy are effective at reducing maternal weight gain in pregnancy (evidence quality was moderate) at birth compared with usual care. Typical dietary interventions include a balanced diet consisting of carbohydrates, proteins and fat and maintenance of a food diary. Typical physical activity-based interventions include light-intensity resistance training, weight-bearing exercises and walking for 30 minutes. They do not increase the risk of small-for-gestational-age or low-birthweight babies (evidence quality was high). Interventions that are mainly based on diet are effective at reducing obstetric outcomes such as gestational hypertension, pre-eclampsia, and shoulder dystocia and trend towards reduction in gestational diabetes (evidence quality was low to high). There were no changes in other neonatal morbidity or mortality outcomes with the interventions.

Implications for practice

The evidence is in favour of employing dietary interventions as opposed to other methods to reduce gestational weight gain in pregnancy and obstetric complications in both normal-weight and obese or overweight women. Mothers should be informed about the degree of benefit gained with weight management measures, especially diet, for various outcomes. Women can be reassured that there is no evidence of harm associated with the interventions to manage weight in pregnancy.

Recommendations for further research

Individual patient data meta-analyses will add value to the study-level data analysis reported here. There is a need for further research to identify the facilitators and barriers to the implementation of the interventions in various health-care settings. For interventions to be taken up by the women and provided by staff, the acceptability of the various components needs to be ascertained. If interventions are introduced on the basis of their effect on maternal weight change, there needs to be an evaluation alongside of their effects on other outcomes, as well as adverse outcomes. If randomised controlled trials are undertaken they should focus on clinically relevant outcomes.

[Note: The results of this systematic review for effectiveness of weight management interventions in pregnancy includes only studies published before March 2011. The findings with the updated search (until January 2012) can be accessed at *BMJ* 2012;**344**:e2088 doi10.1136/bmj.e2088.]

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Chapter 1

Background

Aim

The aim of this health technology assessment (HTA) project was to evaluate the effectiveness and harm of dietary and lifestyle interventions in pregnancy for reducing or preventing obesity and on obstetric, fetal and neonatal outcomes, through a systematic review of literature.

Background

Obesity in pregnancy

In total, 50% of women of childbearing age are either overweight [body mass index (BMI) 24.9–29.9 kg/m^2] or obese (BMI ≥ 30 kg/m^2), with 18% starting pregnancy as obese.[1] Currently, in the USA and Europe, 20–40% of women are found to gain more than the recommended weight during pregnancy,[2] resulting in an increased risk of maternal and fetal complications.[3] More than half of women who die during pregnancy, childbirth or the puerperium are either obese or overweight. The Confidential Enquiry into Maternal and Child Health (CEMACH) report identified maternal obesity as a growing overall threat to the childbearing population in the UK.[4] The maternal risks of obesity include maternal death or severe morbidity, cardiac disease, spontaneous first-trimester and recurrent miscarriage, pre-eclampsia, gestational diabetes, thromboembolism, post-caesarean wound infection, infection from other causes such as urinary and respiratory infections, post-partum haemorrhage and low breastfeeding rates.[4,5] There is also an identified, although poorly studied, adverse psychological impact on obese pregnant women. The fetal risks include stillbirth and neonatal death, macrosomia, neonatal unit admission, preterm birth, congenital abnormalities and childhood obesity with associated long-term risks.[5,6]

Excessive weight gain in pregnancy is associated with persistent retention of the weight beyond pregnancy in the mother.[7–10] Interpregnancy weight gain increases the risk of adverse maternal and fetal outcomes in subsequent pregnancies.[11] An increase in BMI of ≥ 3 units between pregnancies doubles the risk of pre-eclampsia, gestational diabetes, stillbirth and large-for-gestational-age (LGA) birth in subsequent pregnancies. Maternal obesity is also a major risk factor for childhood obesity. The obesity rate is doubled in 2- and 4-year-old children born to obese mothers. Excess weight gain during pregnancy is predictive of offspring obesity, independent of other factors.[12] This link is primarily associated with the mother's ability to breastfeed, poor dietary and exercise habits of the mother before and during pregnancy, the parenting practices of overweight and obese mothers and the exposure of the child to poor dietary behaviours and a sedentary lifestyle once they are born.

The joint Royal College of Obstetricians and Gynaecologists (RCOG) and Centre for Maternal and Child Enquiries (CMACE, formerly CEMACH) guidelines[13] and the National Institute for Health and Clinical Excellence (NICE) guidance[14] recommend that women with a BMI of ≥ 30 kg/m^2 should have consultant care rather than midwifery-led care, which places a massive burden on maternity unit resources. Obese women spend an average of 4.83 more days in hospital, resulting in a fivefold increase in the cost of antenatal care.[15] The costs associated with

newborns are also increased, as babies born to obese mothers have a 3.5-fold increased risk of admission to the neonatal intensive care unit (NICU).[4] Obesity now costs the NHS around £1B a year and the UK economy a further £2.3B of indirect costs. Reducing maternal and childhood obesity, through effective obesity treatment programmes, could result in significant advantages for the NHS and society.

The RCOG has identified weight management interventions targeting mothers as an important long-term challenge that needs research.[16] The antenatal period is an ideal time to provide dietary and physical activity interventions to manage weight. Pregnant women are highly motivated to make changes and they have opportunities for regular contact with health professionals.[17] Weight management in pregnancy plays a crucial role not only in reducing women's future risk of obesity but also in reducing their children's behavioural risk factors for obesity. Even a modest fall in BMI of > 1 unit (equivalent to 2.5 kg) between pregnancies reduces the risks of pre-eclampsia, gestational diabetes and LGA birth.[11] There is a need to identify the optimal interventions that can be delivered in pregnancy and which are effective, acceptable and safe in improving the short- and long-term outcomes for the mother and the baby.

Existing guidelines and reviews

Current recommendations from NICE,[14] RCOG[18] and the American Congress of Obstetricians and Gynaecologists (ACOG)[19] for the management of obesity include healthy diet and exercise in pregnancy with referral to a nutritionist if required. The target weights for weight gain in pregnancy are based on the recommendations provided by the Institute of Medicine (IOM),[20] ACOG[19] and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).[21] The recent NICE guidance has recommended a 'life course approach' by focusing on pregnancy and 1 year after childbirth as the crucial periods to target weight management interventions based on behavioural change and dietary and physical activity.[14]

A recent review in this area found insufficient evidence to recommend specific dietary and/or physical activity interventions to moderate gestational weight gain in pregnant women.[22] The latest CMACE/RCOG guideline on the management of obese women in pregnancy provides recommendations on the antenatal, intrapartum and postnatal care of this group of high-risk women;[13] however, gestational weight gain and the role of dietary and lifestyle interventions in pregnancy were prespecified to be outside the scope of the guideline.

Systematic reviews help clinicians, patients and policy-makers make decisions by summarising evidence. The details of the existing reviews evaluating the effect of weight management interventions on maternal and fetal outcomes are provided in *Appendix 1*. Existing reviews of the effectiveness and adverse effects of weight management interventions in pregnancy show deficiencies in quality and evidence when assessed against a validated tool and reporting checklists: PRISMA[23] (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and MOOSE (Meta analysis of Observational Studies in Epidemiology).[24] This is one of the main reasons for their limitations in the role of informing practice. An accurate and reliable summary of the evidence with clear and transparent reporting is needed to maximise their usefulness to clinicians, patients and policy-makers.[3]

Objectives of the project

This HTA project was undertaken to meet the following objectives:

- to determine, primarily, the effectiveness of dietary and lifestyle interventions in pregnant obese and normal-weight women for:
  - maternal weight change
  - fetal and neonatal weight
- to determine, secondarily, the effectiveness of dietary and lifestyle interventions in pregnant obese and normal weight women for:
  - obstetric and medical complications in pregnancy
  - fetal and neonatal morbidity and mortality
- to evaluate the potential short- and long-term adverse effects in mother and baby resulting from the type of intervention in pregnancy.

Figure 1 shows our proposed framework for the work undertaken.

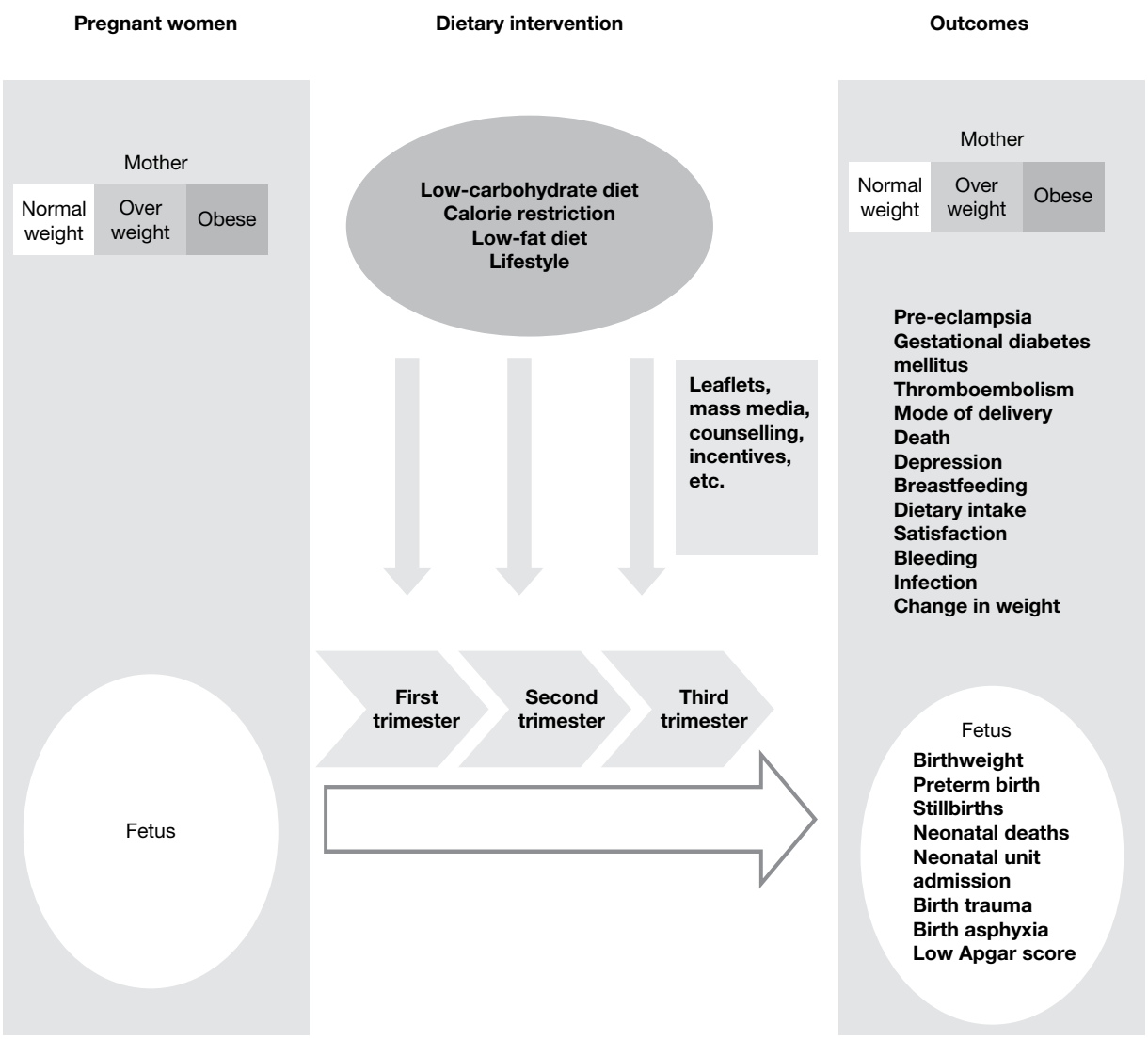

FIGURE 1 A framework to study the effectiveness of dietary and lifestyle interventions for maternal and fetal outcomes.

Chapter 2

Systematic review methods

Protocol development

Systematic reviews of the effectiveness of and harm caused by interventions were carried out using methodology[25–27] in line with the recommendations of the NHS Centre for Reviews and Dissemination and the Cochrane Collaboration, including the Cochrane Adverse Methods Subgroup.[25–33] The systematic reviews of effectiveness and of adverse effects were carried out simultaneously .

The protocol for this review included the following: a detailed literature search to identify all relevant citations, prioritisation of outcomes relevant to clinical practice by Delphi survey, assessment of the risk of bias for the individual studies and evaluation of the strength of evidence for individual outcomes using GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology.

Research question

The structured question addressed by the project is given in *Table 1*.

Methods for effectiveness review

Search strategy

A detailed search of the relevant published and unpublished literature was conducted by constructing a comprehensive search strategy for the effectiveness of dietary and lifestyle interventions in pregnancy. The following databases were searched: MEDLINE, EMBASE, BIOSIS, Latin American and Caribbean Health Sciences Literature (LILACS), Science Citation Index, Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE), HTA database and PsycINFO. In addition, information on studies in progress and unpublished research or research reported in the grey literature were sought by searching a range of relevant databases including Inside Conferences, Systems for Information in Grey Literature (SIGLE), Dissertation Abstracts and ClinicalTrials.gov. Internet searches were also carried out using

TABLE 1 The research question addressed by the project

Question components	Details
Population	Pregnant women who are obese (BMI ≥ 30 kg/m^2) or overweight (BMI 25–29.9 kg/m^2) and pregnant women of normal weight (BMI 18.5–24.9 kg/m^2)
Intervention	Dietary intervention, physical activity-based intervention and mixed approach (see *Table 2*)
Outcomes	Primary outcome: weight-related outcomes
	Secondary outcomes: obstetric outcomes, fetal and neonatal morbidity and mortality (see *Table 3*)
Study design	Systematic review

specialist search gateways (such as OMNI: www.omni.ac.uk/), general search engines (such as Google: www.google.co.uk/) and meta-search engines (such as Copernic: www.copernic.com/). The aim was to identify all studies evaluating the effectiveness of interventions for weight management in pregnancy.

The search strategy was designed in a multistep process by combining search terms related to pregnancy and weight. The search was limited by including search filters for 'human studies' and 'study type' (randomised clinical trials and observational trials without case series and case studies). Existing search strategies or filters, such as the InterTASC Information Specialists' Sub-Group Search Filter Resource, were used to develop the search strategy with some modifications as needed. No further limitations were applied. The detailed search strategy for effectiveness is provided in *Appendix 2*. MEDLINE and EMBASE were searched from inception to May 2010. Other databases were searched from inception to June 2010. The search was repeated and updated until March 2011. A comprehensive master database of articles was constructed using Reference Manager 12.0® software (Thomson Reuters, New York, NY, USA).

Inclusion criteria

The criteria for inclusion of studies in the effectiveness review are described in the following sections.

Population

Pregnant women expecting one or more than one baby (i.e. twins or triplets) were included. We included women who were of normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2) or obese (BMI ≥ 30 kg/m^2). We excluded pregnant women who were underweight (BMI < 18.5 kg/m^2).

Setting

Any setting including primary care or secondary and tertiary units.

Interventions

We included any dietary, physical activity and behavioural change intervention that has the potential to influence weight change in pregnancy. Studies that evaluated interventions mainly based on dietary advice were classified in the dietary interventions group. Interventions primarily based on physical activities such as swimming, running and aerobic exercise were classified in the physical activity group. The mixed approach interventions group included studies that employed diet and physical activity components that may, or may not, be underpinned by behavioural theory. *Table 2* lists the various interventions reviewed.

Comparison

The control group consisted of women with no intervention or routine antenatal care. In women with obstetric or medical complications the care provided was appropriate to the condition (e.g. insulin in diabetic women).

Outcomes

The maternal and fetal outcomes included in the review are provided in *Table 3*.

Study design

We included randomised controlled trials (RCTs) evaluating the effectiveness of dietary and lifestyle weight management interventions in pregnancy for maternal and fetal outcomes. Non-randomised studies (NRSs) and observational studies (cohort and case–control) were included

TABLE 2 Interventions and intervention providers for weight management in pregnancy

Interventions and intervention delivery	Details
Dietary intervention	Energy and intake of total diet and specific food (e.g. low-carbohydrate diet, low-fat diet, high-fibre diet, low-protein diet, balanced diet, Atkins diet, Slimming World diet); dietary patterns, frequency of eating; and meal composition
Physical activity-based intervention	Walking, swimming, aerobic dancing, low-intensity resistance exercise, aqua aerobics and exercise regimes of various intensity
Mixed approach intervention	Intensive counselling regarding diet and physical activity in pregnancy and stepped-care advice. Behavioural change model (e.g. transtheoretical model, theory of planned behaviour, self-determination theory) predominantly underpinning the intervention
Intervention delivery	One-to-one counselling, motivational talk, dietary consultation, group exercise, supermarket tours, cooking demonstration, parentcraft classes, walking group, benefits/incentives, slimming club and mass media (TV, radio, DVD, social websites, NHS websites)
	BMI chart, diet self-monitoring tools, self-weight check, postal questionnaires, IOM weight gain grid; Bassett obstetric chart

TABLE 3 Maternal and fetal outcomes evaluated in the review

Outcomes	Components
Weight-related outcomes (primary)	
Maternal	Change in maternal weight (absolute gain or loss in weight; percentage of weight gained or reduced in comparison with pre-intervention weight), fat content measurement (BMI, skinfold thickness, ponderal index, fat-free mass) and fat distribution measures (waist-to-hip ratio, waist size) in pregnancy
Fetal	Birthweight related to gestational age and sex, fetal fat mass and ponderal index (weight/length^3)
Obstetric and pregnancy-related outcomes	
Fetal and neonatal complications	Pre-eclampsia, gestational diabetes mellitus, gestational hypertension, premature rupture of membranes, caesarean section, post-partum haemorrhage, sepsis, maternal death, preterm labour, abruption, complications of labour and delivery, instrumental delivery, perineal trauma, induction of labour, need for hospitalisation, day-care unit visits in pregnancy and the puerperium, use of intensive care in pregnancy or the puerperium, thromboembolism, stillbirth, perinatal and neonatal death, congenital abnormalities, prematurity, abnormal Apgar score, neonatal respiratory distress, shoulder dystocia, abnormal cord pH at birth, hypoxic–ischaemic encephalopathy, long-term neurological sequelae, need for NICU admission, mechanical ventilation and duration of hospital stay
Childhood and adult outcomes in offspring	Childhood obesity, adult obesity, diabetes mellitus, coronary heart disease, hypertension, stroke, depression and death
Other relevant outcomes	Maternal: cardiac arrest, stroke, psychiatric problems, depression, self-esteem, low back pain, and change in diet and exercise

in the analysis only when the evidence from RCTs was insufficient. Studies that did not provide data to estimate effectiveness measures such as relative risk (RR) or mean difference (MD) were excluded.

Subgroups

The following subgroups were specified a priori and reported in the review:

- intervention: dietary, physical activity and mixed approach interventions
- BMI: obese only, obese and overweight and mixed-group populations
- setting: studies in developed countries and developing countries
- year of publication: studies published before 1990 and since 1990
- diabetes in pregnancy
- responders to the intervention with significant reduction in gestational weight gain.

Study selection

Study selection was conducted in two stages: an initial screening of titles and abstracts against the inclusion criteria to identify potentially relevant papers followed by screening of the full papers of the identified citations without language restrictions. Two reviewers independently assessed each citation (ER and SG) for inclusion in the review. Any differences in opinion were resolved by discussion and by involving a third reviewer. Further information was sought from the study authors if required. The process of study identification and selection is presented in *Figure 2*, consistent with the PRISMA guidelines.

Study quality assessment

The studies were classified by study design according to the NICE guidelines algorithm for classifying quantitative study designs.[34] Quality assessment was carried out separately for the different study designs (RCTs, NRSs and observational studies).

Randomised controlled trials

We assessed the risk of bias – selection bias, performance bias, measurement bias and attrition bias – in line with the recommendations made in the *Cochrane handbook for systematic reviews of interventions*.[35] Study quality was assessed in six domains: sequence generation, allocation sequence concealment, blinding, incomplete outcome data, selective outcome reporting and other potential sources of bias.

Sequence generation

An adequate sequence generation should describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether or not it should produce comparable groups. The use of a random component was considered to be adequate sequence generation. Systematic methods, such as alternation or assignment based on date of birth, case record number or date of presentation, were considered to be inadequate.

Allocation concealment

A study was categorised as being at low risk of bias for allocation concealment if it described the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.

The quality of allocation concealment was chosen using the following criteria:

- adequate concealment of allocation, such as telephone randomisation, consecutively numbered sealed opaque envelopes
- unclear whether adequate concealment of allocation
- inadequate concealment of allocation such as random number tables, sealed envelopes that are not numbered or opaque.

Where the method of allocation concealment was unclear, whenever possible attempts were made to contact authors to provide further details.

Blinding

Adequate blinding described all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. It should also provide any information relating to whether or not the intended blinding was effective. In assessing the risk of bias from blinding, we specifically assessed who was and who was not blinded. Furthermore, we also assessed separately the risk of bias for subjective and objective outcomes.

Incomplete outcome data

We evaluated the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. We assessed whether attrition and exclusions were reported, the numbers in each intervention group (compared with the total number of randomised participants), reasons for attrition or exclusions where reported and any reinclusions in the analyses.

A study was considered to be at low risk of bias for missing outcome data when we were confident that the participants included in the analysis were exactly those who were randomised into the trial. The risk of bias was considered to be unclear if the numbers randomised into each intervention group were not clearly reported. A study was labelled as having a high risk of bias for missing outcome data when there was a difference in the proportion of incomplete outcome data across groups and the availability of outcome data was determined by the participants' true outcomes.

Selective outcome reporting

We compared the outcomes reported in the individual studies with the rest of the studies to assess the possibility of selective outcome reporting. The risk of this bias was assessed at the study level.

Other sources of bias

Any other important concerns about bias not addressed in the above domains were highlighted as other sources of bias. The proportions of studies with various risks of bias are shown in *Appendix 4*. The entries for each domain were marked as 'Yes', 'No' or 'Unclear' as appropriate.

Non-randomised studies

Quality assessment of NRSs was performed using a methodology checklist presented in *Appendix 5*. The Newcastle–Ottawa scale (NOS) was used to assess the quality of the observational comparative studies with cohort and case–control designs.[25] The cohort studies were assessed for the following risks of bias:

- selection of cohorts regarding the representativeness and selection of the exposed cohort, ascertainment of exposure and that the outcome of interest was not present at the start of study
- comparability of the cohorts based on methods or analysis
- assessment of outcome by evaluating the details of outcome assessment, adequacy of length of follow-up for the outcomes to appear and adequacy of follow-up of the cohorts.

The case–control studies were evaluated for the following risks of bias:

- selection of cases and controls, assessing representativeness and adequate definition of the cases and adequate selection and definition of the controls
- comparability of the cases and controls
- ascertainment of exposure, method of ascertaining exposure of the cases and controls and rates of non-response in the groups.

The studies are allocated stars according to the rating. A study can be awarded a maximum of four stars for selection, two for comparability and three for ascertainment of exposure.[36]

Data extraction

Study clinical characteristics and findings were extracted in duplicate by independent reviewers using predesigned and piloted data extraction forms. Any disagreements were resolved by

consensus and/or arbitration involving a third reviewer. Missing information was obtained from investigators if it was crucial to the subsequent analysis. To avoid introducing bias, unpublished information was treated in the same way as published information. In addition to using multiple reviewers to ensure the reproducibility of the overview, sensitivity analyses around important or questionable judgements regarding the inclusion or exclusion of studies, the validity assessments and data extraction were performed. A copy of the data extraction form for the effectiveness review is provided in *Appendix 18*.

Data synthesis

We calculated pooled RRs with 95% confidence intervals (CIs) for dichotomous data. Continuous data were summarised as MD with standard deviation or median change in relation to the baseline. In the case of missing standard deviations, imputation techniques were used based on Cochrane recommendations.[35] Separate analyses were performed on randomised and non-randomised data. Non-randomised data were used for outcomes for which there were no RCTs or a very small number of poor-quality RCTs. The I^2 statistic was used to assess statistical heterogeneity between trials. In the absence of significant heterogeneity, results were pooled using a fixed-effect model. If substantial heterogeneity was detected ($I^2 > 50\%$), possible causes were explored and subgroup analyses for the main outcomes performed. Subgroups defined a priori were BMI of the women, type of intervention, responders, publication year (before and after 1980), study quality and setting. Heterogeneity that was not explained by subgroup analyses was modelled using random-effects analysis where appropriate. For outcomes for which meta-analysis was not appropriate, the RCT and NRS results were presented, where possible, on a forest plot but without summary scores, allowing a visual presentation of the effects of each included trial. For observational studies, a narrative summary of the findings was given. Statistical analysis was performed when sufficient data were presented. RevMan, version 5.0, (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark) was used in the statistical analyses.

Methods for adverse effects review

The review of harm of interventions was undertaken based on recommended methods for systematic reviews, particularly those of observational studies and adverse events, including those of the Cochrane Adverse Effects Subgroup.[30,37–39]

Search strategy

The scope of the review of adverse effects of any dietary intervention on pregnant women and their children was purposefully kept broad. This was to identify a variety of adverse effects that were previously not known or recognised. In addition to the search for relevant reviews and primary studies on the effectiveness of interventions, including those that were excluded from the analysis of benefit, we evaluated studies that specifically provided details of adverse effects resulting from the dietary and lifestyle interventions and weight loss in pregnancy. We designed a separate search strategy to identify studies on harm by including adverse effects text words and indexing terms in the databases previously described in the section on the effectiveness review. Existing search strategies or filters, such as the InterTASC Information Specialist Sub-Group Search Filter Resource, were used to develop the search strategy for this review, with some modifications if needed. The search was limited by including search filters for 'adverse events' , 'human studies' and 'study type' (exclusion of editorials and letters). The detailed search strategy for adverse effects can be found in *Appendix 2*. MEDLINE and EMBASE were searched from inception to June 2010. Other databases were searched from inception to July 2010. The search was updated until March 2011.

Inclusion criteria

The criteria for inclusion of studies in the adverse effects review are described in the following sections.

Population

Pregnant women expecting one or more than one baby (i.e. twins or triplets) were included. We included women who were of normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2) or obese (BMI ≥ 30 kg/m^2). We excluded pregnant women who were underweight (BMI < 18.5 kg/m^2).

Setting

We included studies carried out in any setting including primary care or secondary and tertiary units.

Interventions

Any dietary and physical activity intervention or exposure that has the potential to cause harm to the mother or baby.

Outcomes

We included any clinically significant adverse outcomes in the mother and the child resulting from (1) a dietary intervention or (2) weight change in pregnancy. We also evaluated the most common adverse effects that led to pregnant women discontinuing an intervention.

Study design

Both comparative (RCTs, NRSs and observational studies) and non-comparative studies including case series and case reports were included. This encompassed any publication as an abstract or full text without any language restrictions.

Study selection and quality assessment

Criteria used to assess the quality of studies for the evaluation of adverse effects followed the same concepts as for assessing study quality for effectiveness: assessing risk of bias, inconsistency of results, indirectness of the evidence, imprecision and publication bias. For assessing the risk of bias in estimating adverse event rates associated with weight management interventions in pregnancy[24] we took into account existing checklists for the evaluation of randomised and non-randomised studies,[39,40] including study design and other features associated with outcome [e.g. small for gestational age (SGA), preterm delivery]. Quality assessment and presentation of results were carried out separately for RCTs, NRSs and observational studies with a control group and for observational studies without a control group (case series, case reports). Additionally, information on weight change per se in mother and baby were also extracted as these could be associated with adverse event rates or severity. The methodological quality of all eligible data sets ('risk of bias') was assessed to investigate internal validity (the extent to which the information is probably free of bias) using the following attributes:[41]

- reporting of adverse maternal and fetal outcome definitions to reduce bias in ascertainment of denominator data in the series (any published definition reported vs no definition)
- adequacy of data source to ascertain a capture of denominator data that is as complete as possible (use of multiple data sources, special surveys or clinical studies vs routine registration enrolment in weight loss programmes, in which adequate attribution of cause of harm has been shown to be questionable for maternal and fetal outcomes, leading to substantial under-reporting)

- use of a robust approach to ascertain that the cause of harm is a representation of the underlying condition that is as true as possible (confidential enquiries, use of multiple sources of outcome vs no special efforts to confirm cause)
- a sufficiently high proportion of cases with an attributable cause of harm established (< 5% unclassified).

Data extraction

Methods for study selection and data extraction for the adverse event review were similar to those for the effectiveness review. Study clinical characteristics and findings were extracted in duplicate by independent reviewers using a predesigned and piloted data extraction form (see *Appendix 19*). Any disagreements were resolved by consensus and/or arbitration involving a third reviewer. Missing information was obtained from investigators if it was crucial to subsequent analysis. To avoid introducing bias, unpublished information was treated in the same way as published information. In addition to using multiple reviewers to ensure the reproducibility of the overview, sensitivity analyses around important or questionable judgements regarding the inclusion or exclusion of studies, the validity assessments and data extraction were performed.

Data synthesis

The number of adverse events reported in pregnant women and children was obtained for each intervention to compute a percentage of the total number of women and children in whom the occurrence of a particular adverse event or confirmation of its absence was reported.[41] It is inappropriate to calculate adverse event rates from case studies; thus, a qualitative summary was undertaken. Quantitative adverse event rate calculations were restricted to series of women undergoing weight management interventions and weight change as identified from RCTs and observational studies, with and without controls (case series). The adverse events were quantified as RRs and 95% CIs. The point estimates of proportions and their 95% CIs are represented in forest plots to explore heterogeneity, and the possibility of the differences being due to chance was assessed statistically using Cochran's *Q* test.

Grading of evidence

The quality of the evidence was assessed and reported separately for each outcome following the GRADE methodology. This is because even within one review the quality of the evidence can vary between the outcomes. We defined quality of evidence as 'the extent of confidence that an estimate of effect is correct'.[42] The GRADE system classifies quality of evidence into one of four levels: high, moderate, low and very low (*Table 4*).

To assess the quality, we considered, first of all, the risk of bias (internal validity), that is, the extent to which the design, methods, execution and analysis were not controlled for bias in the assessment of effectiveness.[30] Furthermore, we explored the (in)consistency of results (heterogeneity), (in)directness of the evidence (with respect to the question under consideration, including surrogate parameters), (im)precision of the results and publication bias. We assigned all evidence a 'high' level of quality when it was based on RCTs. If any of the reasons below applied to the body of evidence, for each comparison–outcome pair the quality level was

TABLE 4 Quality of evidence and definitions[27]

High quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very-low quality	Any estimate of effect is very uncertain

downgraded by one level (if the reason was classified as serious) or two levels (if the reason was classified as very serious):

- Risk of bias may arise from limitations in the study design and implementation. We downgraded evidence quality if there was lack of allocation concealment (selection bias), lack of blinding (performance bias), incomplete accounting of patients and outcome events (attrition bias), and other limitations affecting outcome assessment (detection bias).
- Inconsistency referred to heterogeneity in results, which could arise from differences in populations, interventions or outcomes. Widely differing estimates of the effects across studies suggests that there might be true differences in underlying effect. When heterogeneity existed, but investigators failed to identify a plausible explanation, the quality of evidence was downgraded by one or two levels, depending on the magnitude of the inconsistency in the results.
- Indirectness referred to broader or more restricted assessment of the review question components including population, intervention, comparator and outcomes.
- Imprecision of results referred to wide 95% CIs as a result of few participants or few events. We downgraded the quality of evidence because of imprecision if there was a non-significant result or wide CIs.

We tabulated these features and assigned an overall quality grade to the evidence for each comparison–outcome pair. The footnotes in each table (e.g. *Table 10*) provide an explanation as to how we downgraded evidence in light of various deficiencies (*Table 5*).

The secondary maternal and fetal outcomes critical to clinical care of the patient were prioritised by a two-round Delphi survey of clinicians. The Delphi panel of clinicians was chosen for their interest in the field. A structured list of these outcomes (*Box 1*) was sent to 20 clinicians along with a covering letter explaining the purpose of this survey. The questionnaire was sent by e-mail and anonymity was maintained between panellists. In the first round, the experts were asked to rank the outcomes for their importance on a 1–9 scale (1–3 not important; 4–6 important,

TABLE 5 Criteria for assessing risk of bias

Bias	No downgrading	Downgrading by one (possibly two) levels	Downgrading by two or three levels
1. Selection bias	Studies with randomisation, allocation concealment, similarity of groups at baseline	RCTs with some deficiencies in randomisation e.g. lack of allocation concealment, or NRSs with either similarities at baseline or use of statistical methods to adjust for any baseline differences	Non-randomised, with obvious differences at baseline, and without analytical adjustment for these differences
2. Performance bias	Differed only in intervention, which was adhered to without contamination; groups were similar for cointerventions or statistical adjustment was made for any differences	Confounding was possible, but some adjustment was made in the analysis	Intervention was not easily ascertained or groups were treated unequally other than for intervention or there was non-adherence, contamination or dissimilarities in groups and no adjustments made
3. Measurement bias	Outcome measured equally in both groups, with adequate length of follow-up (i.e. at least 2 years after delivery); direct verification of outcome, with data to allow calculation of precision estimates	Inadequate length of follow-up or length not given	Inadequate reporting or verification of maternal mortality or differences in measurement in both groups
4. Attrition bias	No systematic differences in withdrawals between groups and with appropriate imputation for missing values		Incomplete follow-up data, not intention-to-treat analysis or lacking reporting on attrition

BOX 1 List of maternal and fetal outcomes relevant to patient care in the evaluation of weight management interventions in pregnancy

Maternal outcomes

Gestational diabetes mellitus

Pre-eclampsia/pregnancy-induced hypertension

Post-partum haemorrhage

Prolonged labour

Preterm delivery

Induction of labour

Prelabour rupture of membranes

Caesarean section

Instrumental delivery

Perineal trauma

Puerperal pyrexia (≥38°C)

Miscarriage

Need for resuscitation at delivery

Antepartum haemorrhage

Thromboembolism

Admission to the high-dependency unit/intensive care unit

Anaemia

Back pain

Infections

Postnatal incontinence

Postnatal depression

Anxiety

Quality of life

Physical activity

Dietary behaviour

Body fat (%)

Breastfeeding

Threatened miscarriage

Failed instrumental delivery

Coronary artery disease

Non-infective respiratory distress

BOX 1 List of maternal and fetal outcomes relevant to patient care in the evaluation of weight management interventions in pregnancy (*continued*)

Fetal, neonatal and childhood outcomes

Small for gestational age

Large for gestational age

Skinfold thickness (mm)

Fetal fat mass (%)

Abdominal circumference

Head circumference

Ponderal index (g/cm^3 × 100)

Neonate length/crown–heel length

Head-to-abdomen ratio

Birthweight-related outcomes such as BMI

Hypoglycaemia

Hyperbilirubinaemia

Intrauterine death

Respiratory distress syndrome

Admission to NICU

Shoulder dystocia

One or more perinatal complications

Birth trauma

Neural tube defect

Cleft lip or palate or both

Other congenital abnormalities

Abnormal Apgar score

Cardiotocographic abnormalities

Cord pH abnormal

Long-term neurological sequelae

Cord abnormalities

Long-term metabolic sequelae

but not critical; 7–9 critical). They were given the opportunity to add outcomes that were considered to be relevant but not included in the list. Summary statistics such as medians and interquartile ranges (IQRs) were generated for each outcome. The median was used to identify the location on the appropriateness scale and an IQR (i.e. a measure of dispersion generated by taking the difference between the 75th and the 25th percentiles) of ≤ 2 was predefined to indicate consensus. In the second round the experts were asked to reconsider their previous ratings in view of the panel score. The new median scores and IQRs were recalculated. The top 10 outcomes were identified for inclusion in the GRADE evidence profile in addition to the primary weight-related outcomes.

The strength of evidence for each outcome was assessed. The main maternal and fetal weight-related outcomes and those prioritised by the Delphi panel were assessed by GRADE methodology using GRADEpro software version 3.2.2 [GRADEpro (computer program), version 3.2 for Windows; Jan Brozek, Andrew Oxman and Holger Schürmann, 2008]. Two reviewers independently assessed the quality of each study; disagreements were resolved by consensus or arbitration involving a third reviewer. For each comparison–outcome pair we deployed a two-dimensional chart plotting five variables represented on equiangular spokes starting from the same point, each spoke representing one of the domains used in evidence grading.[43] These included study design, risk of bias, inconsistency, indirectness and imprecision. The data length of a spoke was proportional to the magnitude of the quality, ranging from high to moderate to low to very low. A line connected the data values for each spoke generating a pentagon. Consistent use of the same position and angle of the spokes in all comparison–outcome pairs was used for easy visual interpretation in a multiplot format.

Chapter 3

Effectiveness of the interventions

Study selection

At the final update on 31 March 2011, 19,563 potentially relevant citations were identified from the major electronic databases to evaluate the effectiveness of weight management interventions in pregnancy for maternal and fetal outcomes. A further 23 studies were identified from the reference lists of the identified studies. In total, 88 articles were included in the review. *Figure 2* shows the flow diagram of study identification, selection and exclusion.

A total of 56 experimental studies (40 randomised and 16 non-randomised controlled studies;[44–59] involving 8842 women) and 32 observational studies (26 cohort[60–85] and six case–control studies;[86–91] involving 173,297 women) evaluated the effectiveness of dietary, physical activity and other lifestyle interventions in pregnancy for maternal and fetal outcomes. The 40 RCTs included 12 trials on dietary interventions,[92–103] 20 on physical activity[104–123] and eight on mixed approach[124–130] in pregnancy for the prevention or reduction of obesity. *Appendix 3* provides details of the included RCTs.

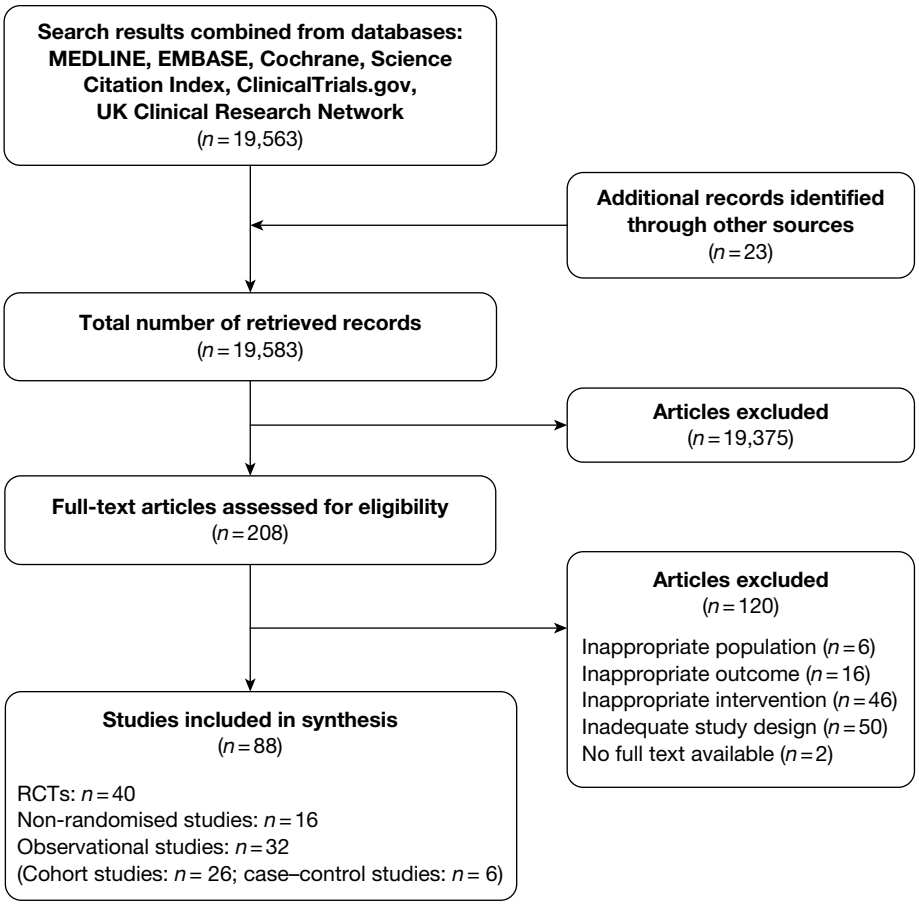

FIGURE 2 Flow chart of study identification and selection in the effectiveness review.

Quality of included studies

Randomised controlled trials

Figure 3 demonstrates the risk of bias of the included RCTs in the seven domains. Two-thirds of studies scored a low risk of bias for selective reporting of outcomes and blinding for objective outcomes. Although there was no obvious evidence of a high risk of bias for sequence generation, allocation concealment and blinding for subjective outcomes, a large proportion of the studies were unclear in their reporting in these domains. *Appendix 4* provides a detailed quality assessment of the individual RCTs.

Non-randomised studies and observational studies

The internal validity of NRSs has been assessed in line with the NICE checklist.[34] *Figure 4* presents the quality of the included NRSs. Further details of the individual study quality for non-randomised and observational studies are provided in *Appendices 5* and *6*. The observational studies were evaluated using the NOS and could score a maximum of nine stars, with four stars for selection, two for comparison and three for outcome assessment. In total, 7/26 (26.9%) cohort studies had a low risk of bias and scored seven or more stars, 18/26 (69.2%) had a medium risk of bias and scored between four and six stars and one study (3.8%) had a high risk of bias (see *Appendix 6*). All six case–control studies had a medium risk of bias.

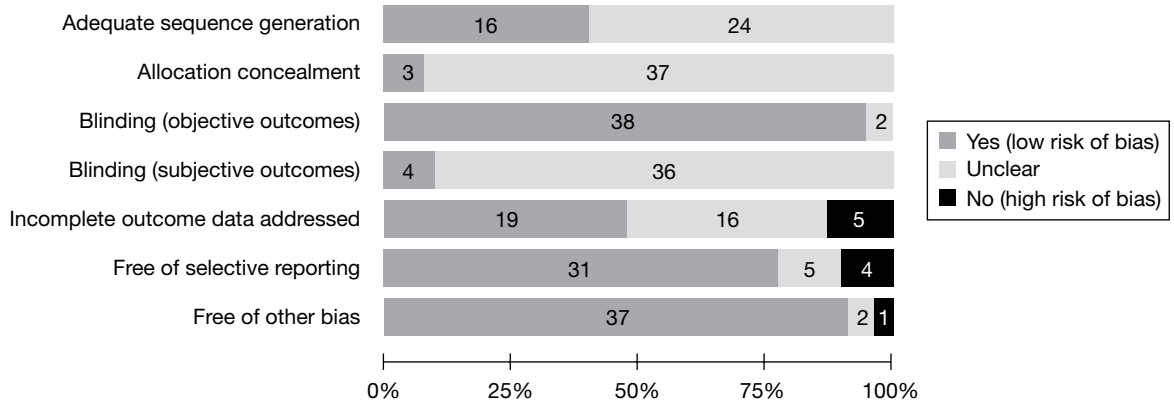

FIGURE 3 Quality assessment of the included RCTs.

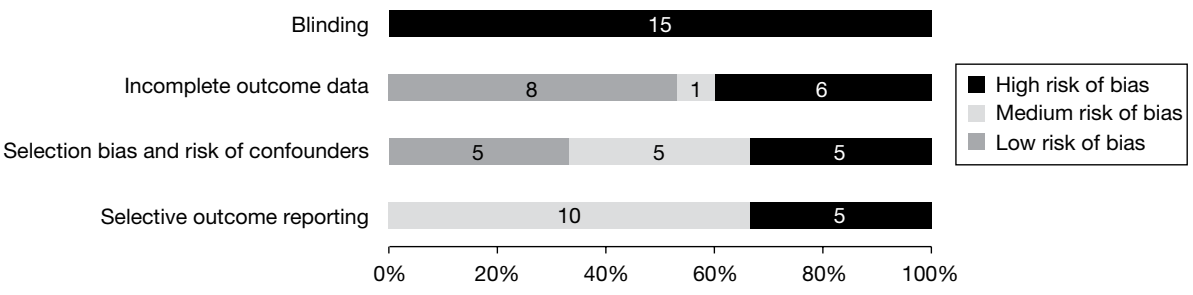

FIGURE 4 Quality assessment of the included NRSs.

Effect of the interventions on weight-related outcomes

Maternal weight-related outcomes

Maternal weight gain in pregnancy

A total of 30 RCTs[17,93–96,99–105,107–109,111–114,116–120,123,124,126–128,130] including 4503 women evaluated the effect of interventions on maternal weight gain in pregnancy. This included nine[93–96,99–103] trials on dietary interventions, six[17,124,126–128,130] on mixed approach and 15[104,105,107–109,111–114,116–120,123] on physical activity interventions. There was a significant decrease in weight gain in pregnancy with interventions of 0.97 kg (95% CI −1.60 kg to −0.34 kg; $p = 0.003$; $I^2 = 87\%$). The largest reduction in weight gain was observed in the dietary intervention studies, with a MD of −3.36 kg (95% CI −4.73 kg to −1.99 kg; $p < 0.00001$; $I^2 = 91\%$), followed by mixed approach, with a MD of −0.57 kg (95% CI −1.60 kg to 0.65 kg; $p = 0.27$; $I^2 = 35\%$). The studies were heterogeneous with an I^2 of 87%. There was a statistically significant difference between the intervention groups ($p = 0.0005$) (*Figure 5*).

Maternal body mass index at delivery

Three RCTs[99,104,113] reported on the effect of interventions on the mother's BMI at delivery. There was a significant reduction in BMI with dietary intervention, with a MD of −1.00 kg/m^2 (95% CI −1.67 kg/m^2 to −0.33 kg/m^2; $p = 0.003$). This effect was not observed with interventions based on physical activity. The overall pooled estimate showed a MD of −0.23 kg/m^2 (95% CI −1.4 kg/m^2 to 0.94 kg/m^2; $p = 0.70$) with a heterogeneity of $I^2 = 58\%$. There was a significant difference between the subgroups ($p = 0.04$) (*Figure 6*).

Exceeding the Institute of Medicine's recommendations on weight gain in pregnancy

The IOM guidelines[131] recommend the optimum weight gain in pregnancy for American women based on their BMI. The recommended gestational weight gain is 11.5–16.0 kg in women with normal BMI (BMI 18.5–24.9 kg/m^2), 7.0–11.5 kg in overweight women (BMI 25–29.9 kg/m^2) and 5.0–9.0 kg in obese women (BMI ≥ 30 kg/m^2). Two RCTs[128,130] reported a reduction in the number of women exceeding IOM recommendations with a dietary and physical activity intervention, which was not statistically significant (*Figure 7*).

Fetal and neonatal weight-related outcomes

Birthweight

A total of 28 RCTs (4573 newborns) evaluated the effect of the interventions on the birthweight of the newborn. This included nine RCTs on dietary interventions,[94–96,98–103] five on a mixed approach intervention[125–128,130] and 14 on physical activity-based interventions.[104,105,107,108,110,113–116,118,119,122,132] Overall, there was a small, but statistically significant, reduction in the mean birthweight of 0.07 kg (95% CI −0.14 kg to −0.01 kg; $p = 0.03$). There was heterogeneity observed among the groups ($I^2 = 68\%$), with no large birthweight reduction in the three intervention subgroups (*Figure 8*).

Large for gestational age at birth

We defined LGA infants as those above the 90th centile or with a birthweight > 4 kg. Twelve RCTs[96,97,99,101,102,105,118,125–128,130] evaluated this outcome in 3021 newborns. There was a 27% reduction (RR 0.73, 95% CI 0.54 to 0.99; $p = 0.05$) in the risk of having a LGA newborn. The results were not heterogeneous, with an I^2 of 33% ($p = 0.13$). This reduction in the incidence of LGA infants was observed with all interventions in pregnancy (*Figure 9*). Five RCTs reported the effects of the interventions on obese and overweight women. There was no significant difference in the incidence of LGA infants between the experimental and control groups of obese and overweight women (RR 1.32, 95% CI 0.55 to 3.16; $p = 0.54$; $I^2 = 78\%$).

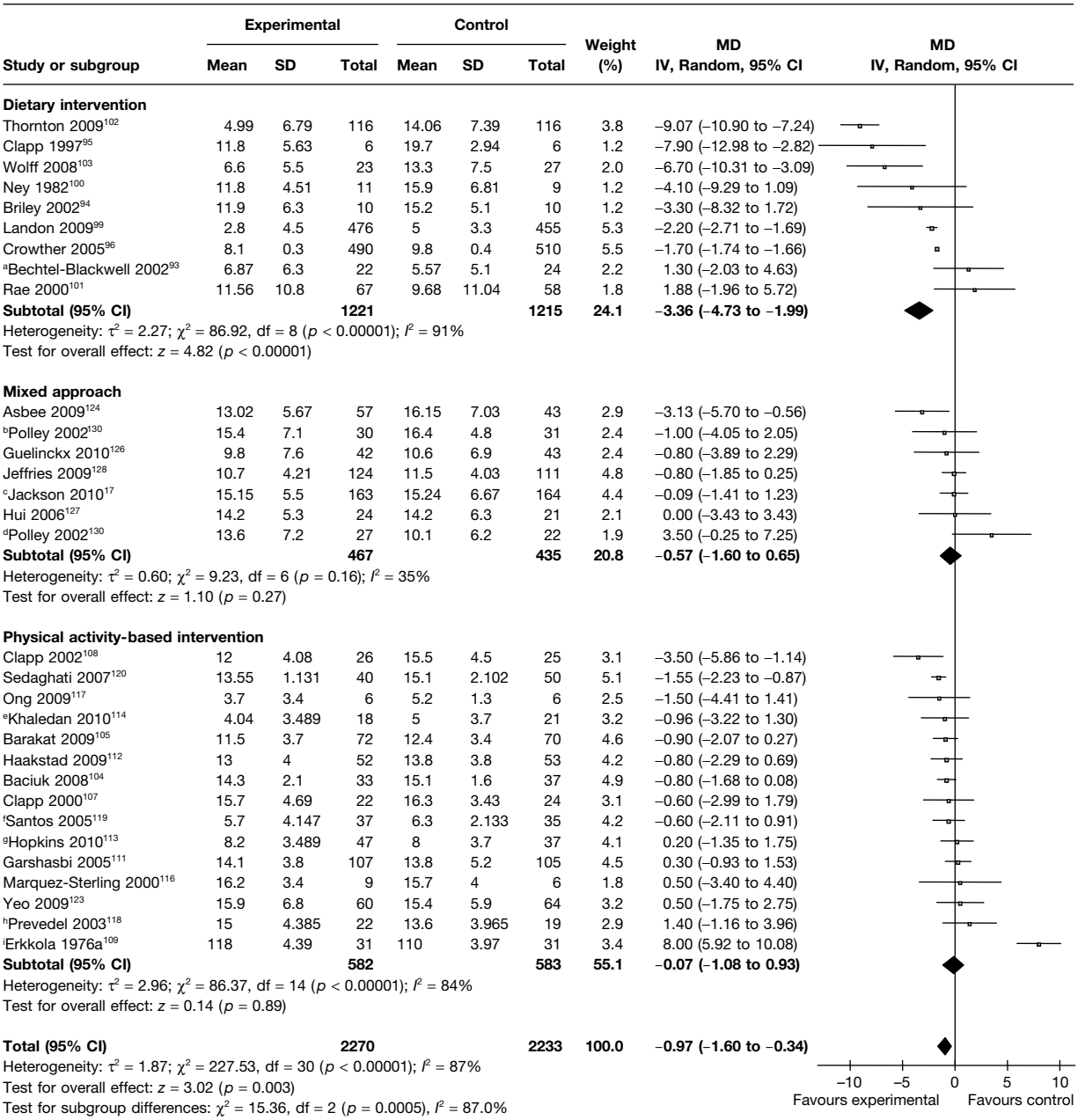

FIGURE 5 Effect of weight management interventions on maternal weight gain in pregnancy. SD, standard deviation. a, SD: from Briley 2002.[94] b, Normal weight women. c, SD: average from Asbee 2009[124] and Jeffries 2009.[128] d, Overweight women. e, SD: average from Baciuk 2008[104], Barakat 2009[105], Garshabi 2005[111], Marquez-Sterling 2000[116], Sedaghati 2007[120] and Yeo 2009.[123] f, SD: average from Barakat 2009[105] and Ong 2009.[117] g, SD: average from Baciuk 2008[104], Barakat 2009[105], Garshabi 2005[111], Marquez-Sterling 2000[116], Sedaghati 2007[120] and Yeo 2009.[123] h, SD: average from Clapp 2000[107] and Clapp 2002.[108] i, SD: average from Clapp 2000[107] and Clapp 2002.[108]

Small for gestational age at birth

Small-for-gestational-age newborns were defined as those with a birthweight below the 10th centile or < 2.5 kg. This outcome served the dual purpose of assessment of the beneficial effect of the intervention and assessment of any adverse effect of the intervention on fetal weight. Eight RCTs[96,98,99,104,105,119,128,130] (2901 newborns) evaluated the effectiveness of the weight management interventions for this outcome. The summary estimate of the RCTs showed no difference in the incidence of SGA infants with a RR of 0.99 (95% CI 0.76 to 1.29). The studies were homogeneous. The effect was consistently observed with all three interventions (*Figure 10*).

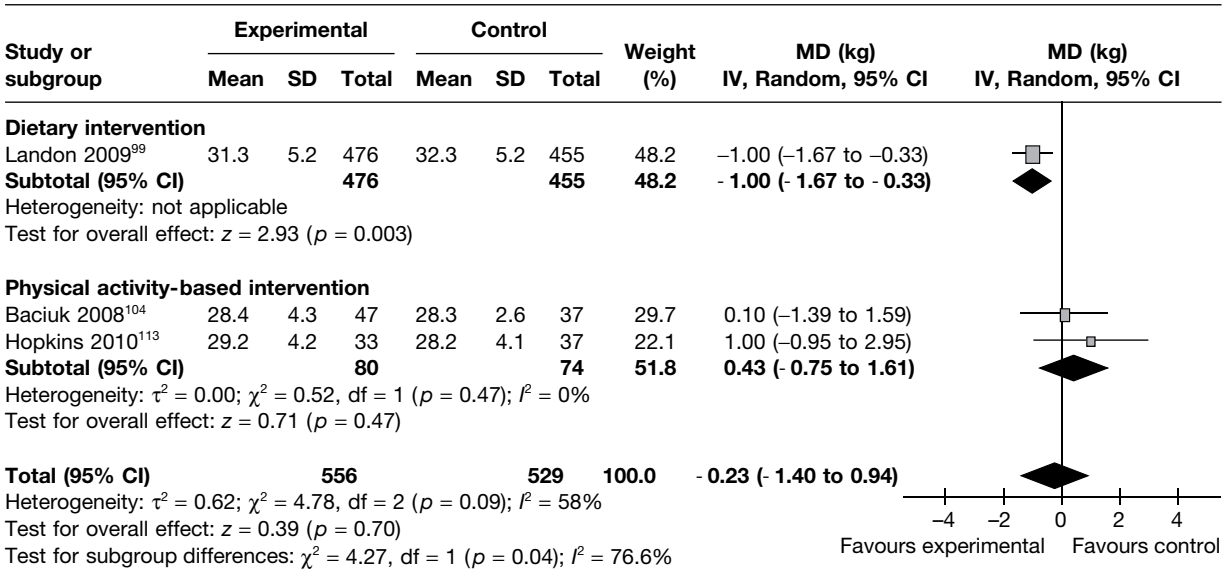

FIGURE 6 Effect of weight management interventions on maternal BMI at delivery. SD, standard deviation.

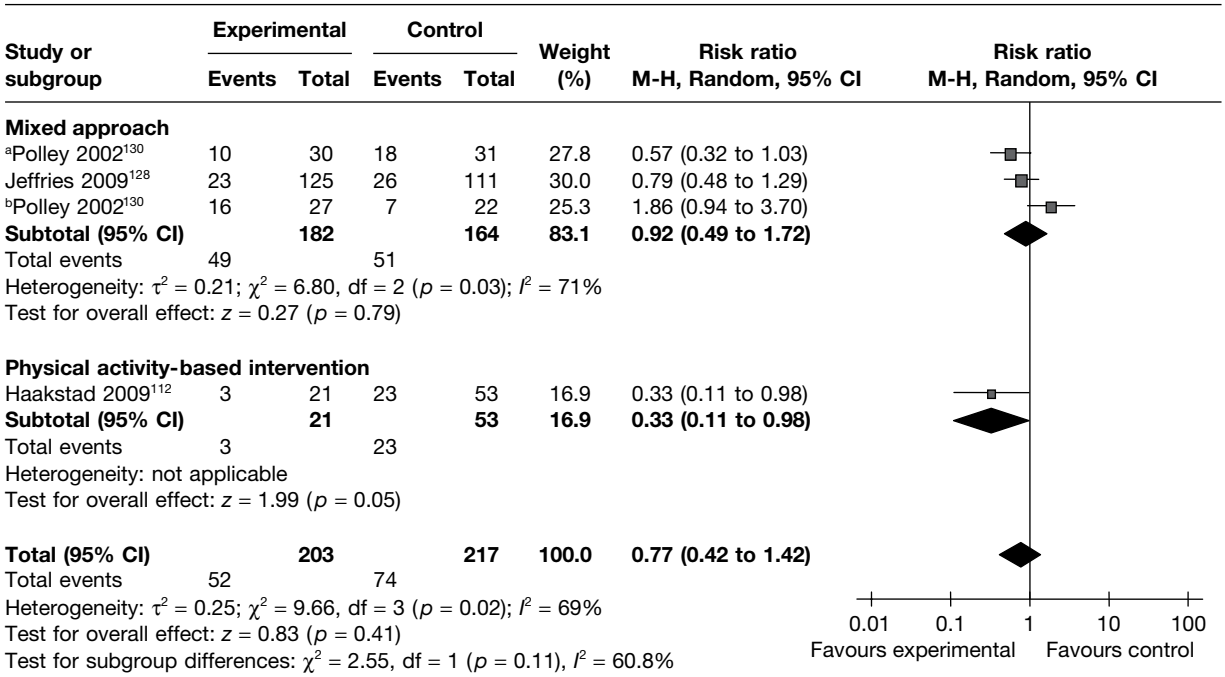

FIGURE 7 Effect of weight management interventions on IOM recommendations. a, Women with normal weight. b, Overweight women.

Ponderal index

The ponderal index for newborns assesses the relationship between the weight of the newborn and its length (kg/m^3). Four RCTs[105,107,108,113] (333 newborns) evaluated the effect of the weight management interventions on the ponderal index. The summary estimate of the trials showed no significant difference in ponderal index of the newborns between the intervention and the control groups, with a MD of –0.09 kg/m^3 (95% CI –0.18 to 0.00 kg/m^3, $I^2 = 72\%$) (*Figure 11*).

Study or subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight (%)	MD IV, Random, 95% CI
Dietary intervention								
Clapp 1997[95]	3.27	0.29	6	4.25	0.27	6	2.5	−0.98 (−1.30 to −0.66)
Crowther 2005[96]	3.335	0.551	506	3.482	0.66	524	5.8	−0.15 (−0.22 to −0.07)
Wolff 2008[103]	3.757	0.617	23	3.895	0.485	27	2.6	−0.14 (−0.45 to 0.17)
Landon 2009[99]	3.302	0.5024	485	3.408	0.5894	473	5.9	−0.11 (−0.18 to −0.04)
Thornton 2009[102]	3.526	0.60836	116	3.586	0.56081	116	4.7	−0.06 (−0.21 to 0.09)
Khoury 2005[98]	3.579	0.649	141	3.542	0.647	149	4.7	0.04 (−0.11 to 0.19)
[a]Rae 2000[101]	3.461	0.502	67	3.267	0.7311	58	3.6	0.19 (−0.03 to 0.42)
Briley 2002[94]	3.54	0.4	10	3.06	0.5	10	1.9	0.48 (0.08 to 0.88)
Ney 1982[100]	3.809	0.823	11	3.313	0.834	9	0.7	0.50 (−0.23 to 1.23)
Subtotal (95% CI)			**1365**			**1372**	**32.3**	**−0.07 (−0.21 to 0.07)**
Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 52.16$, df = 8 ($p < 0.00001$); $I^2 = 85\%$								
Test for overall effect: $z = 1.01$ ($p = 0.31$)								
Mixed approach								
Bung 1991[125]	3.369	0.534	17	3.482	0.502	17	2.2	−0.11 (−0.46 to 0.24)
[b]Polley 2002[130]	3.133	0.468	30	3.2264	0.425	31	3.6	−0.09 (−0.32 to 0.13)
[c]Polley 2002[130]	3.2828	0.463	27	3.349	0.499	22	3.0	−0.07 (−0.34 to 0.21)
Hui 2006[127]	3.402	0.473	24	3.428	0.493	21	2.8	−0.03 (−0.31 to 0.26)
Jeffries 2009[128]	3.416	0.4524	124	3.421	0.5047	111	5.1	−0.00 (−0.13 to 0.12)
Guelinckx 2010[126]	3.492	0.468	42	3.419	0.425	43	4.1	0.07 (−0.12 to 0.26)
Subtotal (95% CI)			**264**			**245**	**20.8**	**−0.02 (−0.10 to 0.07)**
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.76$, df = 5 ($p = 0.88$); $I^2 = 0\%$								
Test for overall effect: $z = 0.37$ ($p = 0.71$)								
Physical activity-based intervention								
Clapp 2002[108]	3.34	0.36	26	3.9	0.35	25	4.0	−0.56 (−0.75 to −0.37)
Marquez-Sterling 2000[116]	3.5154	0.2749	9	3.7223	0.5046	6	1.6	−0.21 (−0.65 to 0.23)
Hopkins 2010[113]	3.426	0.427	47	3.569	0.433	37	4.1	−0.14 (−0.33 to 0.04)
Barakat 2009[105]	3.165	0.411	72	3.307	0.477	70	4.8	−0.14 (−0.29 to 0.00)
Baciuk 2008[104]	3.2222	0.5627	33	3.3127	0.6561	37	2.8	−0.09 (−0.38 to 0.20)
Garshasbi 2005[111]	3.426	0.675	107	3.5	0.431	105	4.7	−0.07 (−0.23 to 0.08)
[d]Prevedel 2003[118]	3.11	0.383	22	3.175	0.425	19	3.3	−0.06 (−0.31 to 0.18)
Khaledan 2010[114]	3.28555	0.33157	18	3.35	0.53715	21	2.9	−0.06 (−0.34 to 0.21)
[e]Lee 1996[115]	3.28626	0.6501	174	3.3247	0.51303	177	5.1	−0.04 (−0.16 to 0.08)
Yeo 2008[122]	3.502	0.772	41	3.528	0.496	38	2.8	−0.03 (−0.31 to 0.26)
Santos 2005[119]	3.363	0.504	46	3.368	0.518	46	3.8	−0.00 (−0.21 to 0.20)
Erkkola 1976[110]	3.584	0.358	23	3.496	0.433	21	3.4	0.09 (−0.15 to 0.32)
Bell 2000[132]	3.589	0.43	33	3.454	0.491	28	3.5	0.13 (−0.10 to 0.37)
Clapp 2000[107]	3.66	4.22	22	3.43	4.41	24	0.1	0.23 (−2.26 to 2.72)
Subtotal (95% CI)			**673**			**654**	**46.9**	**−0.09 (−0.18 to −0.00)**
Heterogeneity: $\tau^2 = 0.02$; $\chi^2 = 30.80$, df = 13 ($p = 0.004$); $I^2 = 58\%$								
Test for overall effect: $z = 1.98$ ($p = 0.05$)								
Total (95% CI)			**2302**			**2271**	**100.0**	**−0.07 (−0.14 to −0.01)**
Heterogeneity: $\tau^2 = 0.02$; $\chi^2 = 88.08$, df = 28 ($p < 0.00001$); $I^2 = 68\%$								
Test for overall effect: $z = 2.24$ ($p = 0.03$)								
Test for subgroup differences: $\chi^2 = 1.59$, df = 2 ($p = 0.45$), $I^2 = 0\%$								

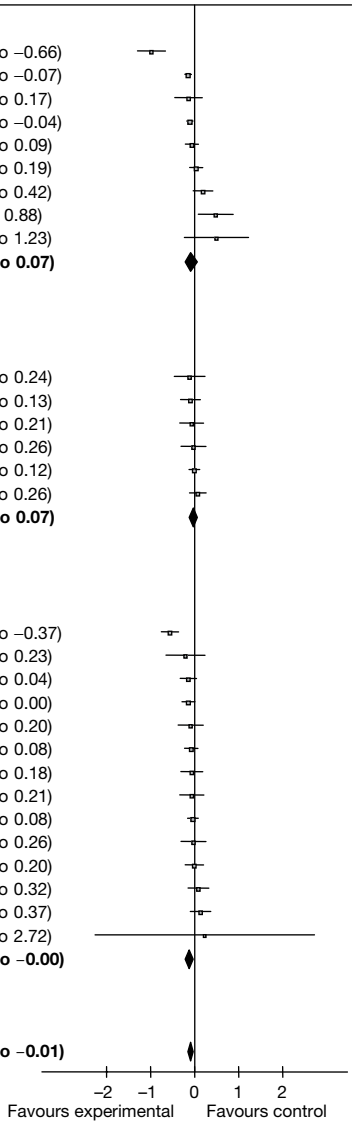

FIGURE 8 Effect of weight management interventions on birthweight. SD, standard deviation. a, SD(EXP): from Landon 2009.[99] b, Women with normal weight; SD: average from Hui 2006[167] and Jeffries 2009.[128] c, Overweight women; SD: from Guelinckx 2010.[126] d, SD: average from Bell 2000[132], Clapp 2002[108], Erkkola 1976.[110] e, Data from Kramer 2006 review.

Fetal fat mass

Fetal fat mass in kilograms was reported in four trials.[95,99,107,108] Dietary interventions resulted in a significant reduction in fetal fat mass in the intervention group, with a MD of −0.04 kg (95% CI −0.06 kg to −0.01 kg; $p = 0.005$; $I^2 = 0\%$) (*Figure 12*).

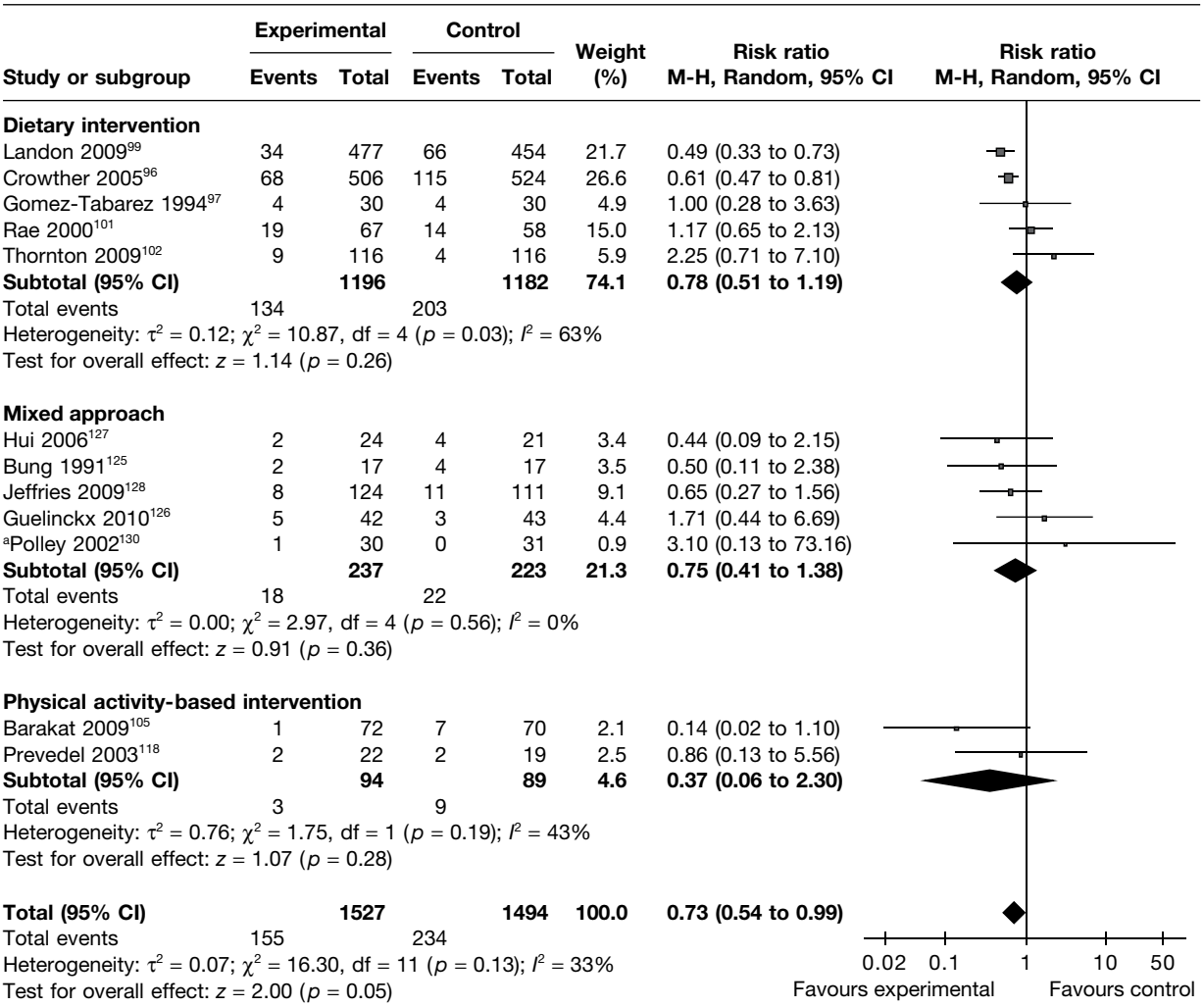

FIGURE 9 Effect of weight management interventions on the incidence of LGA infants. a, Women with normal weight.

Effect of the interventions on obstetric maternal outcomes

Gestational diabetes mellitus

Five RCTs (involving 675 women) reported on the effect of weight management interventions on gestational diabetes mellitus (GDM). Three studies included only obese or overweight pregnant women for the evaluation of a dietary intervention (two RCTs[102,103]) and a mixed approach-based intervention (one RCT[130]). There was an overall reduction in the incidence of GDM of 29% (RR 0.71, 95% CI 0.44 to 1.13; $p = 0.15$), which was not statistically significant (*Figure 13*). Weight management interventions in obese and overweight women showed a reduction of 42% (RR 0.58, 95% CI 0.30 to 1.09; $p = 0.09$). The findings were homogeneous ($I^2 = 0$) across studies and did not reach statistical significance.

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, Fixed, 95% CI
Dietary intervention						
Crowther 2005[96]	33	506	38	524	36.1	0.90 (0.57 to 1.41)
Khoury 2005[98]	11	141	12	149	11.3	0.97 (0.44 to 2.12)
Landon 2009[99]	36	477	29	455	28.7	1.18 (0.74 to 1.90)
Subtotal (95% CI)		**1124**		**1128**	**76.1**	**1.02 (0.75 to 1.37)**
Total events	80		79			
Heterogeneity: $\chi^2 = 0.70$, df = 2 ($p = 0.70$); $I^2 = 0\%$						
Test for overall effect: $z = 0.11$ ($p = 0.91$)						
Mixed approach						
[a]Polley 2002[130]	1	27	2	22	2.1	0.41 (0.04 to 4.20)
Jeffries 2009[128]	9	124	12	111	12.2	0.67 (0.29 to 1.53)
[b]Polley 2002[130]	4	30	3	31	2.9	1.38 (0.34 to 5.64)
Subtotal (95% CI)		**181**		**164**	**17.2**	**0.76 (0.39 to 1.48)**
Total events	14		17			
Heterogeneity: $\chi^2 = 1.04$, df = 2 ($p = 0.59$); $I^2 = 0\%$						
Test for overall effect: $z = 0.82$ ($p = 0.41$)						
Physical activity-based intervention						
Barakat 2009[105]	4	72	4	70	3.9	0.97 (0.25 to 3.74)
Baciuk 2008[104]	3	33	2	37	1.8	1.68 (0.30 to 9.45)
Santos 2005[119]	2	46	1	46	1.0	2.00 (0.19 to 21.30)
Subtotal (95% CI)		**151**		**153**	**6.7**	**1.31 (0.50 to 3.42)**
Total events	9		7			
Heterogeneity: $\chi^2 = 0.39$, df = 2 ($p = 0.82$); $I^2 = 0\%$						
Test for overall effect: $z = 0.56$ ($p = 0.58$)						
Total (95% CI)		**1456**		**1445**	**100.0**	**0.99 (0.76 to 1.29)**
Total events	103		103			
Heterogeneity: $\chi^2 = 3.05$, df = 8 ($p = 0.93$); $I^2 = 0\%$						
Test for overall effect: $z = 0.06$ ($p = 0.95$)						

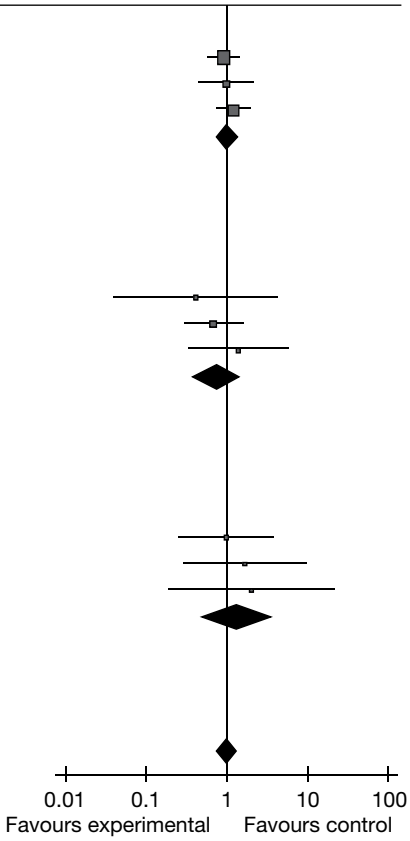

FIGURE 10 Effect of weight management interventions on the incidence of SGA infants. a, Overweight women. b, Women with normal weight.

Study or subgroup	Favours experimental Mean	SD	Total	Control Mean	SD	Total	Weight (%)	MD IV, Random, 95% CI
Physical activity-based intervention								
Clapp 2000[107]	2.49	0.15	26	2.7	0.2	25	25.3	–0.21 (–0.31 to –0.11)
Barakat 2009[105]	2.59	0.26	72	2.68	0.27	70	26.7	–0.09 (–0.18 to –0.00)
Hopkins 2010[113]	2.61	0.27	47	2.69	0.18	37	25.4	–0.08 (–0.18 to 0.02)
Clapp 2002[108]	2.65	0.14	22	2.61	0.25	24	22.6	0.04 (–0.08 to 0.16)
Subtotal (95% CI)			**167**			**156**	**100.0**	**- 0.09 (- 0.18 to 0.00)**
Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 10.68$, df = 3 ($p = 0.01$); $I^2 = 72\%$								
Test for overall effect: $z = 1.86$ ($p = 0.06$)								

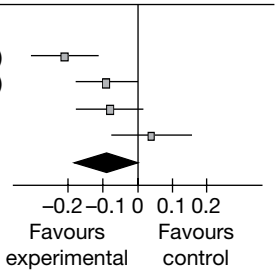

FIGURE 11 Effect of weight management interventions on ponderal index. SD, standard deviation.

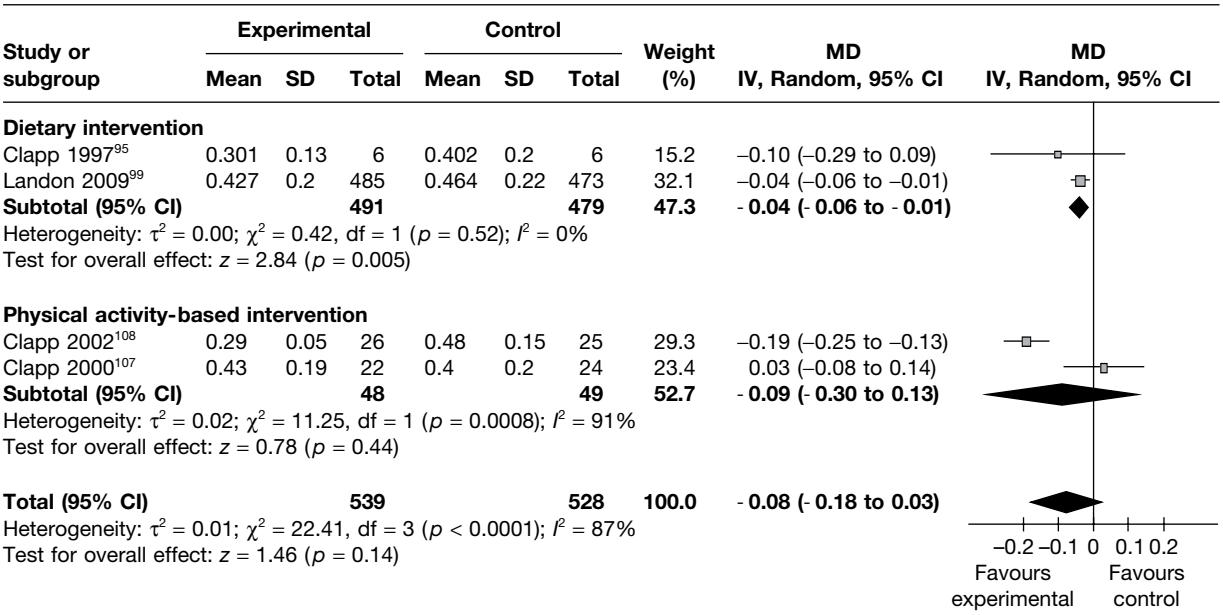

FIGURE 12 Effect of weight management interventions on fetal fat mass. SD, standard deviation.

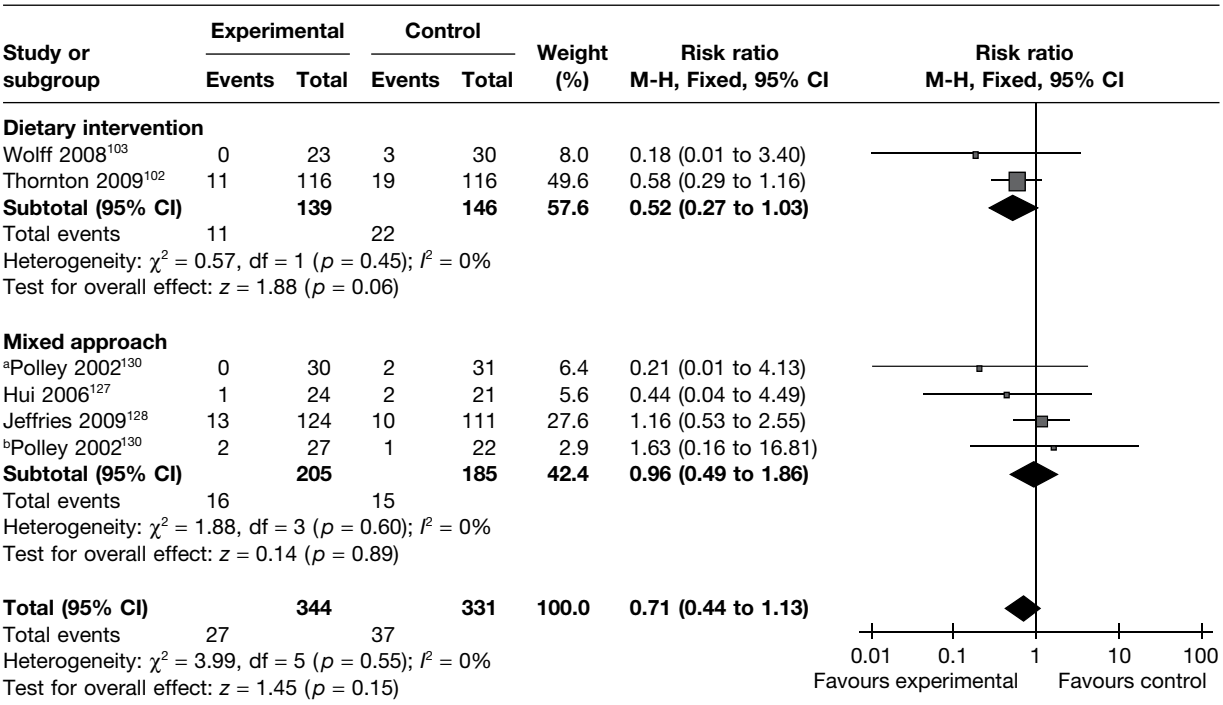

FIGURE 13 Effect of weight management interventions on GDM. a, Women with normal weight. b, Overweight women.

Pre-eclampsia

Ten studies[96,98,99,101–103,122,126,128,130] (involving 3072 women) reported the effect of weight management interventions on the incidence of pre-eclampsia. There was an overall statistically significant reduction in pre-eclampsia of 26% (RR 0.74, 95% CI 0.59 to 0.92; $p = 0.008$; $I^2 = 22\%$). The largest reduction in pre-eclampsia (33%) was observed with dietary intervention (RR 0.67, 95% CI 0.53 to 0.85; $p = 0.0009$) with no heterogeneity ($I^2 = 0$). A similar effect was not observed with physical activity-based intervention or a mixed approach (*Figure 14*). Six studies included only obese and overweight women and showed a significant reduction in pre-eclampsia with the interventions (RR 0.65, 95% CI 0.44 to 0.97; $p = 0.04$; $I^2 = 0$).

Gestational hypertension

Gestational hypertension was evaluated as an outcome in six RCTs.[102,103,122,126,128,130] There was a reduction in gestational hypertension with interventions, which was not statistically significant (RR 0.77, 95% CI 0.54 to 1.1; $I^2 = 37\%$) (*Figure 15*). Dietary intervention (two RCTs)[102,103] in pregnancy showed the greatest benefit by reducing gestational hypertension by 70% (RR 0.30, 95% CI 0.10 to 0.88; $p = 0.03$), with homogeneity between the studies ($I^2 = 0$). Both of the studies on dietary intervention were undertaken in obese and overweight women. The four studies on obese and overweight women[102,103,126,130] showed a reduction in gestational hypertension incidence that was not significant (RR 0.70, 95% 0.30 to 1.16; $p = 0.4$).

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, Fixed, 95% CI
Dietary intervention						
Wolff 2008[103]	0	23	1	27	0.9	0.39 (0.02 to 9.11)
Landon 2009[99]	12	476	25	455	16.3	0.46 (0.23 to 0.90)
Thornton 2009[102]	7	116	11	116	7.0	0.64 (0.26 to 1.58)
Crowther 2005[96]	58	490	93	510	58.1	0.65 (0.48 to 0.88)
Rae 2000[101]	14	63	13	58	8.6	0.99 (0.51 to 1.93)
Khoury 2005[98]	8	141	7	149	4.3	1.21 (0.45 to 3.24)
Subtotal (95% CI)		**1309**		**1315**	**95.3**	**0.67 (0.53 to 0.85)**
Total events	99		150			
Heterogeneity: $\chi^2 = 4.07$, df = 5 ($p = 0.54$); $I^2 = 0\%$						
Test for overall effect: $z = 3.31$ ($p = 0.0009$)						
Mixed approach						
[a]Polley 2002[130]	2	27	3	22	2.1	0.54 (0.10 to 2.97)
Guelinckx 2010[126]	2	42	1	43	0.6	2.05 (0.19 to 21.74)
Jeffries 2009[128]	6	124	2	111	1.3	2.69 (0.55 to 13.03)
Subtotal (95% CI)		**193**		**176**	**4.1**	**1.48 (0.56 to 3.94)**
Total events	10		6			
Heterogeneity: $\chi^2 = 1.96$, df = 2 ($p = 0.38$); $I^2 = 0\%$						
Test for overall effect: $z = 0.79$ ($p = 0.43$)						
Physical activity-based intervention						
Yeo 2008[122]	6	41	1	38	0.7	5.56 (0.70 to 44.09)
Subtotal (95% CI)		**41**		**38**	**0.7**	**5.56 (0.70 to 44.09)**
Total events	6		1			
Heterogeneity: not applicable						
Test for overall effect: $z = 1.62$ ($p = 0.10$)						
Total (95% CI)		**1543**		**1529**	**100.0**	**0.74 (0.59 to 0.92)**
Total events	115		157			
Heterogeneity: $\chi^2 = 11.61$, df = 9 ($p = 0.24$); $I^2 = 22\%$						
Test for overall effect: $z = 2.67$ ($p = 0.008$)						

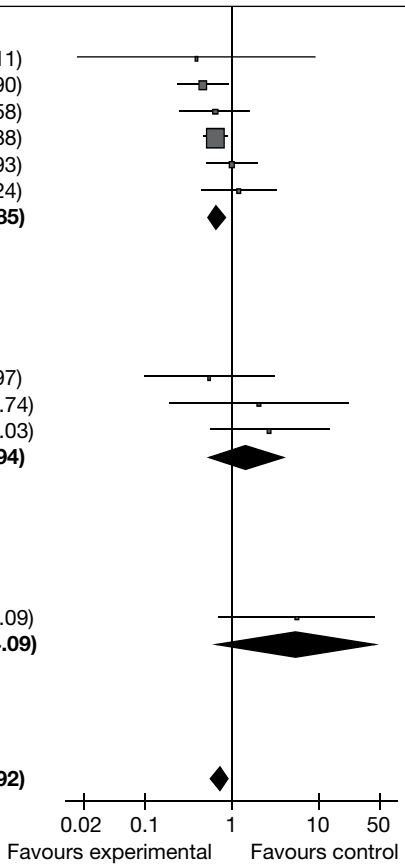

FIGURE 14 Effect of weight management interventions on the incidence of pre-eclampsia. a, Overweight women.

Preterm delivery

Eleven RCTs (involving 2198 women)[94,98,99,102,104,105,118,119,125,128,130] evaluated the effectiveness of weight management interventions in pregnancy on preterm delivery before 37 weeks of gestation. There was no overall difference in the rates of preterm births between the two groups, with a RR of 0.76 (95% CI 0.56 to 1.02) (*Figure 16*). The studies were homogeneous ($I^2 = 0\%$). The four RCTs[94,98,99,102] that evaluated a dietary intervention ($n = 1474$) showed a significant reduction in preterm births of 32% (RR 0.68, 95% CI 0.48 to 0.96; $p = 0.03$; $I^2 = 35\%$). Four RCTs[99,102,119,130] (involving 1305 women) including obese and overweight women showed a reduction in preterm births that was not statistically significant (RR 0.80, 95% CI 0.53 to 1.13; $p = 0.21$, $I^2 = 0\%$).

Gestational age at delivery

A total of 20 RCTs[96,98–105,107,108,110,111,113–116,120,125–127] (4028 women) evaluated the effect of the interventions on the gestational age at delivery. There were no significant differences in the gestational age at delivery between the intervention and control groups, with a MD of 0.03 weeks (95% CI –0.13 weeks to 0.07 weeks; $I^2 = 33\%$) (*Figure 17*). There was low heterogeneity between studies ($I^2 = 33\%$). Dietary intervention (six RCTs, involving 2625 women) resulted in a MD in the gestational age at delivery of 0.05 weeks (95% CI –0.18 weeks to 0.08 weeks; $p = 0.42$; $I^2 = 71\%$).

Mode of delivery

The rate of caesarean section was evaluated as an outcome in 14 RCTs[96,97,99,102–104,114–116,124–126,128,130] involving 3312 women. This included five trials[96,97,99,102,103] on dietary interventions, four[104,114–116] on physical activity-based interventions and five[124–126,128,130] on a mixed approach. There were

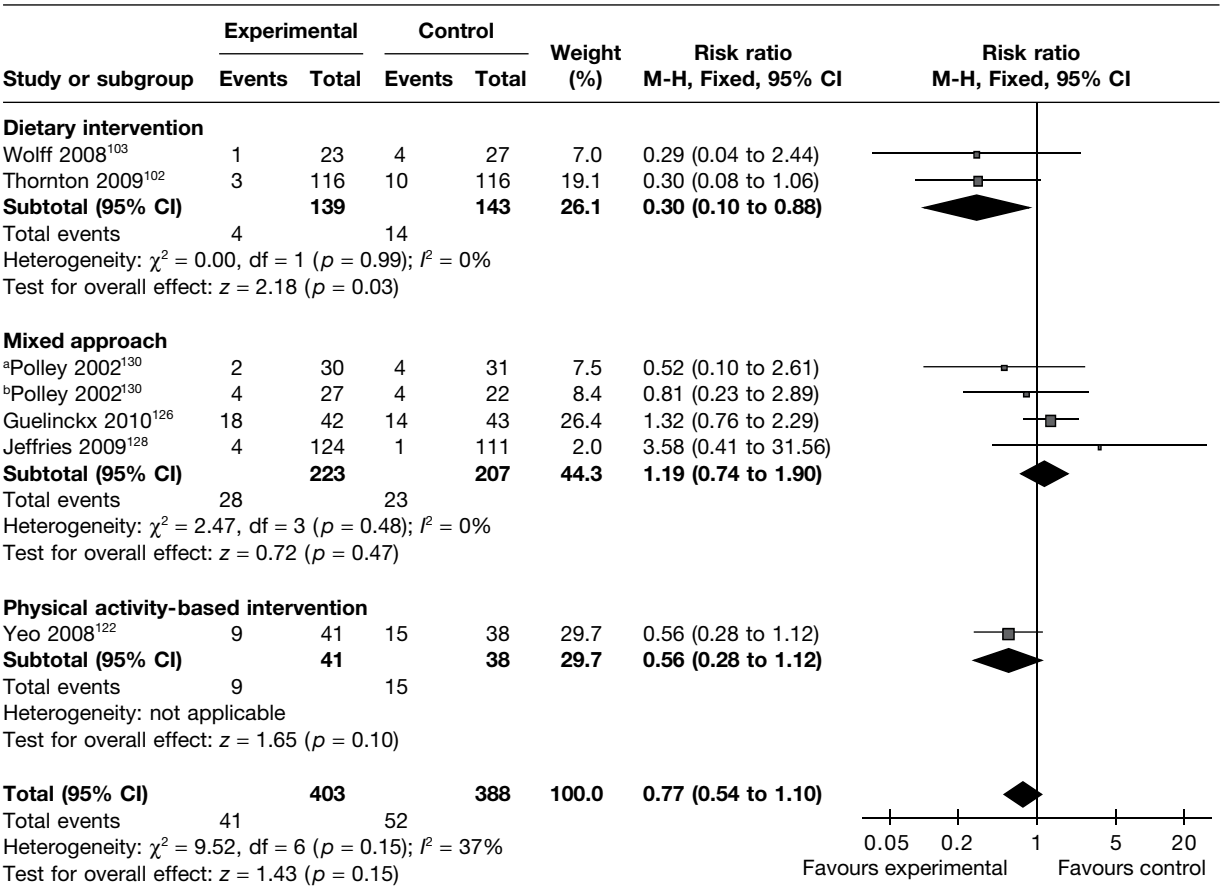

FIGURE 15 Effect of weight management interventions on the incidence of gestational hypertension. a, Women with normal weight. b, Overweight women.

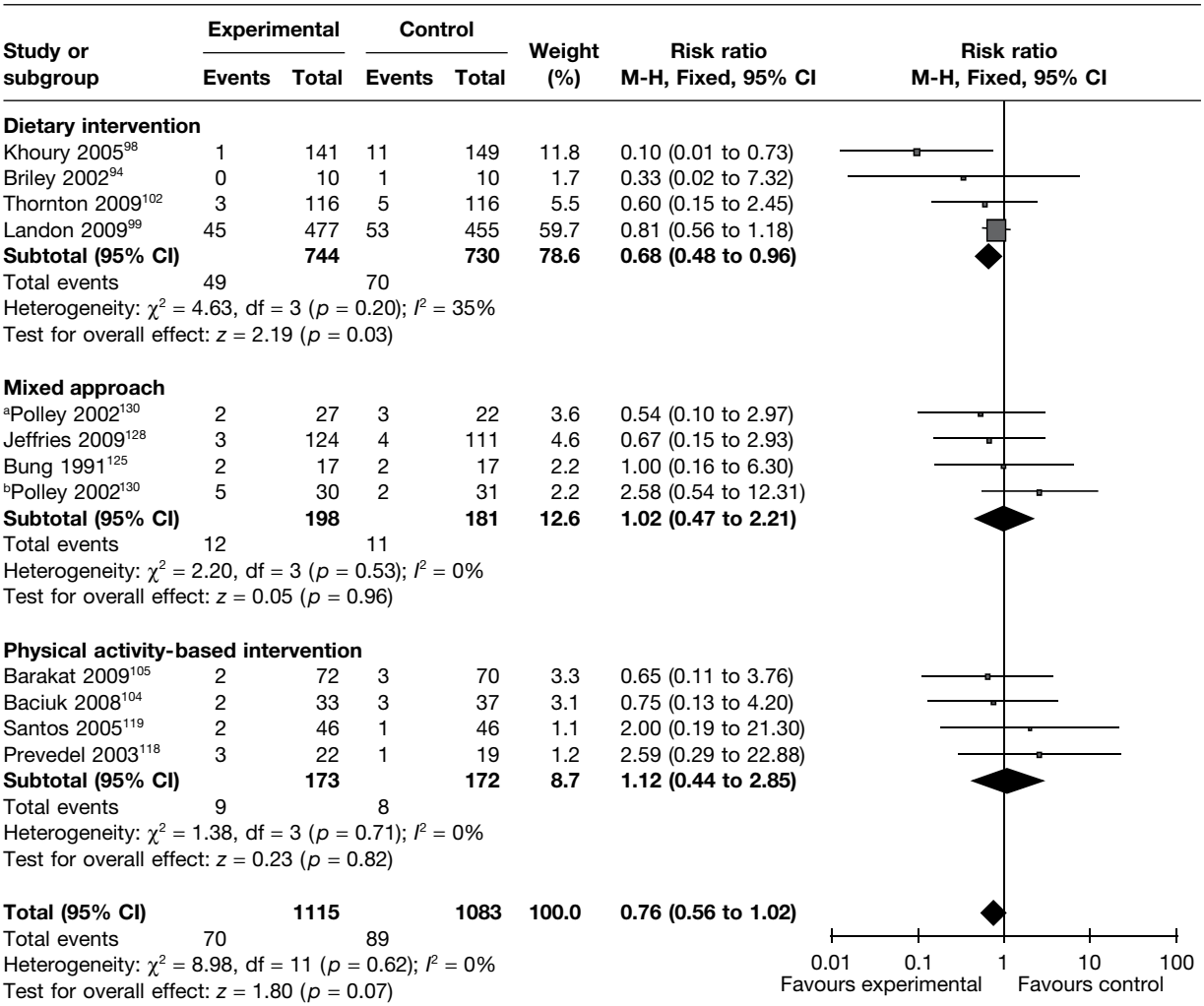

FIGURE 16 Effect of weight management interventions on preterm delivery before 37 weeks of gestation. a, Overweight women. b, Women with normal weight.

no differences between the experimental and the control groups with any intervention. The summary estimate for caesarean section was a RR of 0.93 (95% CI 0.85 to 1.03; $p = 0.15$) (*Figure 18*). There was no significant heterogeneity between the groups ($p = 0.22$, $I^2 = 21\%$). A total of 6 of the 14 RCTs involved obese and overweight women and showed no change in the rate of caesarean section (RR 0.97, 95% CI 0.73 to 1.28; $I^2 = 61\%$).

The rate of vaginal delivery was evaluated in five RCTs.[99,101,104,115,125] There was no difference in the rate of vaginal delivery with any intervention. The pooled estimate showed a RR of 1.00 (95% CI 0.94 to 1.07; $p = 1$). The studies were homogeneous (*Figure 19*). The effect of dietary intervention on vaginal delivery in obese and overweight mothers was studied in two RCTs.[99,101] The rate of vaginal delivery did not change with the intervention, with a RR of 0.97 (95% CI 0.89 to 1.07; $I^2 = 0$).

Induction of labour

The effect of weight management interventions in pregnancy on induction of labour was studied in five RCTs (involving 2362 women).[96,99,101,102,126] There was a slight increase in induction of labour in the intervention arm that was not significantly different from that of the control arm (RR 1.12, 95% CI 1.00 to 1.26; $p = 0.05$; $I^2 = 47\%$) (*Figure 20*). Obese and overweight women only

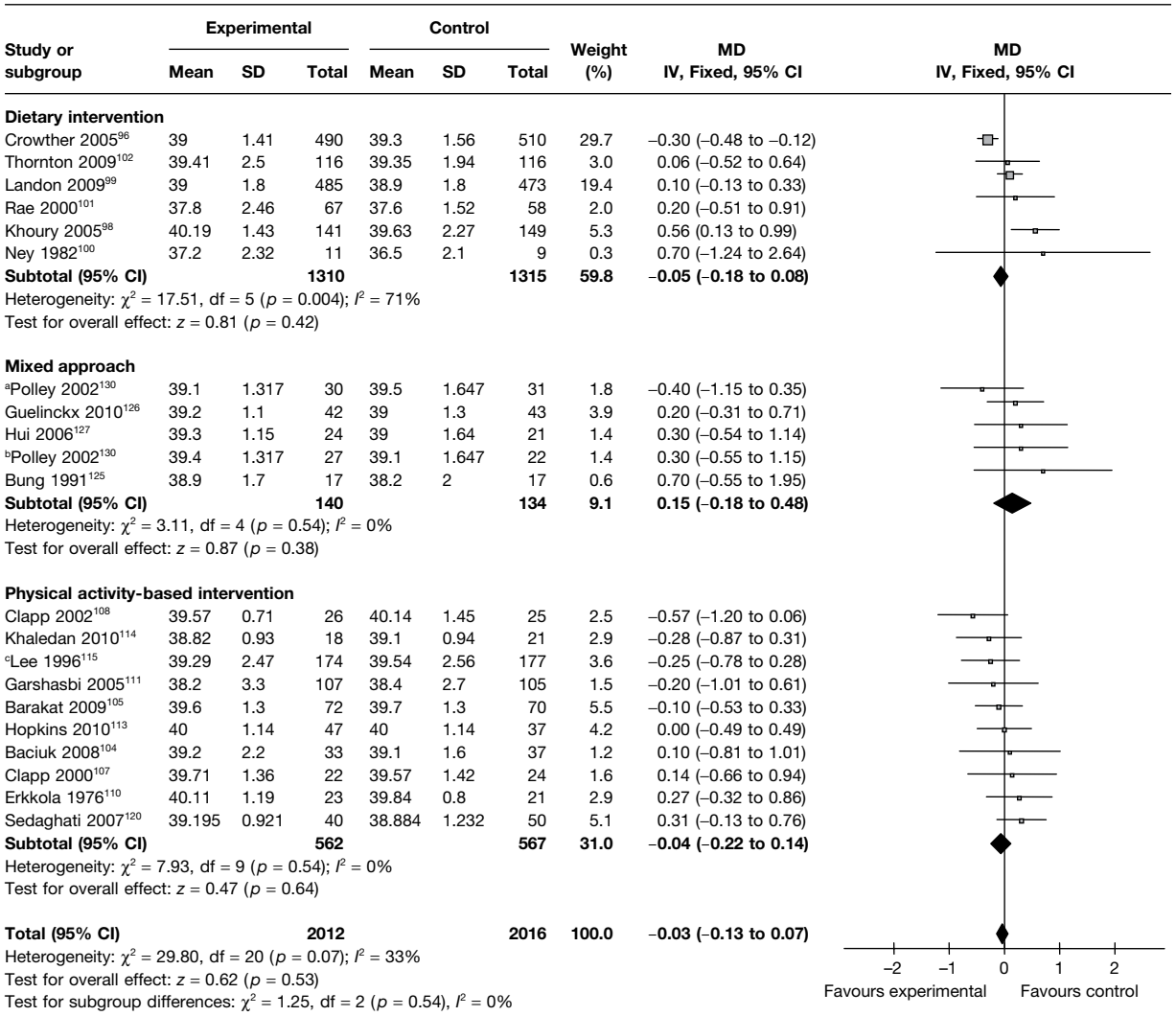

FIGURE 17 Effect of weight management interventions on gestational age at delivery. SD, standard deviation. a, Women with normal weight. b, Overweight women. c, Data from Kramer 2006 review.

were included in four RCTs[99,101,102,126] (involving 1362 women); in these studies there was no difference in the rate of induction of labour between the intervention and control groups (RR 0.99, 95% CI 0.84 to 1.16; $I^2 = 0\%$).

Post-partum haemorrhage

Two RCTs[96,102] ($n = 1232$) compared the rates of post-partum haemorrhage between the weight management intervention group and the control group. The pooled estimate of the studies did not show any significant differences between the groups (RR 0.90, 95% CI 0.57 to 1.42; $I^2 = 0\%$) (*Figure 21*).

Two observational case–control studies[77,78] studied the effect of physical activity-based interventions on post-partum haemorrhage and found no difference between the intervention and control groups.

Low back pain

Low back pain was reported as an outcome in two RCTs[111,126] (involving 302 women) evaluating physical activity-based interventions. The severity of low back pain was increased in one study[111]

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, Fixed, 95% CI
Dietary intervention						
Wolff 2008[103]	2	23	3	27	0.5	0.78 (0.14 to 4.29)
Landon 2009[99]	128	476	154	455	29.2	0.79 (0.65 to0.97)
Crowther 2005[96]	152	490	164	510	29.8	0.96 (0.80 to 1.16)
Thornton 2009[102]	91	116	83	116	15.4	1.10 (0.94 to 1.27)
Gomez-Tabarez 1994[97]	14	30	12	30	2.2	1.17 (0.65 to 2.09)
Subtotal (95% CI)		**1135**		**1138**	**77.1**	**0.93 (0.84 to 1.04)**
Total events	387		416			
Heterogeneity: $\chi^2 = 7.88$, df = 4 ($p = 0.10$); $I^2 = 49\%$						
Test for overall effect: $z = 1.31$ ($p = 0.19$)						
Mixed approach						
[a]Polley 2002[130]	2	27	6	22	1.2	0.27 (0.06 to 1.21)
Asbee 2009[124]	8	57	12	43	2.5	0.50 (0.23 to 1.12)
[b]Polley 2002[130]	2	30	4	31	0.7	0.52 (0.10 to 2.61)
Bung 1991[125]	2	17	3	17	0.6	0.67 (0.13 to 3.50)
Jeffries 2009[128]	41	124	30	111	5.9	1.22 (0.82 to 1.82)
Guelinckx 2010[126]	11	42	7	43	1.3	1.61 (0.69 to 3.75)
Subtotal (95% CI)		**297**		**267**	**12.2**	**0.95 (0.70 to 1.28)**
Total events	66		62			
Heterogeneity: $\chi^2 = 8.87$, df = 5 ($p = 0.11$); $I^2 = 44\%$						
Test for overall effect: $z = 0.33$ ($p = 0.74$)						
Physical activity-based intervention						
Baciuk 2008[104]	12	33	17	37	3.0	0.79 (0.45 to 1.40)
Khaledan 2010[114]	11	18	16	21	2.7	0.80 (0.52 to 1.24)
Marquez-Sterling 2000[116]	3	9	2	6	0.4	1.00 (0.23 to 4.31)
Lee 1996[115]	26	174	25	177	4.6	1.06 (0.64 to 1.76)
Subtotal (95% CI)		**234**		**241**	**10.7**	**0.92 (0.68 to 1.24)**
Total events	52		60			
Heterogeneity: $\chi^2 = 0.93$, df = 3 ($p = 0.82$); $I^2 = 0\%$						
Test for overall effect: $z = 0.57$ ($p = 0.57$)						
Total (95% CI)		**1666**		**1646**	**100.0**	**0.93 (0.85 to 1.03)**
Total events	505		538			
Heterogeneity: $\chi^2 = 17.82$, df = 14 ($p = 0.22$); $I^2 = 21\%$						
Test for overall effect: $z = 1.44$ ($p = 0.15$)						

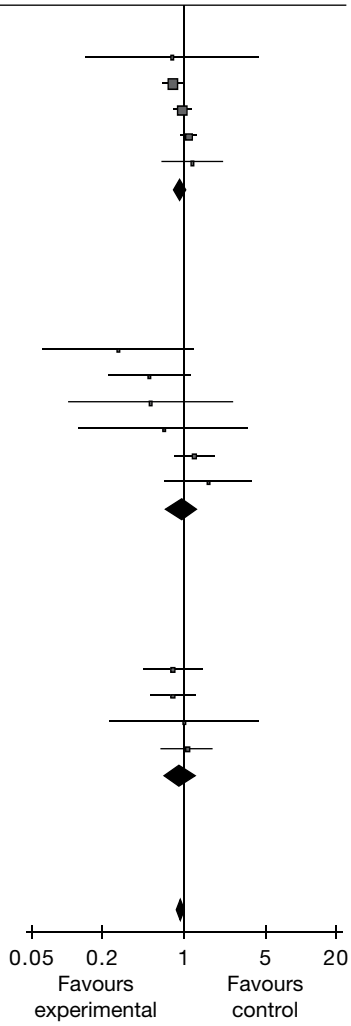

FIGURE 18 Effect of weight management interventions on rate of caesarean section. a, Overweight women. b, Women with normal weight.

and decreased in the other study.[120] The pooled estimate did not show any differences in back pain between the two groups (MD 0.16, 95% CI –10.16 to 10.48; $I^2 = 97\%$) (*Figure 22*).

Effect of the interventions on fetal and neonatal morbidity and mortality

Shoulder dystocia

Four RCTs[96,99,101,128] (2317 newborns) evaluated the effect of interventions (three dietary[96,99,101] and one mixed[128] approach) on the incidence of shoulder dystocia. Overall, there was a 61% reduction in the incidence of shoulder dystocia (RR 0.39, 95% CI 0.22 to 0.70; $p = 0.02$). The studies were homogeneous ($I^2 = 0\%$). The largest proportion of women in the analysis were in the dietary intervention group, which showed a similar effect (*Figure 23*). This beneficial effect was increased in the population of obese and overweight women (RR 0.33, 95% CI 0.14 to 0.74; $p = 0.008$).

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, Fixed, 95% CI
Dietary intervention						
Rae 2000[101]	31	65	30	56	8.8	0.89 (0.63 to 1.27)
Landon 2009[99]	148	174	152	177	41.3	0.99 (0.91 to 1.08)
Subtotal (95% CI)		**239**		**233**	**50.2**	**0.97 (0.89 to 1.07)**
Total events	179		182			
Heterogeneity: $\chi^2 = 0.41$, df = 1 ($p = 0.52$); $I^2 = 0\%$						
Test for overall effect: $z = 0.58$ ($p = 0.56$)						
Mixed approach						
Bung 1991[125]	15	17	12	17	3.3	1.25 (0.88 to 1.78)
Subtotal (95% CI)		**17**		**17**	**3.3**	**1.25 (0.88 to 1.78)**
Total events	15		12			
Heterogeneity: not applicable						
Test for overall effect: $z = 1.24$ ($p = 0.21$)						
Physical activity-based intervention						
Lee 1996[115]	148	174	152	177	41.3	0.99 (0.91 to 1.08)
Baciuk 2008[104]	21	33	20	37	5.2	1.18 (0.79 to 1.74)
Subtotal (95% CI)		**207**		**214**	**46.5**	**1.01 (0.92 to 1.11)**
Total events	169		172			
Heterogeneity: $\chi^2 = 0.80$, df = 1 ($p = 0.37$); $I^2 = 0\%$						
Test for overall effect: $z = 0.25$ ($p = 0.81$)						
Total (95% CI)		**463**		**464**	**100.0**	**1.00 (0.94 to 1.07)**
Total events	363		366			
Heterogeneity: $\chi^2 = 2.71$, df = 4 ($p = 0.61$); $I^2 = 0\%$						
Test for overall effect: $z = 0.01$ ($p = 1.00$)						

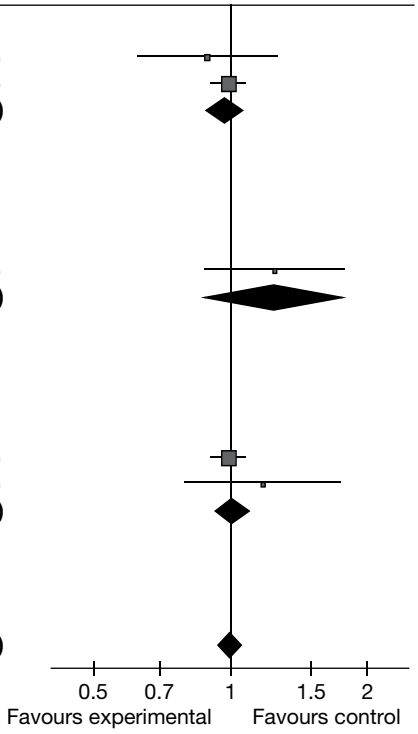

FIGURE 19 Effect of weight management interventions on rate of vaginal delivery.

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, Fixed, 95% CI
Dietary intervention						
Thomton 2009[102]	22	116	31	116	8.9	0.71 (0.44 to 1.15)
Landon 2009[99]	130	476	122	455	35.8	1.02 (0.82 to 1.26)
Rae 2000[101]	29	63	23	51	7.3	1.02 (0.68 to 1.53)
Crowther 2005[96]	189	490	150	510	42.1	1.31 (1.10 to 1.56)
Subtotal (95% CI)		**1145**		**1132**	**94.1**	**1.12 (0.99 to 1.27)**
Total events	370		326			
Heterogeneity: $\chi^2 = 7.55$, df = 3 ($p = 0.06$); $I^2 = 60\%$						
Test for overall effect: $z = 1.81$ ($p = 0.07$)						
Mixed approach						
Guelinckx 2010[126]	24	42	21	43	5.9	1.17 (0.78 to 1.75)
Subtotal (95% CI)		**42**		**43**	**5.9**	**1.17 (0.78 to 1.75)**
Total events	24		21			
Heterogeneity: not applicable						
Test for overall effect: $z = 0.76$ ($p = 0.44$)						
Total (95% CI)		**1187**		**1175**	**100.0**	**1.12 (1.00 to 1.26)**
Total events	394		347			
Heterogeneity: $\chi^2 = 7.58$, df = 4 ($p = 0.11$); $I^2 = 47\%$						
Test for overall effect: $z = 1.93$ ($p = 0.05$)						

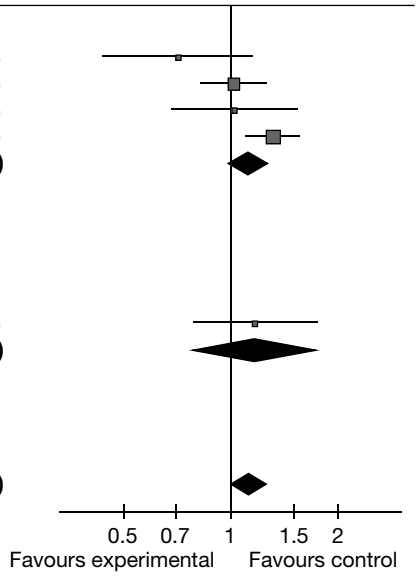

FIGURE 20 Effect of weight management interventions on induction of labour.

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, Fixed, 95% CI
Dietary intervention						
Thomton 2009[102]	3	116	5	116	13.8	0.60 (0.15 to 2.45)
Crowther 2005[96]	29	490	32	510	86.2	0.94 (0.58 to 1.54)
Subtotal (95% CI)		**606**		**626**	**100.0**	**0.90 (0.57 to 1.42)**
Total events	32		37			
Heterogeneity: $\chi^2 = 0.35$, df = 1 ($p = 0.55$); $I^2 = 0\%$						
Test for overall effect: $z = 0.47$ ($p = 0.64$)						

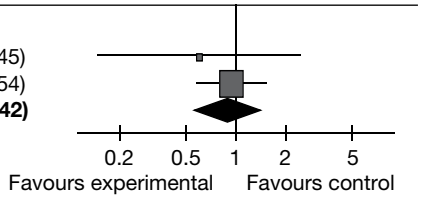

FIGURE 21 Effect of weight management interventions on post-partum haemorrhage.

Study or subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight (%)	MD IV, Random, 95% CI
Physical activity-based intervention								
Sedaghati 2007[120]	0.8	3.0817	40	5.82	5.025	50	50.8	–5.02 (–6.71 to –3.33)
Garshasbl 2005[111]	6.88	10.65	107	1.37	12.46	105	49.2	5.51 (2.39 to 8.63)
Subtotal (95% CI)			**147**			**155**	**100.0**	**0.16 (–10.16 to 10.48)**
Heterogeneity: $\tau^2 = 53.80$, $\chi^2 = 33.79$, df = 1 ($p < 0.00001$); $I^2 = 97\%$								
Test for overall effect: $z = 0.03$ ($p = 0.98$)								
Test for subgroup differences: not applicable								

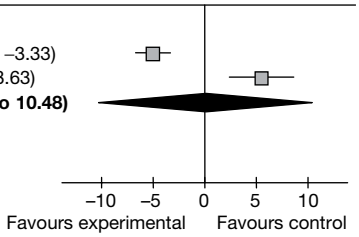

FIGURE 22 Effect of weight management interventions on low back pain in pregnancy. SD, standard deviation.

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, Fixed, 95% CI
Dietary intervention						
Rae 2000[101]	0	67	3	54	9.9	0.12 (0.01 to 2.19)
Landon 2009[99]	7	476	18	455	47.1	0.37 (0.16 to 0.88)
Crowther 2005[96]	7	506	16	524	40.3	0.45 (0.19 to 1.09)
Subtotal (95% CI)		**1049**		**1033**	**97.3**	**0.38 (0.21 to 0.69)**
Total events	14		37			
Heterogeneity: $\chi^2 = 0.79$, df = 2 ($p = 0.68$); $I^2 = 0\%$						
Test for overall effect: $z = 3.18$ ($p = 0.001$)						
Mixed approach						
Jeffries 2009[128]	1	124	1	111	2.7	0.90 (0.06 to 14.14)
Subtotal (95% CI)		**124**		**111**	**2.7**	**0.90 (0.06 to 14.14)**
Total events	1		1			
Heterogeneity: not applicable						
Test for overall effect: $z = 0.08$ ($p = 0.94$)						
Total (95% CI)		**1173**		**1144**	**100.0**	**0.39 (0.22 to 0.70)**
Total events	15		38			
Heterogeneity: $\chi^2 = 1.12$, df = 3 ($p = 0.77$); $I^2 = 0\%$						
Test for overall effect: $z = 3.14$ ($p = 0.02$)						

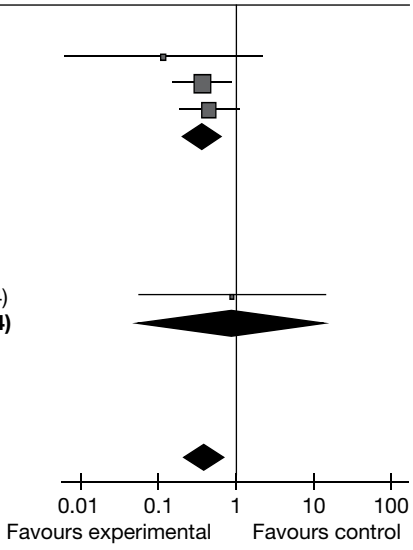

FIGURE 23 Effect of weight management interventions on shoulder dystocia.

Intrauterine death

Two RCTs[96,98] (involving 1320 women) evaluated the effect of dietary intervention on stillbirths. There was a reduction in the incidence of intrauterine death, which was not statistically significant (RR 0.15, 95% CI 0.02 to 1.20; $p = 0.07$; $I^2 = 0\%$) (*Figure 24*).

One observational cohort study by Perichart *et al.*[82] evaluated the effect of a dietary intervention compared with no intervention on intrauterine death. There were no significant differences between the groups. This effect was consistent for women with type 2 diabetes [unadjusted odds ratio (OR) 0.96, 95% CI 0.12 to 1.09] or GDM (unadjusted OR 1.00, 95% CI 0.06 to 16.57).

Respiratory distress syndrome

Two RCTs[96,99] (involving 1962 women) evaluated respiratory distress syndrome with the newborn in mothers undergoing a weight management intervention in pregnancy. The two studies were on dietary interventions and the pooled estimate did not show a difference between the intervention and control groups (RR 1.05, 95% CI 0.48 to 2.28; $I^2 = 58\%$) (*Figure 25*).

Admission to the neonatal intensive care unit

Admission to NICU was reported as an outcome in two RCTs[96,99] (involving 1962 women) evaluating dietary interventions. The studies were heterogeneous ($I^2 = 77\%$) and the pooled estimate did not show any difference between the groups (RR 0.98, 95% CI 0.66 to 1.47) (*Figure 26*). One observational study[82] evaluating a dietary intervention in pregnancy reported on NICU admission in two groups: women with type 2 diabetes and those with GDM. The reported

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, Fixed, 95% CI
Dietary intervention						
Crowther 2005[96]	0	506	5	524	78.7	0.09 (0.01 to 1.70)
Khoury 2005[98]	0	141	1	149	21.3	0.35 (0.01 to 8.57)
Subtotal (95% CI)		**647**		**673**	**100.0**	**0.15 (0.02 to 1.20)**
Total events	0		6			

Heterogeneity: $\chi^2 = 0.38$, df = 1 ($p = 0.54$); $I^2 = 0\%$
Test for overall effect: $z = 1.79$ ($p = 0.07$)

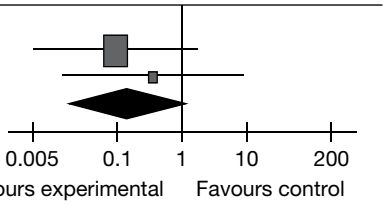

FIGURE 24 Effect of weight management interventions on intrauterine death.

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, Random, 95% CI
Dietary intervention						
Landon 2009[99]	9	477	13	455	42.4	0.66 (0.29 to 1.53)
Crowther 2005[96]	27	506	19	524	57.6	1.47 (0.83 to 2.61)
Subtotal (95% CI)		**983**		**979**	**100.0**	**1.05 (0.48 to 2.28)**
Total events	36		32			

Heterogeneity: $\tau^2 = 0.19$, $\chi^2 = 2.38$, df = 1 ($p = 0.12$); $I^2 = 58\%$
Test for overall effect: $z = 0.12$ ($p = 0.91$)

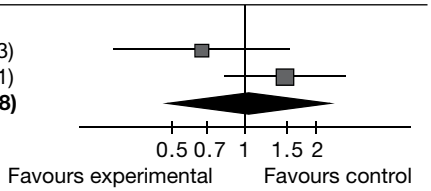

FIGURE 25 Effect of weight management interventions on respiratory distress syndrome.

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, Random, 95% CI
Dietary intervention						
Landon 2009[99]	43	477	53	455	39.8	0.77 (0.53 to 1.13)
Crowther 2005[96]	357	506	321	524	60.2	1.15 (1.05 to 1.26)
Subtotal (95% CI)		**983**		**979**	**100.0**	**0.98 (0.66 to 1.47)**
Total events	400		374			

Heterogeneity: $\tau^2 = 0.07$, $\chi^2 = 4.40$, df = 1 ($p = 0.04$); $I^2 = 77\%$
Test for overall effect: $z = 0.08$ ($p = 0.93$)

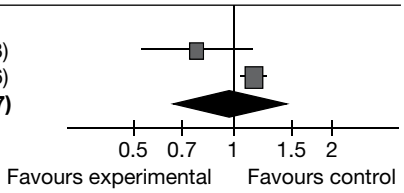

FIGURE 26 Effect of weight management interventions on admission to NICU.

unadjusted OR was significant only in the case of women with type 2 diabetes (OR 0.21, 95% CI 0.03 to 0.51).

Apgar scores

Apgar scores were evaluated as an outcome in six RCTs[96,102,105,115,116,128] studying the effect of weight management interventions in pregnancy. Three studies[96,102,128] reported scores of < 7 at 5 minutes and three studies[105,115,116] provided the scores at 5 minutes for comparison. There were no differences in the abnormal scores (< 7 at 5 minutes) (RR 0.64, 95% CI 0.27 to 1.49; $p = 0.3$, $I^2 = 0\%$; *Figure 27*) or in the mean scores (MD 0.0, 95% CI −0.05 to 0.05; $p = 0.94$; *Figure 28*) between the two groups.

Infant hypoglycaemia

Hypoglycaemia in the first few days after birth is defined as blood glucose < 40 mg/dl. In preterm infants, repeated blood glucose levels of < 50 mg/dl may be associated with neurodevelopmental delay. Five RCTs[96,99,101,125,128] reported the rate of hypoglycaemia among the children of studied mothers. Neither a comprehensive approach nor dietary interventions had any significant influence on hypoglycaemia rate (*Figure 29*).

Infant hyperbilirubinaemia

Two RCTs[96,99] evaluated the effect of dietary interventions on the rates of hyperbilirubinaemia in 1898 newborns. The studies were homogeneous. There was a trend towards a reduction in hyperbilirubinaemia with the interventions, which was not significant (*Figure 30*).

Birth trauma

Two RCTs[96,99] evaluated the effect of dietary interventions on the risk of birth trauma. The studies showed a reduction in the risk of birth trauma (RR 0.36, 95% CI 0.11 to 1.23; $I^2 = 0\%$), which was not statistically significant (*Figure 31*).

Effect of interventions on neonatal anthropometric measurements at birth

Child's birth length

Five RCTs[95,103,105,125,126] (323 newborns) evaluated the birth length of the newborn. The birth length of the newborn was reduced with the interventions, but the difference was not statistically significant (*Figure 32*).

Abdominal circumference of the newborn

Two RCTs[103,107] evaluated the effect of dietary weight management interventions on abdominal circumference in 62 newborns. The studies were heterogeneous and overall there was no

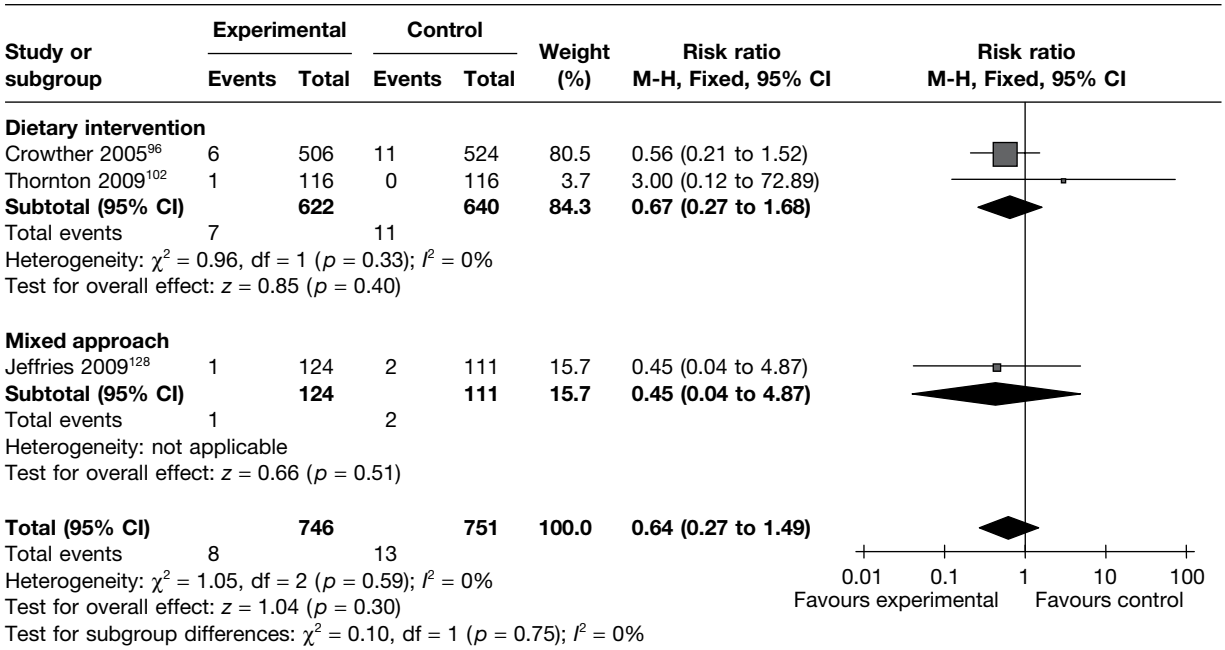

FIGURE 27 Effect of weight management interventions on abnormal Apgar scores (< 7 at 5 minutes).

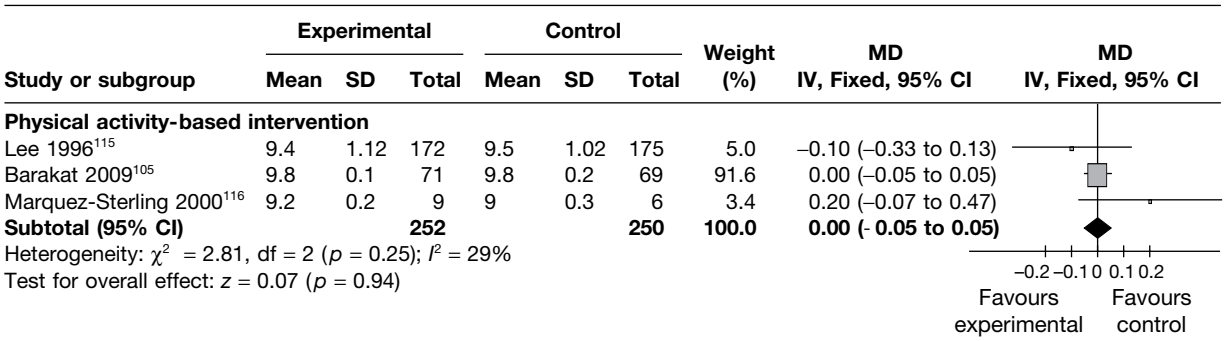

FIGURE 28 Effect of weight management interventions on Apgar scores at 5 minutes. SD, standard deviation.

significant change in the intervention group in comparison with the control group (MD –1.26 cm, 95% CI –3.71 cm to 1.19 cm; $p = 0.31$; $I^2 = 91\%$) (*Figure 33*).

Crown–heel length

Three RCTs[107,108,113] evaluated the effect of physical activity based weight management interventions on crown–heel length in 181 newborns. The studies were heterogeneous and overall there was no significant change in the intervention group in comparison with the control group (MD –0.18 cm, 95% CI –1.80 cm to 1.44 cm; $p = 0.83$; $I^2 = 92\%$) (*Figure 34*).

Subgroup analyses

Subgroup analyses on the basis of period of publication, country of study (developed vs developing), GDM status and risk of bias from allocation concealment showed no differences in the summary estimates of gestational weight gain, birthweight and incidence of LGA and SGA infants. The type of intervention resulted in significant differences ($p = 0.003$) between the groups for weight gain in pregnancy, with the maximum reduction in gestational weight gain

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, Fixed, 95% CI
Dietary intervention						
Rae 2000[101]	22	59	25	50	24.1	0.75 (0.48 to 1.15)
Landon 2009[99]	62	381	55	357	50.5	1.06 (0.76 to 1.47)
Crowther 2005[96]	35	506	27	524	23.6	1.34 (0.82 to 2.18)
Subtotal (95% CI)		**946**		**931**	**98.2**	**1.05 (0.83 to 1.33)**
Total events	119		107			
Heterogeneity: $\chi^2 = 3.39$, df = 2 ($p = 0.18$); $I^2 = 41\%$						
Test for overall effect: $z = 0.40$ ($p = 0.69$)						
Mixed approach						
Bung 1991[125]	2	17	1	17	0.9	2.00 (0.20 to 20.04)
Jeffries 2009[128]	3	124	1	111	0.9	2.69 (0.28 to 25.44)
Subtotal (95% CI)		**141**		**128**	**1.8**	**2.35 (0.47 to 11.76)**
Total events	5		2			
Heterogeneity: $\chi^2 = 0.03$, df = 1 ($p = 0.86$); $I^2 = 0\%$						
Test for overall effect: $z = 1.04$ ($p = 0.30$)						
Total (95% CI)		**1087**		**1059**	**100.0**	**1.07 (0.85 to 1.35)**
Total events	124		109			
Heterogeneity: $\chi^2 = 4.47$, df = 4 ($p = 0.35$); $I^2 = 10\%$						
Test for overall effect: $z = 0.59$ ($p = 0.55$)						

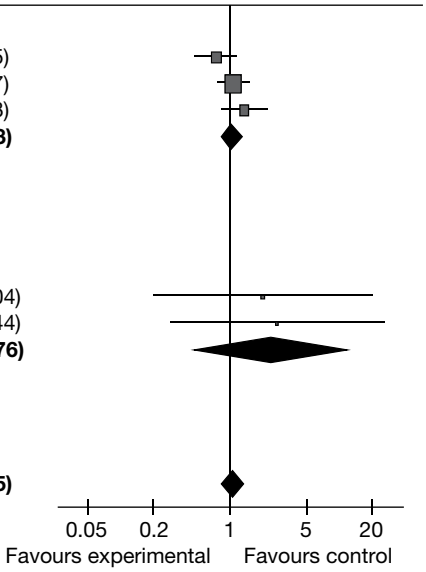

FIGURE 29 Effect of weight management interventions on infant hypoglycaemia.

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, Fixed, 95% CI
Dietary intervention						
Crowther 2005[96]	44	506	48	524	45.7	0.95 (0.64 to 1.40)
Landon 2009[99]	43	450	54	418	54.3	0.74 (0.51 to 1.08)
Subtotal (95% CI)		**956**		**942**	**100.0**	**0.84 (0.64 to 1.10)**
Total events	87		102			
Heterogeneity: $\chi^2 = 0.81$, df = 1 ($p = 0.37$); $I^2 = 0\%$						
Test for overall effect: $z = 1.30$ ($p = 0.19$)						

Test for subgroup differences: not applicable

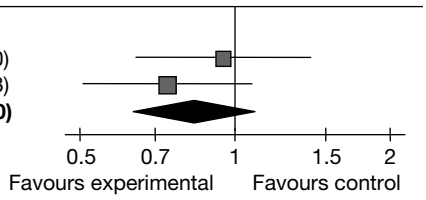

FIGURE 30 Effect of weight management interventions on infant hyperbilirubinaemia.

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, Fixed, 95% CI
Dietary intervention						
Crowther 2005[96]	0	506	3	524	35.9	0.15 (0.01 to 2.86)
Landon 2009[99]	3	476	6	455	64.1	0.48 (0.12 to 1.90)
Subtotal (95% CI)		**982**		**979**	**100.0**	**0.36 (0.11 to 1.23)**
Total events	3		9			
Heterogeneity: $\chi^2 = 0.51$, df = 1 ($p = 0.48$); $I^2 = 0\%$						
Test for overall effect: $z = 1.63$ ($p = 0.10$)						

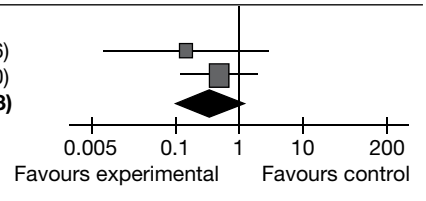

FIGURE 31 Effect of weight management interventions on birth trauma.

Study or subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight (%)	MD IV, Random, 95% CI
Dietary intervention								
Clapp 1997[95]	50.3	1.71	6	53.1	1.23	6	15.9	–2.80 (–4.49 to –1.11)
Wolff 2008[103]	52	3	23	53	2	27	18.1	–1.00 (–2.44 to 0.44)
Subtotal (95% CI)			**29**			**33**	**34.0**	**- 1.84 (- 3.61 to - 0.08)**
Heterogeneity: $\tau^2 = 0.98$, $\chi^2 = 2.53$, df = 1 ($p = 0.11$); $I^2 = 61\%$								
Test for overall effect: $z = 2.05$ ($p = 0.04$)								
Mixed approach								
Bung 1991[125]	49.3	2	17	51	3	17	15.7	–1.70 (–3.41 to 0.01)
Guelinckx 2010[126]	50.6	2	42	50	1.8	43	24.2	0.60 (–0.21 to 1.41)
Subtotal (95% CI)			**59**			**60**	**39.9**	**- 0.42 (- 2.66 to 1.82)**
Heterogeneity: $\tau^2 = 2.18$, $\chi^2 = 5.66$, df = 1 ($p = 0.02$); $I^2 = 82\%$								
Test for overall effect: $z = 0.37$ ($p = 0.71$)								
Physical activity-based intervention								
Barakat 2009[105]	49.5	1.8	72	49.7	1.8	70	26.1	–0.20 (–0.79 to 0.39)
Subtotal (95% CI)			**72**			**70**	**26.1**	**- 0.20 (- 0.79 to 0.39)**
Heterogeneity: not applicable								
Test for overall effect: $z = 0.66$ ($p = 0.51$)								
Total (95% CI)			**160**			**163**	**100.0**	**- 0.80 (- 1.81 to 0.21)**
Heterogeneity: $\tau^2 = 0.93$, $\chi^2 = 16.78$, df = 4 ($p = 0.002$); $I^2 = 76\%$								
Test for overall effect: $z = 1.55$ ($p = 0.12$)								

MD IV, Random, 95% CI

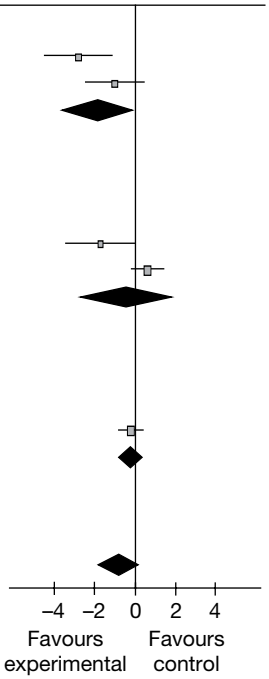

FIGURE 32 Effect of weight management interventions on birth length. SD, standard deviation.

Study or subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight (%)	MD IV, Random, 95% CI
Dietary intervention								
Clapp 2000[107]	29.9	0.75	6	32.4	0.98	6	50.5	–2.50 (–3.49 to –1.51)
Wolff 2008[103]	34	2	23	34	2	27	49.5	0.00 (–1.11 to 1.11)
Subtotal (95% CI)			**29**			**33**	**100.0**	**- 1.26 (- 3.71 to 1.19)**
Heterogeneity: $\tau^2 = 2.84$, $\chi^2 = 10.85$, df = 1 ($p = 0.0010$); $I^2 = 91\%$								
Test for overall effect: $z = 1.01$ ($p = 0.31$)								

MD IV, Random, 95% CI

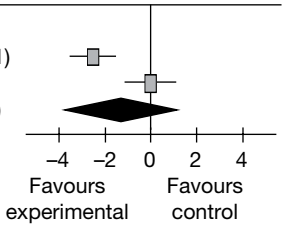

FIGURE 33 Effect of weight management interventions on abdominal circumference. SD, standard deviation.

Study or subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight (%)	MD IV, Random, 95% CI
Physical activity-based intervention								
Clapp 2002[108]	51.1	1.53	26	52.6	1	25	34.1	–1.50 (–2.21 to –0.79)
Hopkins 2010[113]	50.8	2.4	47	51	1.9	37	32.6	–0.20 (–1.12 to 0.72)
Clapp 2000[107]	51.8	1.4	22	50.6	1.47	24	33.3	1.20 (0.37 to 2.03)
Subtotal (95% CI)			**95**			**86**	**100.0**	**- 0.18 (- 1.80 to 1.44)**
Heterogeneity: $\tau^2 = 1.87$, $\chi^2 = 23.67$, df = 2 ($p < 0.00001$); $I^2 = 92\%$								
Test for overall effect: $z = 0.21$ ($p = 0.83$)								

MD IV, Random, 95% CI

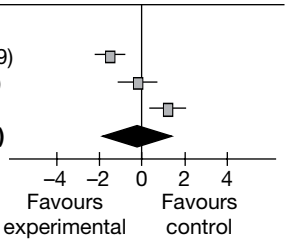

FIGURE 34 Effect of weight management interventions on crown–heel length. SD, standard deviation.

seen in the dietary intervention group (MD –3.36 kg, 95% CI –4.73 kg to –1.99 kg). Women with diabetes in pregnancy showed a significant reduction in the incidence of pre-eclampsia with weight management interventions (RR 0.65, 95% CI 0.50 to 0.84) compared with women without diabetes (RR 1.16, 95% CI 0.70 to 1.93), and the difference in the summary estimates between the groups was statistically significant ($p = 0.04$). There was a significant reduction in pre-eclampsia in the responders – women with significantly reduced gestational weight gain with intervention (RR 0.61, 95% CI 0.47 to 0.79) – compared with the group with no significant change in weight (RR 1.33, 95% CI 0.84 to 2.11) ($p = 0.004$). There was a significant difference between the responders (MD –0.29 kg, 95% CI –0.46 kg to –0.12 kg) and non-responders (MD –0.02 kg, 95% CI –0.06 kg to –0.03 kg) for birthweight ($p = 0.002$). Subgroup analysis of the summary estimates of birthweight and incidence of LGA and SGA infants did not show a statistically significant difference according to the type of intervention (*Table 6*).

Sensitivity analysis that excluded studies on women with diabetes in pregnancy consistently showed a overall reduction in gestational weight gain with interventions (MD –0.88 kg, 95% CI –1.85 kg to 0.09 kg; $p = 0.001$), including diet (MD –5.18 kg, 95% CI –9.44 kg to –0.91 kg; $p < 0.00001$) and physical activity (MD –0.07 kg, 95% CI –1.08 kg to 0.93 kg; $p < 0.00001$). The reduction in birthweight with intervention persisted (MD –0.08 kg, 95% CI –0.16 kg to 0.0 kg; $p = 0.04$) with no differences in the incidence of SGA and LGA infants or shoulder dystocia between the groups. The estimates of other studies for the effect of diet on the incidence of gestational hypertension, preterm birth, vaginal delivery, caesarean section and SGA infants were similar after excluding studies on women with diabetes. There was a trend towards a reduction in the incidence of pre-eclampsia with diet in these studies.

Summary

This review on the effectiveness of weight management interventions has identified a large number of RCTs, especially for the primary weight-related outcomes in the mother and the fetus. Two-thirds of the included studies showed a low risk of bias for addressing incomplete outcome data, selective reporting and blinding for objective outcomes. Fewer than one-sixth of the studies showed a high risk of bias for addressing incomplete outcome data and selective reporting. The commonly reported outcomes were maternal weight gain in pregnancy and birthweight of the newborn.

Weight management interventions in pregnancy resulted in a statistically significant reduction in weight-related outcomes such as maternal weight gain in pregnancy, and birthweight of the newborn. However, there were no differences between the intervention and control groups for incidence of SGA fetuses. Although we did not observe a beneficial effect of reduction in growth restriction in the babies with intervention, it was a reassuring finding because there have been concerns over fetal weight reduction with weight management interventions.

There was a significant decrease in the rates of key obstetric outcomes such as pre-eclampsia and shoulder dystocia in the analysis of outcomes for all interventions. It is likely that this reduction in shoulder dystocia will be of greatest benefit in women with GDM or pre-existing diabetes. There was a trend towards a reduction in the rates of obstetric complications such as GDM, gestational hypertension and preterm birth before 37 weeks with weight management interventions.

TABLE 6 Subgroup analyses for trial methodology, clinical characteristics and publication for maternal and fetal outcomes in the evaluation of weight management interventions in pregnancy

	Gestational weight gain (kg)			Pre-eclampsia			Birthweight (kg)			LGA infants			SGA infants		
Subgroup	No. of studies	MD (95% CI)	*p*-value for interaction	No. of studies	RR (95% CI	*p*-value for interaction	No. of studies	MD (95% CI)	*p*-value for interaction	No. of studies	RR (95% CI)	*p*-value for interaction	No. of studies	RR (95% CI	*p*-value for interaction
Publication year															
After 1990	28	–1.22 (–1.77 to –0.66)	0.57	–	–	–	26	–0.08 (–0.15 to –0.02)	0.11	–	–	–	–	–	–
Before 1990	2	2.19 (–9.66 to 14.04)		–	–		2	0.14 (–0.13 to 0.41)		–	–		–	–	
Country status															
Developed countries	24	–1.09 (–1.92 to –0.27)	0.42	–	–	–	23	–0.08 (–0.15 to 0.00)	0.77	10	0.72 (0.51 to 1.03)	0.63	6	0.97 (0.74 to 1.27)	0.40
Developing countries	6	–0.64 (–1.39 to 0.12)		–	–		5	–0.06 (–0.16 to 0.04)		2	0.95 (0.33 to 2.75)		2	1.79 (0.44 to 7.23)	
Intervention type															
Diet	9	–3.36 (–4.73 to –1.99)	0.003	6	0.67 (0.53 to 0.85)	0.05	9	–0.07 (–0.21 to 0.07)	0.45	5	0.78 (0.51 to 1.19)	0.73	3	1.02 (0.75 to 1.37)	0.61
Mixed	6	–0.36 (–1.40 to 0.68)		1	5.56 (0.70 to 44.09)		14	–0.02 (–0.10 to 0.07)		5	0.75 (0.41 to 1.38)		2	0.76 (0.39 to 1.48)	
Physical activity	15	–0.07 (–1.08 to 0.93)		3	1.48 (0.56 to 3.94)		5	–0.09 (–0.18 to 0.00)		2	0.37 (0.06 to 2.30)		3	1.31 (0.50 to 3.42)	
Diabetic status															
Women with diabetes	5	–1.84 (–2.36 to –1.32)	0.09	3	0.65 (0.50 to 0.84)	0.04	5	–0.06 (–0.17 to 0.05)	0.75	4	0.65 (0.46 to 0.92)	0.30	2	1.03 (0.74 to 1.42)	0.73
Normal women	25	–0.86 (–1.85 to 0.13)		7	1.16 (0.70 to 1.93)		23	–0.08 (–0.16 to 0.00)		8	0.91 (0.53 to 1.59)		6	0.93 (0.59 to 1.46)	

continued

TABLE 6 Subgroup analyses for trial methodology, clinical characteristics and publication for maternal and fetal outcomes in the evaluation of weight management interventions in pregnancy *(continued)*

	Gestational weight gain (kg)			Pre-eclampsia			Birthweight (kg)			LGA infants			SGA infants		
Subgroup	No. of studies	MD (95% CI)	*p*-value for interaction	No. of studies	RR (95% CI	*p*-value for interaction	No. of studies	MD (95% CI)	*p*-value for interaction	No. of studies	RR (95% CI)	*p*-value for interaction	No. of studies	RR (95% CI	*p*-value for interaction
Risk of bias – allocation concealment															
High risk	27	–0.81 (–1.60 to –0.01)	0.18	8	0.77 (0.60 to 0.98)	0.48	25	–0.08 (–0.15 to 0.00)	0.85	11	0.82 (0.57 to 1.16)	0.06	5	0.88 (0.62 to 1.26)	0.33
Low risk	3	–1.79 (–2.98 to –0.60)		2	0.62 (0.36 to 1.06)		3	–0.06 (–0.16 to 0.03)		1	0.49 (0.33 to 0.73)		3	1.15 (0.77 to 1.70)	
Maternal weight change with intervention															
Significantly reduced gestational weight gain				4	0.61 (0.47 to 0.79)	0.004	6	–0.29 (–0.46 to –0.12)	0.002	3	0.67 (0.41 to 1.07)	0.36	2	1.03 (0.74 to 1.42)	0.73
No significant change in gestational weight gain				6	1.33 (0.84 to 2.11)		22	–0.02 (–0.06 to –0.03)		9	0.88 (0.60 to 1.30)		7	0.93 (0.59 to 1.46)	

Of the three interventions, dietary intervention showed the most beneficial effect by significantly reducing rates of obstetric complications such as gestational hypertension, preterm births, pre-eclampsia and shoulder dystocia. The significant reduction in the rate of preterm births with dietary interventions is likely to be reflected in the finding of increased gestational age with dietary interventions. For fetal outcomes the evidence was limited to dietary interventions only and showed a trend towards a reduction in rates of intrauterine deaths, birth trauma and hyperbilirubinaemia.

The dietary components of the interventions evaluated a balanced diet of carbohydrates, fat and protein, moderate energy and caloric restriction based on individual requirements, low-fat and -cholesterol diets and the use of a food diary for monitoring. The physical activity-based interventions included weight-bearing sessions, walking for 30 minutes a day and low-intensity resistance training. The mixed approach group included dietary and physical activity interventions with associated in-depth behavioural risk assessments and tailored counselling.

The main strengths of the effectiveness review were the peer-reviewed protocol, the comprehensive search strategy without any language restrictions and the use of randomised data to draw inferences. Non-randomised data were included only when there was a paucity of evidence. This review has identified the largest body of evidence on this topic, for both weight-related outcomes and clinically relevant obstetric and fetal outcomes. Dietary interventions in pregnancy have consistently shown a beneficial effect on weight-related, obstetric and fetal and neonatal outcomes compared with other interventions. The review findings are limited by the lack of detail about the components of the intervention in some of the included studies,

gestational age at which the intervention was commenced, its frequency and the method of delivery. Furthermore, there are very few studies for important clinical outcomes such as intrauterine death, maternal admission to the high-dependency unit (HDU) and neonatal admissions to NICU. There are no data available to assess the long-term effects of these outcomes on the mother and the fetus.

[Note: The results of this systematic review for effectiveness of weight management interventions in pregnancy includes only studies published before March 2011. The findings with the updated search (until January 2012) can be accessed at *BMJ* 2012;**344**:e2088 doi10.1136/bmj.e2088.]

Chapter 4

Adverse effects of interventions

Study selection

From a systematic search of the literature to identify the maternal and fetal adverse effects of weight management interventions in pregnancy, 14,832 potentially relevant records were obtained (up to 31 March 2011). A search of the reference lists of the relevant articles led to the identification of 26 further citations. After reviewing the abstracts, the full texts of 180 papers were obtained for detailed assessment. After exclusion of 154 publications, 26 papers were included in the review. *Figure 35* provides details of the process of study selection.

Of the included studies, two were RCTs (involving 277 women)[129,132] and 24 were observational studies (19 cohort studies and five case–control studies, involving 468,581 women).[63,64,67,68,70,73–77,80,85,89,133–143] The studies evaluated the effect of dietary, physical activity and other lifestyle interventions in pregnancy on maternal and fetal outcomes. *Appendices 7* and *10* provide details of the included RCTs and observational studies, respectively, that assessed the adverse effects of outcomes.

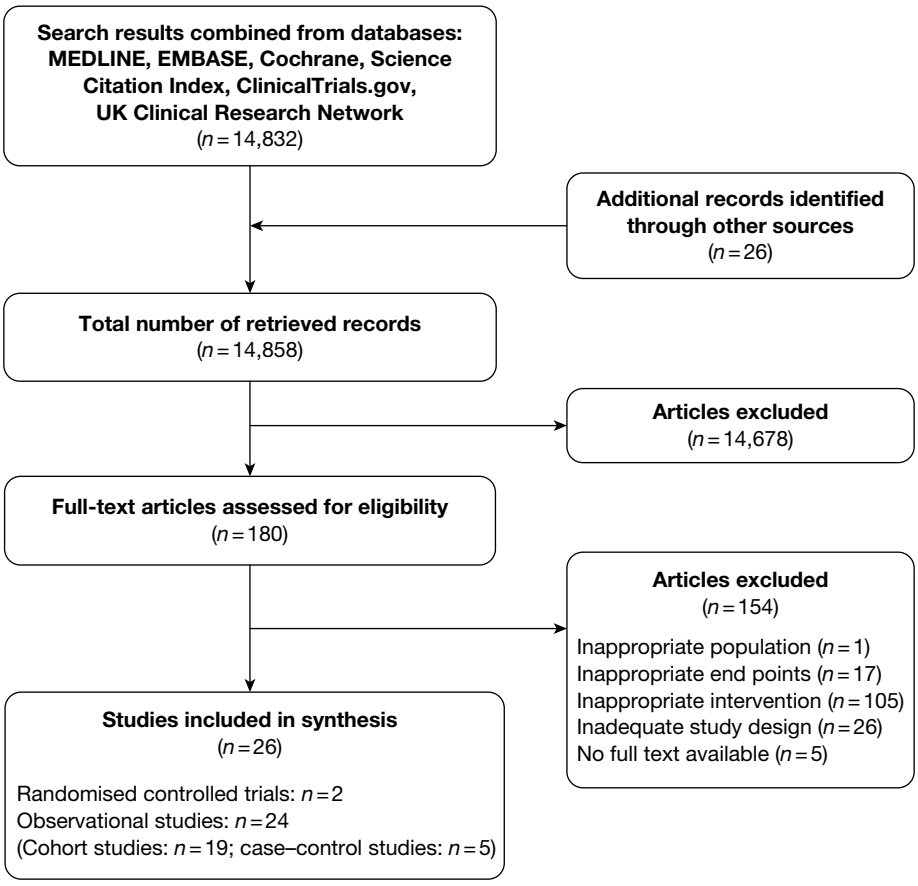

FIGURE 35 Flow chart of study identification and selection for the evaluation of adverse maternal and fetal outcomes.

Quality of the included studies

Randomised controlled trials

The quality of the two included RCTs[129,132] is shown in *Figure 36*. The details regarding sequence generation, allocation concealment and blinding for subjective outcomes were unclear in both studies. A detailed quality assessment of the included RCTs is provided in *Appendix 8*.

Observational studies

The 24 observational studies included 19 cohort studies and five case–control studies.[63,64,67,68,70,73–77,80,85,89,133–143] The quality assessment of the cohort and case–control studies is summarised in *Appendix 9*. The studies, evaluated using NOS, could score a maximum of nine stars, with four stars for selection, two for comparison and three for outcome assessment. In total, 3/19 (15.8%) cohort studies had a low risk of bias and scored seven or more stars; 16/19 (84.2%) had a medium risk of bias and scored between four and six stars.

Results

The adverse outcomes included in the review were defined as those that occurred unintentionally with potential harm to the mother or baby. We also included those outcomes that may have been the direct result of the intervention itself, for example risk of preterm delivery due to strenuous physical exercise.

Randomised clinical trials

The two RCTs[129,132] were conducted in women already planning to exercise in pregnancy and pregnant athletes. Kulpa *et al.*[129] reported on the outcomes of meconium-stained amniotic fluid, uterine atony and chorioamnionitis. Estimated RRs for the above outcomes were 0.62 (95% CI 0.20 to 1.90; $p = 0.40$), 0.93 (95% CI 0.22 to 3.89; $p = 0.92$) and 3.69 (95% CI 0.15 to 88.13; $p = 0.42$) respectively. Bell and Palma[132] evaluated the effect of vigorous exercise in pregnancy (exercising five or more times per week) on the risk of reduction in birthweight. There was no difference in birthweight between the vigorous exercise group and the control group.

Observational studies

A total of 18 studies[68,73–76,80,85,89,133–139,141–143] observed the effect of diet on maternal and fetal outcomes. The majority of the included studies produced data on the effects of a severe reduction in caloric intake in extreme conditions such as war or famine (*Table 7*). The studies on physical activity included women undergoing exercises of various intensities or other recreational

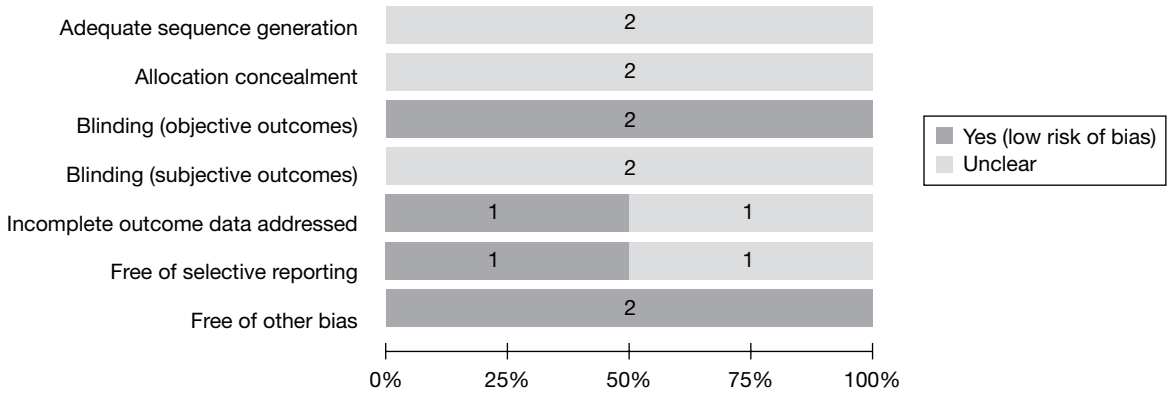

FIGURE 36 Quality of the included RCTs for the adverse effects review.

TABLE 7 Adverse outcomes associated with any diet or physical activity in pregnancy

Outcome	Study	Characteristics of intervention or exposure	Types of intervention	Total *N*	Intervention or exposure (*n*/*N*)	Control (*n*/*N*)	OR or HR (95% CI)
NTD	Carmichael 2003[133]	Diet to lose weight	Diet	1077	29/538	14/539	OR 2.1 (1.1 to 4.1)[a]
		Fasting diet			17/538	3/539	OR 5.8 (1.7 to 20.0)[a]
		Other special diet			17/538	3/539	OR 1.0 (0.3 to 3.1)[a]
		Eating disorder			18/538	11/539	OR 1.7 (0.8 to 3.6)[a]
		Any special diet or eating disorder			61/538	31/539	OR 2.1 (1.3 to 3.3)[a]
		Binge eating (self-reported dieting behaviour for any time during 3 months before pregnancy or during pregnancy)			36/538	44/539	OR 0.8 (0.5 to 1.3)[a]
NTD	Yazdy 2010[143]	Glycaemic index low < 60	Diet	1394	522/698	594/696	OR 2.0 (1.5 to 2.6)[a]
		Glycaemic index high ≥ 60			176/698	102/696	OR 1.5 (1.1 to 2.0)[b]
		Glycaemic load low < 205			668/698	683/696	OR 2.4 (1.2 to 4.6)[a]
		Glycaemic load high ≥ 205			30/698	13/696	OR 1.8 (0.8 to 4.0)[b]
		Glycaemic index low < 60		Subgroup BMI ≥ 30 kg/m^2 (100)	23/36	53/64	OR 2.7 (1.1 to 7.0)[a]
		Glycaemic index high ≥ 60			13/36	11/64	OR 2.0 (0.6 to 7.3)[b]
		Glycaemic load low < 205			32/36	59/64	OR 1.5 (0.4 to 5.9)[a]
		Glycaemic load high ≥ 205			4/36	5/64	OR 0.9 (0.2 to 4.7)[b]
		Glycaemic index low < 60		Subgroup BMI < 30 kg/m^2 (816)	138/185	540/631	OR 2.0 (1.4 to 3.0)[a]
		Glycaemic index high ≥ 60			47/185	91/631	OR 1.7 (1.1 to 2.7)[b]
		Glycaemic load low < 205			177/185	623/631	OR 3.8 (1.4 to 10.5)[a]
		Glycaemic load high ≥ 205			8/185	8/631	OR 3.3 (1.0 to 10.6)[b]
Cord abnormalities	Magann 2002[77]	Exercise: various intensities	Physical activity	750			
		Light			15/222	18/217	OR 0.80 (0.39 to 1.63)[a]
		Moderate			7/73		OR 1.17 (0.47 to 2.93)[a]
		Heavy			9/238		OR 0.43 (0.19 to 0.99)[a]
Coronary heart disease (adult)	Roseboom 2000[139]	Diet: famine	Diet	736			
		Exposed in late gestation			3/120	6/232	Exposed in late gestation vs not exposed prenatally: OR 0.8 (0.2 to 2.8)
		Exposed in mid-gestation			1/108	8/208	Exposed in mid-gestation: OR 3.0 (0.0 to 2.2)
		Exposed in early gestation			6/68		Exposed early gestation: OR 3.0 (1.1 to 8.0)
	de Rooij 2006[134]	Diet: famine	Diet	694			OR 0.79 (0.42 to 1.49)[a]

continued

TABLE 7 Adverse outcomes associated with any diet or physical activity in pregnancy (*continued*)

Outcome	Study	Characteristics of intervention or exposure	Types of intervention	Total *N*	Intervention or exposure (*n*/*N*)	Control (*n*/*N*)	OR or HR (95% CI)
Metabolic syndrome (adult)	de Rooij 2007[68]	Diet: famine	Diet	783			OR 1.2 (0.9 to 1.7)
	de Rooij 2006[134]	Diet: famine	Diet	694			OR 1.09 (0.78 to 1.51)[a]
Hypertension (adult)	Lumey 2009[76]	Diet: famine	Diet	638	224/344	168/294	OR 1.40 (1.02 to 1.93)[a]
Breast cancer	Painter 2008[135]	Diet: famine	Diet	475			HR (all exposed) 2.6 (0.9 to 7.7)[a]
		Exposed in late gestation			3/82	1/126	HR 2.6 (0.9 to 7.7)[b]
		Exposed in mid-gestation			3/77	4/144	HR 2.5 (0.8 to 7.4)[b]
		Exposed in early gestation			4/46		HR 4.0 (1.1 to 14.5)[b]
Cleft lip, cleft palate or both	Vujkovic 2007[142]	Diet: Western vs prudent	Diet	381			
		Western (by tertile)					
		T1 (127)			58/203	69/178	T1: ref.
							T2: OR 1.3 (0.8 to 2.2)[a]
							T3: OR 1.9 (1.2 to 3.1)[a]
		T2 (127)			67/203	60/178	T2: OR 1.2 (0.7 to 2.1)[b]
							T3: OR 1.7 (1.0 to 3.0)[b]
		T3 (127)			78/203	49/178	T2: OR 1.2 (0.8 to 2.1)[b]
							T3: OR 1.8 (1.0 to 2.9)[b]
		Prudent (by tertile)					
		T1 (127)			68/203	59/178	T1: ref.
							T2: OR 0.9 (0.5 to 1.4)[a]
							T3: OR 1.1 (0.7 to 1.8)[a]
		T2 (127)			64/203	63/178	T2: OR 0.8 (0.5 to 1.4)[b]
							T3: OR 1.3 (0.8 to 1.8)[b]
		T3 (127)			71/203	56/178	T2: OR 0.7 (0.5 to 1.2)[b]
							T3: OR 1.0 (0.6 to 1.7)[b]

Outcome	Study	Characteristics of intervention or exposure	Types of intervention	Total *N*	Intervention or exposure (*n*/*N*)	Control (*n*/*N*)	OR or HR (95% CI)
Antisocial personality disorder	Neugebauer 1999[80]	Diet: famine, western Holland	Diet	76,630			
		By trimester					
		First, second or third			26/14,310	50/45,007	OR 1.6 (1.02 to 2.6)
							OR 2.0 (1.2 to 3.3)[b]
		First and/or second			20/9252		OR 2.0 (1.2 to 3.5)
							OR 2.5 (1.5 to 4.2)[b]
		First only			6/2443		OR 2.2 (0.95 to 5.0)
							OR 2.9 (1.2 to 6.7)[b]
		First and second only			6/2223		OR 2.4 (1.04 to 5.7)
							OR 3.0 (1.3 to 7.0)[b]
		Second only			9/4586		OR 1.8 (0.9 to 3.6)
							OR 2.1 (1.03 to 4.4)[b]
		Thirrd only			5/5058		OR 0.9 (0.4 to 2.2)
							OR 1.1 (0.4 to 2.7)[b]
		By severity					
		Severely exposed			26/14,310	50/45,007	OR 1.9 (1.02 to 2.6)
							OR 2.0 (1.2 to 3.3)[b]
		Moderately exposed			10/9615		OR 0.9 (0.6 to 1.9)
							OR 0.7 (0.3 to 1.6)[b]
Dyslipidaemia (adult)	Lumey 2009[76]	Diet: famine	Diet	638	96/344	85/294	OR 0.95 (0.61 to 1.34)[a]
Obesity (adult)	Ravelli 1976[136]	Diet: famine (by trimester)	Diet	307,700			
		Third			51/6200	148/11,200	OR 0.62 (0.45 to 0.85)[a]
		Second and third			126/7500	286/17,600	OR 1.03 (0.84 to 1.28)[a]
		First and second			119/4300	230/15,900	OR 1.94 (1.55 to 2.43)[a]
		First			41/2500	162/10,500	OR 1.06 (0.75 to 1.50)[a]

continued

TABLE 7 Adverse outcomes associated with any diet or physical activity in pregnancy (*continued*)

Outcome	Study	Characteristics of intervention or exposure	Types of intervention	Total *N*	Intervention or exposure (*n*/*N*)	Control (*n*/*N*)	OR or HR (95% CI)
IGT or type 2 diabetes (adult)	Stanner 1997[141]	Diet: famine	Diet	357			
Known diabetes					4/169	7/188	OR 0.63 (0.18 to 2.18)[a]
Newly diagnosed diabetes					3/169	5/188	OR 0.66 (0.16 to 2.81)[a]
IGT					16/169	16/188	OR 1.12 (0.54 to 2.32)[a]
	Ravelli 1998[137]	Diet: famine	Diet	702			
		Exposed in late gestation			24/116	33/221	General: OR 1.19 (0.79 to 1.79)[a]
		Exposed in mid-gestation			14/100	30/202	
		Exposed in early gestation			10/63		
Meconium in fluid	Clapp 1990[64]	Physical activity: exercise regularly or at >50% of their preconceptional level throughout pregnancy	Physical activity	131	12/87	11/44	OR 0.48 (0.19 to 1.20)[a]
Abnormal heart rate	Clapp 1990[64]	Physical activity: exercise regularly or at >50% of their preconceptional level throughout pregnancy	Physical activity	131	12/87	11/44	OR 0.48 (0.19 to 1.20)[a]
Nuchal cord	Clapp 1990[64]	Physical activity: exercise regularly or at >50% of their preconceptional level throughout pregnancy	Physical activity	131	23/87	24/44	OR 0.30 (0.14 to 0.64)[a]
Threatened abortion	Dale 1982[67]	Physical activity: running	Physical activity	33	1/21	1/11	OR 0.50 (0.03 to 8.85)[a]
Chorioamnionitis secondary to prolonged rupture of membranes	Dale 1982[67]	Physical activity: running	Physical activity	33	0/21	1/11	OR 0.16 (0.01 to 4.35)[a]
Asphyxia/ meconium staining/fetal distress	Dale 1982[67]	Physical activity: running	Physical activity	33	0/21	4/11	OR 0.04 (0.00 to 0.81)
Sepsis	Dale 1982[67]	Physical activity: running	Physical activity	33	0/21	1/11	OR 0.16 (0.01 to 4.35)[a]

HR, hazard ratio; IGT, impaired glucose tolerance.
a Unadjusted value.
b Adjusted value.

physical activity in pregnancy. The rates of congenital abnormalities such as neural tube defects (NTDs) were observed in those following dietary interventions that aimed to significantly reduce weight[133] or in those intaking food with a very high- or a very low-glycaemic index.[143] The risks of coronary artery disease, metabolic syndrome, breast cancer and diabetes were studied in infants born to mothers who were severely diet restricted owing to famine.[68,135,139]

The observational studies on physical activity in pregnancy did not show any significant adverse maternal or fetal outcomes. This was consistently observed for different activities of varying severity.

The detailed clinical characteristics of the included studies for the evaluation of adverse effects are provided in *Appendix 10*.

Summary

The review of adverse effects identified two RCTs and a relatively large number of observational studies. The data from the observational studies showed a possible association between extremes of diet (exposure to famine) and adverse outcomes; however, there was no evidence to suggest that dietary interventions evaluated in the review or currently offered in clinical practice could be associated with adverse maternal or fetal outcomes. Physical activity in pregnancy and maternal and fetal outcomes were studied in the randomised trials and observational studies. Various forms of physical activity such as structured exercises, running and recreational activities of differing intensities were not associated with adverse maternal and fetal outcomes.

The strength of the review is the systematic search for evidence using a broad search strategy. The inclusion of both randomised and non-randomised data including case series has ensured that the review identifies the evidence for all potential adverse effects of interventions. The review was limited by the RCTs being of poor quality. A large proportion of the evidence from the observational studies was devoted to extremes of diet rather than the components of a balanced healthy diet. There was insufficient evidence on popular diets such as the Atkins diet, the Slimming World diet and 'high-protein' diets. The studies on physical activity in pregnancy were mainly concerned with cord abnormalities and abnormal fetal heart rate patterns. The data from RCTs on women undergoing physical activity in pregnancy show no effect on gestational age at delivery or preterm delivery provide reassuring evidence on the safety of these interventions for these outcomes.

Chapter 5

Grading of Recommendations Assessment, Development and Evaluation (GRADE) findings

Prioritisation of outcomes

The primary outcomes were weight-related outcomes. There were numerous secondary outcomes. These were ranked through a two-iteration Delphi survey.

First iteration

A total of 19 clinicians (19/20, 95%) completed the questionnaire. Five maternal outcomes – GDM, pre-eclampsia and pregnancy-induced hypertension, caesarean section, thromboembolism and admission to the HDU/intensive therapy unit (ITU) – had a median score of ≥ 8 with an IQR of ≤ 2. The six fetal outcomes that were scored in a similar fashion were SGA infants, intrauterine death, admission to NICU, shoulder dystocia, birth trauma and long-term neurological sequelae. In addition to the outcomes provided, the panel considered breastfeeding, back pain, threatened miscarriage, failed instrumental delivery, maternal coronary artery disease, maternal non-infective respiratory distress, cord abnormalities and long-term metabolic sequelae in the infant to be relevant to the question posed. These outcomes were added to the initial outcomes and sent for scoring for importance in the second round.

Second iteration

A total of 16 panellists (16/19, 84%) participated in the second round of the survey. For maternal outcomes there was evidence of consensus for GDM, thromboembolism and admission to HDU/ITU, as reflected in the median scores of 8 and a fall in IQR from the first round score. Pre-eclampsia continued to be considered as a critically important outcome, with a median score of > 8, although there was an increase in the IQR from 1.5 to 2. Induction of labour scored a median of 8 and was included in the final list of outcomes. Caesarean section as an outcome scored lower (median 7) than in the first round.

For fetal outcomes there was consistency in the ranking, with median scores of > 8 and IQRs of ≤ 1.25 for birth trauma, intrauterine death, admission to NICU and shoulder dystocia. All of the selected fetal outcomes consistently demonstrated a narrowing of the IQR scores in the second round, demonstrating consensus between the participants. The ten outcomes considered to be critical to patient care are provided in *Box 2*. The scores for the outcomes in the two rounds of the Delphi survey are provided in *Appendix 11*.

Grading of evidence for the effectiveness and adverse effects of interventions

The grading of the evidence for the primary outcomes related to maternal and fetal weight commissioned by the HTA programme and the outcomes considered to be critically important for patient management are summarised graphically in *Figure 37*. This two-dimensional chart

BOX 2 Delphi panel list of outcomes of critical importance in the management of maternal weight in pregnancy

GDM

Pre-eclampsia/gestational hypertension

Admission to HDU/ITU

Thromboembolism

Induction of labour

SGA infants

Shoulder dystocia

Birth trauma

Admission to NICU

Long-term neurological sequelae

plots five variables represented by equiangular spokes, which represent the quality domains used in evidence grading for each comparison–outcome pair. For each of the spokes, the length represents the magnitude of the quality, ranging from very low at the centre of the plot to high at its maximum length.

Details of the quality assessment are provided in *Appendix 12*. The overall strength of evidence for weight gain in pregnancy and birthweight was moderate for all interventions considered together. The strength of evidence for all interventions together was moderate for shoulder dystocia and high for SGA infants. The quality of the pooled evidence for all interventions was moderate for gestational hypertension in obese and overweight women and intrauterine death, and low for reduction in pre-eclampsia and birth trauma. The trend in reduction of GDM was graded low (*Table 8*). Although thromboembolism, maternal admission to HDU/ITU and long-term neurological sequelae to the fetus were considered to be critically important to the clinicians, we did not identify relevant evidence for these outcomes. Dietary interventions in pregnancy were graded moderate to high for the important outcomes more often than the other interventions (see *Appendix 13*).

The quality of the evidence for adverse outcomes for studies reporting diet and physical activity in pregnancy is provided in *Table 9*. The strength of evidence was very low for all of the outcomes evaluated for dietary intervention. Poor quality of evidence was also observed for physical activity interventions in pregnancy.

Summary

The Delphi survey prioritised outcomes that were considered to be critical in the management of women in pregnancy. The evidence quality on the primary outcomes related to weight, maternal weight gain in pregnancy and birthweight was graded as moderate. The strength of evidence was low for secondary outcomes such as pre-eclampsia, GDM, gestational hypertension and caesarean section and low to high for preterm birth, induction of labour, shoulder dystocia, birth trauma, incidence of SGA and LGA infants and intrauterine death for all interventions. The strength of evidence for adverse outcomes due to diet and physical activity was mostly very low reflecting the paucity of evidence in this area.

TABLE 8 The GRADE profile of the RCTs on the effects of weight management interventions in pregnancy on the primary and clinically important outcomes

	Illustrative comparative risks[a] (95% CI)				
Outcomes	**Assumed risk, control**	**Corresponding risk, all weight management interventions**	**Relative effect (95% CI)**	**No. of participants (studies)**	**Quality of the evidence (GRADE)[b]**
Gestational weight gain (kg)		The mean gestational weight gain (kg) in the intervention groups was 0.94 kg lower (1.57 kg to 0.3 kg lower)		4595 (30)	⊕⊕⊕⊖ Moderate[c,d,e]
Birthweight (kg)		The mean birthweight (kg) in the intervention groups was 0.07 kg lower (0.14 kg to 0.01 kg lower)		4573 (28)	⊕⊕⊕⊖ Moderate[c,d,f]
LGA	157 per 1000	115 per 1000 (85 to 155)	RR 0.73 (0.54 to 0.99)	3021 (12)	⊕⊕⊕⊖ Moderate[c,d,g]
SGA	71 per 1000	70 per 1000 (54 to 92)	RR 0.99 (0.76 to 1.29)	2901 (8)	⊕⊕⊕⊕ High[h]
Pre-eclampsia	103 per 1000	76 per 1000 (61 to 95)	RR 0.74 (0.59 to 0.92)	3072 (10)	⊕⊕⊖⊖ Low[h,i,j]
Gestational hypertension	134 per 1000	103 per 1000 (72 to 147)	RR 0.77 (0.54 to 1.1)	791 (6)	⊕⊕⊖⊖ Low[k]
GDM	112 per 1000	80 per 1000 (49 to 127)	RR 0.71 (0.44 to 1.13)	675 (5)	⊕⊕⊖⊖ Low[h,l,m]
Preterm birth	82 per 1000	62 per 1000 (46 to 84)	RR 0.76 (0.56 to 1.02)	2198 (11)	⊕⊕⊕⊖ Moderate[c,d,g]
Caesarean section	327 per 1000	304 per 1000 (278 to 337)	RR 0.93 (0.85 to 1.03)	3312 (14)	⊕⊕⊖⊖ Low[c,d,g,m]
Induction of labour	295 per 1000	330 per 1000 (295 to 372)	RR 1.12 (1.0 to 1.26)	2362 (5)	⊕⊕⊕⊖ Moderate[c,d,g]
Post-partum haemorrhage	59 per 1000	53 per 1000 (24 to 84)	RR 0.90 (0.57 to 1.43)	1232 (2)	⊕⊕⊖⊖ Low[g,n]
Intrauterine death	9 per 1000	1 per 1000 (0 to 11)	RR 0.15 (0.02 to 1.2)	1320 (2)	⊕⊕⊕⊖ Moderate[h]
Admission to NICU	382 per 1000	374 per 1000 (252 to 562)	RR 0.98 (0.66 to 1.47)	1962 (2)	⊕⊖⊖⊖ Very low[c,d,g,i,l]
Shoulder dystocia	33 per 1000	13 per 1000 (7 to 23)	RR 0.39 (0.22 to 0.7)	2317 (4)	⊕⊕⊕⊖ Moderate[g]
Birth trauma	9 per 1000	3 per 1000 (1 to 11)	RR 0.36 (0.11 to 1.23)	1961 (2)	⊕⊕⊖⊖ Low[g,h]
Neonatal hypoglycaemia	103 per 1000	110 per 1000 (88 to 139)	RR 1.07 (0.85 to 1.35)	2146 (5)	⊕⊖⊖⊖ Very low[g,l,m]

a Poor information about allocation concealment which was assess as not strongly significant.
b Poor information about blinding of subjective outcomes which was assessed as not strongly significant.
c High risk of bias regarding incompleteness of outcome data addressed and selective reporting.
d High risk of bias regarding incompleteness of outcome data addressed.
e Women with gestational diabetes.
f Allocation concealment not clear but not considered to be necessary for downgrading.
g Qualitative difference in the summary estimate.
h Significant dubgroup effect observed for women with gestational diabetes.
i Heterogeneity I2 = 48%.
j Wide confidence interval crossing line of no effect.
k Slight skew in funnel plot for given outcome.
l Difficult to interpret as only two studies.
m Evidence only for one group of interventions.

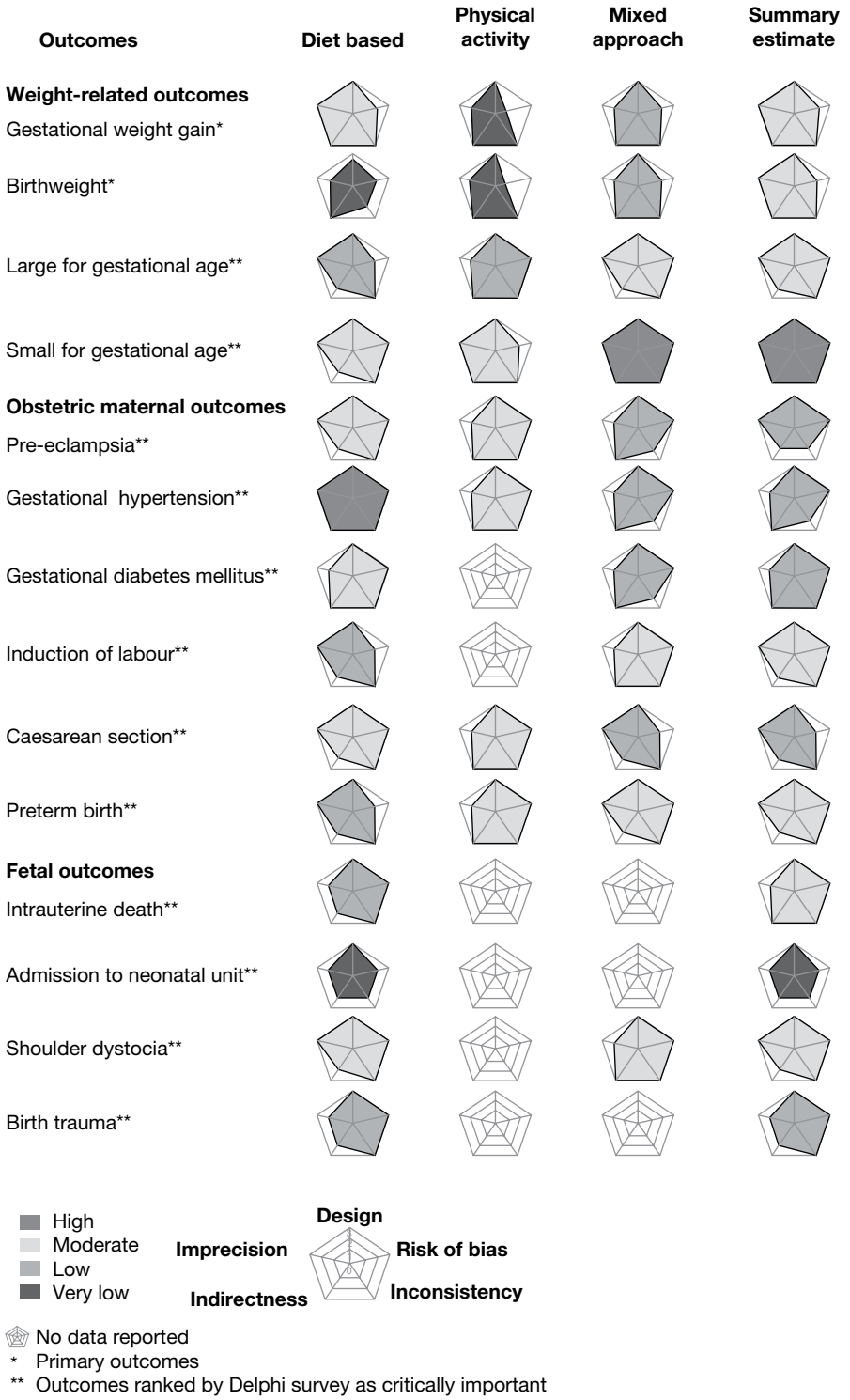

FIGURE 37 Graphic display of the evidence quality for the effect of various interventions on weight-related and clinically important outcomes.

TABLE 9a GRADE profile for adverse effects due to diet and physical activity in pregnancy: diet in pregnancy

Outcomes	Illustrative comparative risks[a] (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)[b]
	Assumed risk, control	Corresponding risk, diet			
NTD	See comment o	See comment o	Not estimable	0 (2)	⊕⊖⊖⊖ Very low[c,d,e]
Coronary heart disease: long-term outcome in children	32 per 1000	90 per 1000 (35 to 209)[f]	OR 3 (1.1 to 8.0)	508 (1)	⊕⊖⊖⊖ Very low[e,g,h]
Metabolic syndrome: long-term outcome in children	1 per 1000	1 per 1000 (1 to 2)[i]	OR 1.2 (0.9 to 1.7)	59,317 (1)	⊕⊖⊖⊖ Very low[g,h]
Hypertension: long-term outcome in children	571 per 1000	651 per 1000 (576 to 720)	OR 1.4 (1.02 to 1.93)	638 (1)	⊕⊖⊖⊖ Very low[h,j]
Antisocial personality disorder: long-term outcome in children	1 per 1000	2 per 1000 (1 to 3)[i]	OR 2.0 (1.2 to 3.3)	59,317 (1)	⊕⊖⊖⊖ Very low[e,g,h]
Dyslipidaemia	289 per 1000	279 per 1000 (199 to 353)	OR 0.95 (0.61 to 1.34)	638 (1)	⊕⊖⊖⊖ Very low[h,j,k]
Obesity: in adulthood: long-term outcome in children	13 per 1000[l]	8 per 1000 (6 to 11)[l]	OR 0.62 (0.45 to 0.85)	17,400 (1)	⊕⊖⊖⊖ Very low[h,m]
Obesity: in adulthood: long-term outcome in children	14 per 1000[n]	27 per 1000 (22 to 33)[n]	OR 1.94 (1.55 to 2.43)	20,200 (1)	⊕⊖⊖⊖ Very low[h,m]
IGT: long-term outcome in children	85 per 1000	94 per 1000	OR 1.12 (0.54 to 2.32)	357 (1)	⊕⊖⊖⊖ Very low[g,h]

IGT, impaired glucose tolerance; max., maximum.

a The basis for the *assumed risk* (e.g. the median control group risk across studies) is provided in footnotes. The *corresponding risk* (and its 95% CI) is based on the assumed risk in the comparison group and the *relative effect* of the intervention (and its 95% CI).

b GRADE Working Group grades of evidence: *high quality*: further research is very unlikely to change our confidence in the estimate of effect; *moderate quality*: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *low quality*: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *very-low quality*: we are very uncertain about the estimate.

c Poor information about definition of controls, ascertainment of exposure and non-response rate in Yazdy 2010[143] study.

d No explanation was provided.

e OR > 2.

f Exposed early.

g Observational study, 5 points (9 max.) in NOS questionnaire.

h Singleton men and women born between January 1945 and March 1946 whose mothers were exposed or not to the Dutch famine during pregnancy.

i During first, second or third trimester.

j Observational study, 6 points (9 max.) in NOS questionnaire.

k Wide CI.

l During third trimester of pregnancy.

m Observational study, 4 points (9 max.) in NOS questionnaire.

n During first and second trimester of pregnancy.

o Data heterogeneous and not suitable for pooling of estimates.

TABLE 9b GRADE profile for adverse effects due to diet and physical activity in pregnancy: physical activity in pregnancy

Outcomes	Illustrative comparative risks[a] (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)[b]
	Assumed risk, control	Corresponding risk, physical activity			
Cord abnormalities	83 per 1000	37 per 1000 (17 to 82)[c]	OR 0.43 (0.19 to 0.99)	455 (3)	⊕⊖⊖⊖ Very low[d]
Stimulation for abnormal labour pattern	205 per 1000	115 per 1000 (43 to 303)	RR 0.56 (0.21 to 1.48)	131 (1)	⊕⊖⊖⊖ Very low[d,e]
Meconium in amniotic fluid	170 per 1000	105 per 1000 (34 to 323)	RR 0.62 (0.2 to 1.9)	85 (1)	⊕⊕⊖⊖ Low[e,f,g,h]
Abnormal fetal heart rate	250 per 1000	138 per 1000 (60 to 286)	OR 0.48 (0.19 to 1.2)	131 (1)	⊕⊖⊖⊖ Very low[d,e]
Nuchal cord	545 per 1000	264 per 1000 (144 to 434)	OR 0.3 (0.14 to 0.64)	131 (1)	⊕⊖⊖⊖ Very low[d]
Threatened abortion	91 per 1000	48 per 1000 (3 to 470)	OR 0.5 (0.03 to 8.85)	32 (1)	⊕⊖⊖⊖ Very low[e,i]
Failure to progress with oxytocin augmentation	273 per 1000	142 per 1000 (26 to 503)	OR 0.44 (0.07 to 2.7)	32 (1)	⊕⊖⊖⊖ Very low[e,i]
Chorioamnionitis	26 per 1000	0 per 1000	OR 3.69 (0.15 to 88.13)	85 (1)	⊕⊕⊖⊖ Low[e,f,g,h]
Maternal anaemia	182 per 1000	143 per 1000 (24 to 541)	OR 0.75 (0.11 to 5.3)	32 (1)	⊕⊖⊖⊖ Very low[e,i]
Maternal sepsis	91 per 1000	16 per 1000 (1 to 303)	OR 0.16 (0.01 to 4.35)	32 (1)	⊕⊖⊖⊖ Very low[e,i]
Uterine atony	85 per 1000	79 per 1000 (19 to 331)	RR 0.93 (0.22 to 3.89)	85 (1)	⊕⊕⊖⊖ Low[e,f,g,h]

max., maximum.

a The basis for the *assumed risk* (e.g. the median control group risk across studies) is provided in footnotes. The *corresponding risk* (and its 95% CI) is based on the assumed risk in the comparison group and the *relative effect* of the intervention (and its 95% CI).

b GRADE Working Group grades of evidence: *high quality*: further research is very unlikely to change our confidence in the estimate of effect; *moderate quality*: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *low quality*: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; *very-low quality*: we are very uncertain about the estimate.

c Exercise (heavy).

d Observational study, 6 points (9 max.) in NOS questionnaire.

e Wide CI.

f Limited information about allocation concealment, assessed as not strongly significant.

g Limited information about blinding of subjective outcomes, assessed as not strongly significant.

h Limited information about adequate sequence generation, assessed as not strongly significant.

i Observational study, 4 points (9 max.) in NOS questionnaire.

The weight-related outcomes were regarded as critical in the HTA commissioning brief (HTA No. 09/27/06) for an evaluation of the reduction or prevention of obesity in pregnancy. In addition to the large benefits observed with dietary intervention, the strength of evidence for this intervention was also rated better than that for the other interventions. The evidence for gestational weight gain was of moderate quality for dietary interventions and low for the physical activity and mixed approach interventions. For subgroups of overweight women and obese women the strength of evidence was low to very low for all three interventions. This was a result of the imprecision in the estimates and incomplete reporting of the outcome data. The quality of evidence for the incidence of SGA infants, which showed no significant differences between

the intervention and control groups, was moderate to high for all of the interventions. This finding is reassuring to an extent as it negates the perceived risks of interventions for the growth of the fetus.

The evidence quality for reduction in the rate of pre-eclampsia was moderate for dietary intervention, which showed the largest reduction in risk. In the subgroups of obese and overweight women the beneficial effect of dietary intervention in reducing pre-eclampsia scored a moderate-to-high grade for the quality of evidence. Overall, there was moderate-quality evidence that weight management interventions reduce the risks of shoulder dystocia, with the potential to reduce associated morbidity and mortality. The strength of evidence was low for the trend towards a reduction in the incidence of GDM. It is possible that a different panel may have identified a different group of clinically important outcomes.

The graphic display has captured the quality of the evidence for many comparisons and outcomes simultaneously in one diagram making it possible to comprehend large numbers of data in one glance. The diagram, once understood, allows for appraisal of key issues concerning risk of bias, heterogeneity, directness of evidence in relation to the question, and precision of results. This critical appraisal alters the trust that we can place in the evidence collated for decision-making.

The GRADE profile findings are limited because of the paucity of evidence for some important outcomes such as thromboembolism, maternal admission to HDU/ITU, long-term neurological sequelae and more than one perinatal complication. Further research is likely to have an important impact on the confidence of our estimate and is likely to change the estimate. We have refrained from assessing the quality of evidence across outcomes as it is in the domain of the guideline developers. As systematic reviewers we have limited ourselves to the GRADE profiling of the important outcomes.

Chapter 6

Discussion

Introduction

This review evaluated the effects of dietary and lifestyle interventions, including physical activity, on the prevention and reduction of obesity in pregnancy, an important area of public health given the increasing prevalence of obesity. We undertook three distinct but related pieces of work:

1. a systematic review of the evidence to evaluate the effect of dietary and lifestyle interventions on maternal and fetal weight (primary outcome), obstetric outcomes and fetal and neonatal morbidity and mortality
2. a systematic review of the evidence to evaluate the risks of adverse effects in the mother or fetus as a result of interventions in pregnancy
3. grading of the quality of evidence for critical and important outcomes.

This work has been described in detail in the previous sections. This chapter summarises the key findings and limitations of the work undertaken. It draws conclusions and makes recommendations for research.

Main findings

- Interventions to manage weight in pregnancy were effective at reducing weight gain in pregnancy, with dietary interventions being the most effective.
- The commonest diet evaluated in the studies was a balanced calorie regime with low fat or cholesterol and high fibre. Interventions were delivered in both primary and secondary care. Physical activity involved moderate exercise with low-intensity resistance training.
- The small reduction in birthweight appeared to be of benefit by reducing the risk of LGA fetuses. This reduction in birthweight did not show as an increase in the incidence of SGA fetuses.
- Dietary intervention showed benefit in reducing obstetric complications such as pre-eclampsia, gestational hypertension and preterm delivery compared with other interventions. Dietary intervention also reduced the risks of shoulder dystocia of the fetus. There was no effect on any other fetal and neonatal morbidity and mortality outcomes with any intervention.
- There was no evidence of maternal or fetal harm resulting from the diet and physical activity interventions recommended in current clinical practice.
- Evidence quality for effectiveness outcomes was more often graded moderate or high compared with evidence quality for adverse effects. The quality of evidence for adverse effects for both diet and physical activity was very low.

Strengths of the report

This systematic review comprehensively addressed the benefits and harms of the various weight management interventions in pregnancy. In doing so, compared with other reviews, it identified

the largest quantity of evidence, especially RCTs. A Delphi survey of clinicians was the first attempt to rank the outcomes according to their importance. The grading of the strength of evidence for the outcomes prioritised provides the much-needed clarity to make judgements about effects and generate recommendations.

Limitations of the report

- It was not possible to provide effectiveness data for all of the outcomes and subgroups; however, the critical and important outcomes are well covered.
- The interpretation of the findings is limited by the paucity of descriptive information on the intensity and duration of intervention, means of provision, patient compliance and any management that can potentially facilitate or hinder implementation. The estimate of reduced gestational weight gain with diet was associated with significant heterogeneity.
- No studies performed a face-to-face comparison of various interventions, thereby restricting the ranking of interventions based on effectiveness.
- The grading of evidence was often limited by the poverty of reporting. The poor quality of evidence on adverse effects was a particular problem.
- There was no evidence on popular diets such as the 'high-protein, low-carbohydrate', 'no carbohydrate', Slimming World and Atkins diets.
- There were no relevant data on the quality of life of the participants.

Overall conclusion

Despite the above limitations some clear conclusions can be made. There is benefit from weight management interventions, especially dietary intervention, in reducing weight gain in pregnancy (evidence quality moderate). Interventions reduced the risk of pre-eclampsia and shoulder dystocia (evidence quality low to high). Interventions based on diet are effective in reducing the main obstetric complications such as pre-eclampsia, gestational hypertension and shoulder dystocia (evidence quality moderate to moderate). Weight management interventions reduce the risk of having large babies. There is no evidence of harm to the mother or fetus from the diet or physical activity components of the interventions currently used.

Recommendations for research

These recommendations are guided by gaps identified and the evidence grading:

- If RCTs are undertaken they should focus on clinically relevant outcomes.
- Individual patient data meta-analysis can improve the interpretation of current data.
- The long-term effects of the interventions on the mother and fetus and the safety of the interventions needs further evaluation.
- Engagement with pregnant women can identify the outcomes that they consider relevant to themselves and their babies.
- Cost-effectiveness can be assessed by undertaking a model-based health economic evaluation.
- If weight management interventions are implemented based on current evidence and ongoing studies, service evaluation should include an assessment of uptake, compliance and adverse effects.

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Contribution of authors

ST developed the protocol, conducted the review, drafted the manuscript and led the project. ER and SG undertook the literature searches, study selection, data extraction and data analysis. WD, JW and EB provided input into the review conduct and the drafting of the initial manuscript. JT and KJ provided input into the protocol development and the drafting of the manuscript. TR was involved in the review of adverse effects of interventions. RK provided input into the use of GRADE. AC and BWM were involved in project development and provided input at all stages. KSK provided input into the development of the protocol, the conduct of the review and the final version of the manuscript.

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Appendix 1

List of reviews evaluating the effect of weight management interventions on maternal and fetal outcomes

Review	Question	Search criteria	Studies included
Dodd 2008[144]	**Population:** overweight and obese women during pregnancy **Intervention:** dietary and lifestyle interventions (alone or in combination) to limit weight gain with the intention of improving maternal, fetal and infant health outcomes **Outcomes:** weight gain, maternal, fetal and infant health outcomes **Design of included studies:** RCTs	**Databases searched:** MEDLINE, The Cochrane Library, Australian (ACTR) and International (ICTN) Clinical Trials Registry **Hand searching:** not stated **Search restrictions:** none stated	**RCTs:** Polley 2002,[130] Rae 2000[101]
Dodd 2010[145]	**Population:** pregnant women who are overweight or obese **Intervention:** antenatal dietary or lifestyle interventions **Outcomes:** LGA infants, mean gestational weight gain, hypertension, pre-eclampsia or eclampsia, GDM, preterm birth before 37 weeks of gestation, infection, need for induction of labour, caesarean section, post-partum haemorrhage requiring blood transfusion, perinatal death (stillbirth and neonatal death), congenital anomalies, infant birthweight of > 4500 g, infant birthweight of < 2500 g, Apgar score of < 7 at 5 minutes of age, hypoglycaemia requiring intravenous treatment, hyperbilirubinaemia requiring treatment, admission to NICU and birth trauma. Childhood outcomes of relevance relate to body size (including height, weight, and BMI) and body composition **Study design:** RCTs	**Databases searched:** PubMed, CENTRAL, ACTR, ICTN **Hand searching:** yes **Search restrictions:** no	**RCTs:** Asbee 2008, Brankston 2004, Guelinckx 2008, Magee 1990, Polley 2002,[130] Rae 2000,[101] Santos 2005,[119] Thornton 2009,[102] Wolff 2008[103]
Kuhlmann 2008[146]	**Population:** pregnant or post-partum women **Intervention:** exercise **Outcomes:** pregnancy weight gain in excess of the IOM recommendations or post-partum weight retention **Design of included studies:** RCTs	**Databases searched:** MEDLINE, EMBASE, PsycINFO, Sociological Abstracts, Cumulative Index to Nursing and Allied Health Literature (CINAHL) **Hand searching:** yes **Search restrictions:** studies published January 1985 to August 2007, English language	**RCTs:** Leermakers 1998, O'Toole 2003, Polley 2002,[130]

Review	Question	Search criteria	Studies included
Leet 2003[147]	**Population:** pregnant women **Intervention:** exercise **Outcomes:** infant birthweight **Design of included studies:** RCTs, non-randomised controlled studies, observational studies	**Databases searched:** MEDLINE, Doctor Dissertation Abstracts Online **Hand searching:** yes **Search restrictions:** English language	**Experimental:** Bell 2000,[132] Carr 1992, Clapp 2000,[107] Clapp 2002,[108] Collings 1983,[52] Erkkola 1976, Lee 1996,[115] Marquez-Sterling 2000[116] **Quasi-experimental:** Brenner 1995, Lewis 1998, Webb 1988 **Observational:** Bell 1995,[60] Botkin 1991, Burger 1988, Clapp 1984,[62] Clapp 1990, Clapp 1992, Clapp 1995,[51] Clapp 1998, Dale 1982,[67] Hatch 1993,[70] Horns 1996,[71] Jackson 1995,[72] Johson 1994, Madison 1989, Melgar 1997, Piravej 2001,[83] Rice 1991, Sternfeld 1995
Liu 2005[148]	**Population:** pregnant women **Intervention:** an intervention applicable to public health practice consistent with Ontario's Mandatory Health Programs and Services Guidelines; primary prevention and *not* designed specifically for pregnant women who are obese or diabetic (pregnant or obese women can be included in the study population) **Outcomes:** proportion of women exceeding the upper limit of the IOM recommended gestational weight gain range **Design of included studies:** RCTs, non-randomised controlled studies, prospective studies with control group	**Databases searched:** MEDLINE, EMBASE, CINAHL, PsycINFO, Sociological Abstracts, SPORTDiscus **Hand searching:** yes **Search restrictions:** studies published 1980 to 2005, English language	**RCTs:** Clapp 1995,[51] Olson 2004,[81] Polley 2002[130]
Ronnberg 2010[149]	**Population:** pregnant women **Exclusion:** women with diabetes mellitus **Intervention:** intervention studies specifically designed to prevent excessive gestational weight gain **Outcomes:** weight gain in pregnancy **Study design:** RCTs, NRSs, observational studies	**Databases searched:** PubMed, The Cochrane Library, CINAHL, Physiotherapy Evidence Database (PEDro) **Hand searching:** yes **Search restrictions:** limited to English and Scandinavian languages	**RCTs:** Asbee 2008, Bechtel-Blackwell 2002,[93] Polley 2002,[130] Wolff 2008[103] **NRSs and observational:** Claesson 2008,[49] Gray-Donald 2000,[54] Kinnunen 2007,[57] Olson 2004[81]
Scharr 2010[22]	**Population:** pregnant women expecting a single baby, women seeking preconception advice, women actively planning a pregnancy **Intervention:** dietary and/or physical activity advice, personal one-to-one and group counselling, physical activity groups or classes, educational and informative literature given to pregnant women, monitoring by health professionals or self-assessment, tracking of progress and tailoring programmes to meet current needs of pregnant women **Outcomes:** weight-related outcomes, dietary and physical activity outcomes, other mother-related outcomes, outcomes relating to the infant **Design of included studies:** RCTs, NRSs, observational studies	**Databases searched:** MEDLINE, EMBASE, The Cochrane Library, Science Citation Index, ClinicalTrials.com, UK Clinical Research Network Portfolio, other: Applied Social Sciences Index and Abstracts (ASSIA) via CSA, British Nursing Index via OVID SP, CINAHL via OVID SP, EconLit via OVID SP, Maternity and Infant Care via OVID SP, PsycINFO via OVID SP, Social Science Citation Index via Web of Science **Hand searching:** yes **Search restrictions:** searches were limited by year (1990–2008) and to human studies (where this option was available)	**RCTs:** Asbee 2008, Guelinckx 2008, Hui 2002, Polley 2002,[130] Wolff 2008[103] **NRSs:** Claesson 2008,[49] Gray-Donald 2000,[54] Kardel 1998,[56] Kinnunen 2007,[57] Olson 2004[81] **Case series:** Galletly 1996, Mendelson 1991 **Observational:** Bergmann 1997, Bungum 1999, Cambell 2001, Cogswell 1996, Conway 1999,[66] Gunderson 2004, Horns 1996,[71] Keppel 1993, Lof 2008, Mumford 2008, Olson 2003, Sternfeld 1995, Symons Downs 2007, Taffel 1993

Review	Question	Search criteria	Studies included
Schlüssel 2008[150]	**Population:** pregnant women **Intervention:** physical activity for pregnant women: (1) occupational physical activities and (2) leisure-time physical activities **Outcomes:** pre-eclampsia, gestational arterial hypertension, GDM, gestational weight gain, miscarriage, mode of delivery, fetal growth or development, birthweight, length at birth or prematurity **Design of included studies:** cross-sectional, case–control or follow-up (cohort) epidemiological studies	**Databases searched:** MEDLINE, LILACS **Hand searching:** yes **Search restrictions:** published between 1980 and 2005, Portuguese, English, or Spanish language	**Cohort:** Begun 2000, Bell 1995, Clapp 1989, Clapp and Little 1995, Dempsey 2004, Florack 1993, Florack 1995, Hatch 1993, Hatch 1998, Henriksen 1995, Horns 1996, Jarrett and Sppelday 1983, Klebanoff 1990, Koemeester 1995, Magann 2002, Misra 1998, Rabkin 1990, Rao 2003, Rose 1991, Saftlas 2004, Stamfeld 1995, Takito 2005 **Case–control:** Alderman 1998, Berkowitz 1983, Campbell and Mottola 2001, Carmichael 2002, Dempsey 2004, El Metwall 2001, Letke 1999, Marcoux 1989, Schramm 1996, Sorensen 2003, Spinillo 1995, Spinillo 1996 **Cross-sectional:** Dye 1997, Leiferman and Evenson 2003
Skouteris 2010[151]	**Population:** pregnant women **Intervention:** intervention studies specifically designed to prevent excessive gestational weight gain; interventions specifically targeting diabetes mellitus and/or designed for adolescents or post-partum women were excluded **Outcomes:** excessive weight gain in pregnancy **Study design:** RCTs, NRSs, observational studies	**Databases searched:** CINAHL, Global Health, MEDLINE, PsycINFO, Academic Search Premier **Hand searching:** not stated **Search restrictions:** limited to English papers published between January 2000 and April 2010	**RCTs:** Asbee 2008, Guelinckx 2008, Hui 2002, Jeffries 2009,[128] Polley 2002,[130] Wolff 2008[103] **NRSs:** Claesson 2008,[49] Gray-Donald 2000,[54] Kinnunen 2007,[57] Olson 2004[81]

Appendix 2

Search strategies

Search strategy in MEDLINE for the effect of dietary and lifestyle interventions in pregnancy on maternal and fetal outcomes

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1950 to present.

#	Searches	Results
1	Pregnancy/	605,292
2	pregnan*.tw.	299,525
3	Gravidity/	495
4	gravid*.tw.	8201
5	gestation*.tw.	116,230
6	Pregnant Women/	4361
7	pregnant wom#n.tw.	47,172
8	(child adj3 bearing).tw.	1653
9	childbearing.tw.	6924
10	matern*.tw.	141,495
11	or/1-10	746,528
12	Weight Gain/ph [Physiology]	2614
13	weight gain*.tw.	32,374
14	Weight Loss/ph [Physiology]	2846
15	weight loss*.tw.	38,743
16	weight change*.tw.	5183
17	Obesity/dh, me, ph, pc, px, th [Diet Therapy, Metabolism, Physiology, Prevention & Control, Psychology, Therapy]	33,441
18	obes*.tw.	111,828
19	Adiposity/ph [Physiology]	609
20	adipos*.tw.	43,101
21	Overweight/dh, me, ph, pc, px, th [Diet Therapy, Metabolism, Physiology, Prevention & Control, Psychology, Therapy]	1397
22	overweight*.tw.	21,881
23	Body Mass Index/	50,740
24	bmi.tw.	41,380
25	or/12-24	249,023
26	exp Randomised Controlled Trial/	289,035
27	"randomised controlled trial".pt.	289,035
28	"controlled clinical trial".pt.	81,125
29	(random$ or placebo$).tw,sh.	695,701
30	((singl$ or double$ or triple$ or treble$) and (blind$ or mask$)).tw,sh.	119,769

#	Searches	Results
31	single-blind method/	13,834
32	double-blind method/	105,956
33	exp Case-Control Studies/	460,490
34	(case$ and control$).tw.	239,150
35	exp Cohort Studies/	757,527
36	cohort$.tw.	157,621
37	observational study.tw.	17,760
38	non-randomised study.tw.	577
39	Evaluation Studies/	132,483
40	Comparative Study/	1,477,175
41	or/26-40	3,133,968
42	11 and 25 and 41	6878
43	exp Animals/	14,612,094
44	(rat$ or mouse or mice or hamster$ or animal$ or dog$ or cat$ or bovine or sheep or lamb$).af.	7,246,173
45	43 or 44	15,284,475
46	Humans/	11,152,314
47	human$.tw,ot,kf.	1,568,770
48	46 or 47	11,413,435
49	45 not (45 and 48)	3,949,418
50	42 not 49	5941

Search strategy in MEDLINE for the adverse effects of dietary and lifestyle interventions in pregnancy on maternal and fetal outcomes

Ovid MEDLINE(R) 1950 to May week 4 2010.

#	Searches	Results
1	Pregnancy/	608,934
2	pregnan*.tw.	294,859
3	Gravidity/	502
4	gravid*.tw.	8054
5	gestation*.tw.	11,4581
6	Pregnant Women/	4376
7	pregnant wom#n.tw.	46,264
8	(child adj3 bearing).tw.	1621
9	childbearing.tw.	6805
10	matern*.tw.	139,237
11	or/1-10	741,261
12	(ae or to).fs.	1,363,123
13	exp safety/	40,253
14	(safe or safety).tw.	296,532
15	side effect$.tw.	136,451
16	(adverse and (reaction$ or event$ or response$)).tw.	98,046

#	Searches	Results
17	((adverse or undesirable or harms$ or serious or toxic) adj3 (effect$ or reaction$ or event$ or outcome$)).tw.	204,126
18	exp Clinical Trials, Phase IV as Topic/	150
19	(toxicity or complication$ or noxious or tolerability).tw.	649,502
20	harm$.tw,hw.	60,216
21	((undesired or undesirable) and (result$ or effect$)).tw.	9837
22	or/12-21	2,131,088
23	exp diet/	155,881
24	diet$.tw.	290,808
25	energy intake/	25,172
26	energy intake.tw.	10,074
27	calor$.tw.	42,201
28	nutrition$.tw.	131,024
29	(food adj3 intake).tw.	27,605
30	Fasting/	24,834
31	fast$.tw,kf.	246,556
32	Starvation/co, dh, me, ph [Complications, Diet Therapy, Metabolism, Physiology]	2421
33	starvation.tw,kf.	16,448
34	or/23-33	720,466
35	exp EXERCISE/	51,394
36	exp Exercise Therapy/	21,162
37	exercis$.af.	205,665
38	(aerobics or physical therapy or physical activity or physical inactivity).af.	71,067
39	(fitness adj (class$ or regime$ or program$)).af.	526
40	(aerobics or physical therapy or physical training or physical education).af.	55,042
41	dance therapy.af.	161
42	Yoga.tw.	911
43	pilates.tw.	43
44	swimming.tw.	12,793
45	aerobic$.tw.	41,405
46	aquarobic$.tw.	1
47	(aqua adj3 aerobic$).tw.	7
48	fitness.tw.	24,492
49	(Body adj3 ball).tw.	31
50	(Aqua adj3 fitness).tw.	2
51	(Nordic adj3 walking).tw.	26
52	(Recreational adj3 activit*).tw.	1633
53	(brisk adj3 walking).tw.	230
54	walking.tw.	28,317
55	cycling.tw.	24,848

#	Searches	Results
56	bicycle.tw.	8940
57	treadmill.tw.	18,047
58	jogging.tw.	921
59	(training adj3 exercise$).tw.	9097
60	(upper adj3 extremity adj3 exercise$).tw.	119
61	Stretching.tw.	10,794
62	Dancing.tw.	656
63	(Tai adj3 chi).tw.	449
64	(tai adj3 ji).tw.	7
65	(belly adj3 dancing).tw.	4
66	(motor adj3 activit*).tw.	13,891
67	(Occupational adj3 activit*).tw.	1528
68	(household adj3 activit*).tw.	461
69	(locomot* adj3 activit*).tw.	13,405
70	(daily adj3 physic* adj3 activit*).tw.	1092
71	or/35-70	398,556
72	34 or 71	1,072,658
73	11 and 22 and 72	9858
74	exp Animals/	14,729,014
75	(rat$ or mouse or mice or hamster$ or animal$ or dog$ or cat$ or bovine or sheep or lamb$).af.	7,120,771
76	74 or 75	15,216,122
77	Humans/	11,246,110
78	human$.tw,ot,kf.	1,550,517
79	77 or 78	11,474,007
80	76 not (76 and 79)	3,800,283
81	letter.pt.	680,151
82	comment.pt.	411,317
83	editorial.pt.	256,472
84	81 or 82 or 83	1,004,073
85	73 not 80	6997
86	73 not (80 or 84)	6883

Appendix 3

Clinical characteristics of the randomised controlled trials evaluating the effect of diet, physical activity and a mixed approach for weight management in pregnancy on maternal and fetal outcomes

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Asbee 2009[124] English	**Method of randomisation:** randomisation was performed using computer-generated random allocation. Randomisation occurred in consecutive order at the time of the antenatal visit **Allocation concealment:** study randomisation was numbered and sealed in an opaque envelope **Blinding:** no blinding used	**Inclusion criteria:** antenatal care established at 6–16 weeks of gestation; age 18–49 years; all antenatal care received at the resident obstetrics clinic; English speaking, Spanish speaking or both; singleton pregnancy **Exclusion criteria:** antenatal care established at more than 16 weeks of gestation; non-English speaking or non-Spanish speaking; multiple pregnancy; BMI > 40 kg/m^2; pre-existing diabetes, untreated thyroid disease or hypertension requiring medication or other medical conditions that might affect body weight; delivery at institution other than Carolinas Medical Centre-Main; pregnancy ending in premature delivery (< 37 weeks); limited prenatal care (fewer than four visits) **Number of participants:** experimental 57, control 43	Programme of intensive counselling regarding diet and lifestyle during pregnancy. The intervention provided education and feedback about weight gain, appropriate exercise in pregnancy and pregnancy-specific dietary counselling At the initial visit the study group met with a registered dietitian to receive a standardised counselling session, including information on pregnancy-specific dietary and lifestyle choices. The counselling consisted of recommendations for a patient-focused caloric value divided in a 40% carbohydrate, 30% protein and 30% fat ratio. Patients were instructed to engage in moderate-intensity exercise at least three times per week and preferably five times per week. They also received information on the appropriate weight gain during pregnancy using the IOM guidelines. Each participant met with the dietitian only at the time of enrolment At each routine obstetric appointment the participant's weight was measured using a balance beam scale and charted on an IOM Gestational Weight Gain Grid in front of the participant. The health-care provider (physician or nurse practitioner) informed the participant whether or not her weight gain was at the appropriate level. If her weight gain was within the IOM guidelines, the patient was praised and encouraged to continue her current diet and exercise regimen. If her weight gain was not within the IOM guidelines, the participant's diet and exercise regimen was reviewed and she was advised on increasing or decreasing her food intake and increasing or decreasing exercise	No intervention	IOM adherence, caesarean delivery rate, weight gain from prepregnancy to delivery

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Baciuk 2008[104] English	**Method of randomisation:** computer-generated randomisation list of numbers; volunteers were enrolled sequentially and randomised to one of the two study groups **Allocation concealment:** each sequential number corresponded to a sealed opaque envelope containing the information on the randomisation group **Blinding:** outcome assessors	**Inclusion criteria:** pregnant women of < 20 weeks of gestation; singleton pregnancy; no gestational risk factors; receiving prenatal care at the research institution and intending to give birth there **Exclusion criteria:** practising regular physical exercise; two or more caesarean sections; clinical and/or laboratory diagnoses of neurological, cardiovascular, pulmonary, musculoskeletal or endocrine disorders; any disorder that could represent a risk to the woman's health, such as morbid obesity, severe anaemia or vaginal bleeding during pregnancy **Number of participants:** experimental 34, control 37	**Physical activity:** water aerobics The intervention was the regular, moderate practise of water aerobics for 50 minutes three times a week in an indoor swimming pool with water warmed at 28–30°C. Water aerobics was initiated following the first physical evaluation and continued up to delivery. The moderate intensity of exercises during the sessions was assured by monitoring the patient's heart rate using a heart rate monitor and keeping the rate at around 70% of their predicted maximum heart rate	No intervention	Request for analgesia, caesarean section, Apgar score at 1 minute ≥ 7, vaginal delivery, preterm birth (< 37 weeks), low birthweight (< 2500 g), adequacy of neonatal weight to gestational age, length of labour (minutes), birthweight, gestational age, weight gain, body fat (%), fat-free mass (%), BMI
Badrawi 1992[92] English	**Method of randomisation:** participants were divided 'randomly' into two groups **Allocation concealment:** not reported **Blinding:** no blinding used	Obese pregnant mothers, aged between 25 and 35 years **Number of participants:** 100	Balanced calorie diet 1500–2000 kcal/day	No intervention	Pregnancy-induced hypertension

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Barakat 2009[105] English	**Method of randomisation:** not reported **Allocation concealment:** the researcher in charge of randomly assigning participants did not know in advance which treatment the next person would receive and did not participate in assessment **Blinding:** outcome assessors	**Inclusion criteria:** gravida with singleton and uncomplicated gestation; not at high risk for preterm delivery (no history of recurrent spontaneous preterm birth, i.e. number of previous preterm deliveries ≤ 1); 25–35 years of age; being sedentary before gestation (exercising < 20 minutes on < 3 days/week); being under medical follow-up throughout the entire pregnancy period (and planning to give birth) in the same obstetrics hospital department (Hospital Severo Ochoa, Madrid, Spain); having no absolute or relative contraindication to exercise participation during pregnancy [such as, among others, haemodynamically significant heart disease, restrictive lung disease, pregnancy-induced hypertension, severe anaemia, maternal cardiac arrhythmia, chronic bronchitis, type 1 diabetes or extreme morbid obesity (BMI 40 kg/m^2)] **Exclusion criteria:** women not planning to give birth in the same obstetrics hospital department (Hospital Severo Ochoa, Madrid, Spain); women not under medical follow-up throughout the entire pregnancy period; women with any serious medical condition preventing them from exercising safely **Number of participants:** experimental 80, control 80	Light-intensity resistance exercise training performed during the second and third trimesters The training intensity was carefully and individually controlled and was kept to light to moderate with relatively low cardiovascular stress (i.e. heart rate 80% of age-predicted maximum heart rate value, calculated as 220 minus age) Three sessions per week for about 26 weeks (originally planned an average of 80 training sessions for each participant in the event of no preterm delivery) Each session consisted of 35–40 minutes of exercise divided into a low-intensity (60% of maximal heart rate) warm-up period (8 minutes), followed by toning and very light resistance exercises (20 minutes) and finishing with a low-intensity cool-down (8 minutes) period The core portion consisted of toning and joint mobilisation exercises involving major muscle and joint groups. Exercises included shoulder shrugs and rotations, arm elevations, leg lateral elevations, pelvic tilts, and rocks. Resistance exercises included one set of 10–12 repetitions of abdominal curls, biceps curls, arm extensions, arm side lifts, shoulder elevations, seated bench press, seated lateral row, lateral leg elevations, leg circles, knee extensions, knee (hamstring) curls, and ankle flexion and extensions. The women used barbells (3 kg per exercise) or low- to medium-resistance bands (Therabands) All participants wore a heart rate monitor (Accurex Plus, Polar Electro OY, Finland) during the training sessions, so heart rate was continuously monitored. To further minimise cardiovascular stress, the researchers specifically instructed participants to avoid the Valsalva manoeuvre All resistance exercise training sessions were performed under observation and supervision in an exercise room. Exercise training facilities from the primary care medical centre in which the participants were monitored throughout the pregnancy were used	No intervention	Birthweight, preterm delivery, weight gain from prepregnancy to delivery, birth length, ponderal index, head circumference, Apgar score at 1 minute, Apgar score at 5 minutes, gestational age

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
			To reduce participant drop-out and to maintain adherence to the training programme, all sessions were accompanied by music and were performed in an airy, well-lit exercise room. A qualified fitness specialist worked with groups of 10–12 women The exercise training programme started in the second trimester (weeks 12–13) and was continued until the end of pregnancy (weeks 38–39)		
Bechtel-Blackwell 2002[93] English	**Method of randomisation:** not reported **Allocation concealment:** unclear **Blinding:** patients	**Inclusion criteria:** African-American adolescent primigravidas, age 13–18 years; receiving prenatal care from an adolescent prenatal clinic **Number of participants:** experimental 30, control 30	Nutritional education intervention The nutrition assessment using CASI (computer-assisted self-interviewing) and GWDCF (Gestational Weight Data Collection Form) was administered to all participants at four separate times: on admission to the study in the first trimester, at 24–26 weeks' gestation (second trimester), at 32–34 weeks' gestation (third trimester) and 6 weeks post partum. The nutrition education intervention consisted of three 20-minute group sessions that addressed the nutritional needs specific to the women's stage of pregnancy	No intervention	Gestational weight, post-partum weight retention
Briley 2002[94] English	**Method of randomisation:** randomly assigned to either an intervention or a control group **Allocation concealment:** none reported **Blinding:** no blinding used	**Inclusion criteria:** African-American women with representative rates of low birthweight similar to those of the USA **Number of participants:** experimental 15, control 12	Prenatal nutrition intervention: counselling The intervention protocol was adapted from Widga and Lewis[152] Included a minimum of six individualised in-home nutrition assessment and counselling visits. Visits were scheduled weekly for the first 4 weeks and then monthly for two more visits	No intervention	Preterm birth, weight gain, birthweight

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Bung 1991[125] English	**Method of randomisation:** not reported **Allocation concealment:** not reported **Blinding:** no blinding used	Women with gestational diabetes diagnosed by 3-hour glucose tolerance test **Inclusion criteria:** persistent fasting plasma glucose > 5.88 mmol but < 7.22 mmol, which would then require insulin by standard clinical protocol; up to 33 weeks gestational age (to allow minimum exercise training programme of 4 weeks) **Exclusion criteria:** other medical or obstetric complications of pregnancy; patients at risk for premature labour **Number of participants:** experimental 21, control 20	Physical activity and diet (30 kcal/kg diet) (EXE – EXercise) At enrolment and then every 4 weeks subjects in the EXE study underwent a symptom-limited VO_{2max} test on a bicycle ergometer. The result of this test determined a standardised exercise prescription for all subjects at 50% of VO_{2max} and reflected in heart rates identified at this workload. This exercise routine assured a comparable exercise prescription for all subjects All EXE subjects were instructed to conduct a non-sedentary lifestyle and return to the exercise laboratory three times a week to exercise under medical supervision. In the laboratory, the subjects exercised on a recumbent bicycle at 50% of their last determined maximum aerobic capacity. The total duration of the exercise was 45 minutes, divided into three periods of 15 minutes, interspersed with two 5-minute rest periods to facilitate fetal monitoring. This exercise routine was judged to be moderate and to generate an approximate energy use 5–7.5 times the resting metabolic rate Each exercise session was preceded by a 10-minute rest-monitoring period. Before and immediately after the exercise sessions, the subjects' plasma glucose concentrations and blood pressures were obtained and recorded. Throughout the exercise sessions maternal heart rate and uterine activity were continuously monitored	Insulin and diet (30 kcal/kg diet)	Spontaneous vaginal delivery, vacuum or forceps delivery, caesarean section, macrosomia, neonatal hypoglycaemia, premature labour, gestational age at delivery, birthweight, birth length

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Clapp 1997[95] English	**Method of randomisation:** not reported **Allocation concealment:** not reported **Blinding:** no blinding used	12 healthy women, physically active [training regime throughout pregnancy – supervised exercise consisting of 20 minutes of weight-bearing exercise three times a week at an intensity equal to 55% of each individual's maximum capacity (VO_{2max})] **Number of participants:** experimental 6, control 6	Aboriginal carbohydrate diet, diet containing carbohydrates derived from low-glycaemic sources Diet containing carbohydrates derived from low-glycaemic sources included carbohydrate products made from unprocessed wholegrain, fruits, beans, vegetables and many dairy products. The so-called 'aboriginal'-type carbohydrate diet included most dense wholegrain and multigrain breads, bran cereals, pastas, fresh fruits and vegetables, yogurt, ice cream and nuts. Both diets were designed to contain 17–19% protein, 20–25% fat and 55–60% carbohydrate. Total caloric content was based on fat-free mass and weight stability in the non-pregnant state (35–45 kcal/kg lean body mass/day). During pregnancy all women were allowed to increase caloric intake according to appetite with advancing gestation Dietary compliance was assessed by 24-hour dietary recalls obtained at random times twice each week. Caloric intake, diet composition, the glycaemic index of the carbohydrate portion of the diet and the overall dietary glycaemic index were calculated using a standardised approach	**Cafeteria carbohydrate diet:** isocaloric diet containing similar quantities of protein, fat and carbohydrate whose carbohydrates were derived from high-glycaemic sources Included carbohydrate products that came from highly processed grains, root vegetables and simple sugars. Included many highly refined breads, potatoes, instant rice, most breakfast cereals, deserts and snack-type foods (so-called 'cafeteria' type carbohydrate)	Birthweight, length, head circumference, abdominal circumference, body fat (%), fat mass, lean body mass, weight gain from 8 weeks to delivery, skinfold thickness at five sites
Clapp 2000[107] English	**Method of randomisation:** randomly assigned by envelope draw to a no-exercise control group or an exercise group **Allocation concealment:** not reported **Blinding:** no blinding used	Low-risk pregnant women **Inclusion criteria:** non-substance abusing; viable singleton pregnancy **Number of participants:** experimental 25, control 25	**Physical activity:** one of three forms of weight-bearing exercise (treadmill, step aerobics or stair-stepper) Exercise carried out for 20 minutes three to five times each week for the remainder of pregnancy at an intensity between 55% and 60% of the preconception maximum aerobic capacity. No attempt was made to assess the physical activity associated with everyday life or to challenge the veracity of the women about additional unmonitored recreational physical activity Exercise sessions were monitored and exercise intensity was checked every 2 weeks by means of respiratory calorimetry	No intervention	Birthweight, crown–heel length, ponderal index, head circumference, head–abdomen ratio, percentage body fat, fat mass, lean body mass, weight gain from 8 weeks to delivery, gestational age at delivery

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Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Clapp 2002[108] English	**Method of randomisation:** randomly assigned by envelope draw **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** healthy; regularly exercising (three or more times each week); non-substance abusing; viable singleton pregnancy **Number of participants:** overall randomised 80; completed treatment: Lo-Hi group 26, Mod-Mod group 24, Hi-Lo group 25	**Physical activity:** weight-bearing (treadmill, step aerobics or stair-stepper) exercise regimens, each of which was conducted at a standard intensity (oxygen consumption, 55–60% of prepregnancy VO_{2max}) This design provided between-group variation in weekly exercise volume in both early and late pregnancy that was quantitated with the use of the duration–intensity index (the product of exercise intensity and exercise time) in both early and late pregnancy The three regimens were: (1) 20 minutes 5 days a week through week 20, gradually increasing to 60 minutes 5 days a week by week 24 and maintaining that regimen until delivery (Lo-Hi); (2) 40 minutes 5 days a week from week 8 until delivery (Mod-Mod); (3) 60 minutes 5 days a week through week 20, gradually decreasing to 20 minutes 5 days a week by week 24 and maintaining that regimen until delivery (Hi-Lo) Women in the Lo-Hi group exercised for 1100 units/week in early pregnancy, increasing to 3300 units/week in late pregnancy; the women in the Mod-Mod group exercised for 2200 units/week throughout; and the women in the Hi-Lo group exercised for 3300 units/week in early pregnancy, decreasing to 1100 units/week in late pregnancy. Exercise sessions were monitored, and exercise intensity was checked every 2 weeks with the use of respiratory calorimetry	Women with gradually decreasing exercise by 24 weeks until delivery	Weight gain from 8 weeks to delivery, fat retention, gestational age at delivery, birthweight, crown–heel length, ponderal index, head circumference, head/abdomen ratio, body fat, fat mass, lean body mass

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Crowther 2005[96]	**Method of randomisation:** stratification was according to centre and singleton or twin gestation. Randomisation was performed centrally with the use of numbers generated by computer with variable block sizes of 6, 8 and 10 **Allocation concealment:** not reported **Blinding:** patients and investigators/clinicians	**Inclusion criteria:** singleton or twin pregnancy; between 16 and 30 weeks' gestation; attended antenatal clinics at the collaborating hospitals; had one or more risk factors for GDM on selective screening or a positive 50 g oral glucose challenge test [glucose level 1 hour after glucose challenge at least 7.8 mmol/l (140 mg/dl)]; had a 75 g oral glucose tolerance test at 24–34 weeks' gestation in which the venous plasma glucose level was < 7.8 mmol /l after an overnight fast and was 7.8–11.0 mmol/l (198 mg/dl) at 2 hours **Exclusion criteria:** previously treated GDM or active chronic systemic disease (except essential hypertension); severe glucose impairment **Number of participants:** experimental 490, control 510	**Diet:** dietary advice. The care of the women in the intervention group replicated clinical care in which universal screening and treatment for gestational diabetes are available Interventions included individualised dietary advice from a qualified dietitian, which took into consideration a woman's prepregnancy weight, activity level, dietary intake and weight gain; instructions on how to self-monitor glucose levels, which the woman was then asked to do four times daily until the levels had been in the recommended range for 2 weeks [fasting glucose levels of at least 3.5 mmol/l (63 mg/dl) and no more than 5.5 mmol/l (99 mg/dl), preprandial levels of no more than 5.5 mmol/l, and levels 2 hours postprandially that were no more than 7.0 mmol/l (126 mg/dl)], followed by daily monitoring at rotating times during the day; and insulin therapy, with the dose adjusted on the basis of glucose levels if there were two capillary-blood glucose results during the 2-week period in which the fasting level was at least 5.5 mmol/l or the postprandial level was at least 7.0 mmol/l at ≤ 35 weeks' gestation or at least 8.0 mmol/l (144 mg/dl) at > 35 weeks' gestation, or if there was one capillary-blood glucose result during the 2-week period of at least 9.0 mmol/l (162 mg/dl)	No intervention (the care of the women in the routine care group replicated clinical care in which screening for gestational diabetes is not available)	Perinatal complications (stillbirth, neonatal death, shoulder dystocia, bone fracture, nerve palsy, admission to neonatal nursery, jaundice requiring phototherapy), induction of labour, caesarean delivery, neonatal convulsions, respiratory distress syndrome, LGA infants, macrosomia, SGA infants, 5-minute Apgar score < 7, hypoglycaemia, antenatal admission, antenatal pre-eclampsia, any perineal trauma, post-partum haemorrhage (≥ 600 ml), puerperal pyrexia (≥ 38°C), EPDS (Edinburgh Postnatal Depression Scale) score > 12, birthweight, weight gain (from first prenatal visit to last visit), gestational age at birth, length of postnatal stay, quality of life during pregnancy [SF-36 (Short Form questionnaire-36 items) (questionnaire: emotional role, mental health, overall physical component, overall mental component, health-state utility, anxiety)]

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Erkkola 1976[109] English	**Method of randomisation:** 'randomly' divided into the training group and the control group **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** healthy primigravidae, aged 20–26 years; regular menstruation **Exclusion criteria:** miscarriage, threatened miscarriage, labour before 38th week of gestation, legal abortion **Number of participants:** experimental 38, control 38	Physical activity Training group received both written and oral instructions for training. They were instructed to perform strenuous exercise for 1 hour a day three times a week throughout pregnancy. All subjects exceeded 60 hours in total of training; over half performed more than 80 hours of training. The women themselves controlled the intensity of the training by measuring their pulse, which was supposed to be 140 beats/minute. During first and second trimesters all types of exercise were recommended but during the third trimester exercises with any bumping and compressing effects on the uterus were disallowed **Types of exercise:** walking, running, climbing stairs, cycling, swimming, gymnastics, skiing, training school, ball playing, rowing	No intervention	Weight change from week 26 to week 38 of pregnancy
Garshasbi 2005[111] English	**Method of randomisation:** not reported **Allocation concealment:** sealed envelopes; not clear if they were opaque and numbered **Blinding:** outcome assessors	**Inclusion criteria:** healthy primigravidae; between 20 and 28 years; between 17 and 22 weeks of gestation; housewives; high school educated **Exclusion criteria:** any absolute and relative contraindications to aerobic exercise during pregnancy according to 2002 ACOG guidelines; history of exercise before pregnancy; history of orthopaedic disease or surgery **Number of participants:** experimental 161, control 105	Physical activity: exercise programme during second half of pregnancy This programme was designed to strengthen the abdominal muscles and hamstrings muscles and increase traction of the iliopsoas and paravertebral muscles. The exercise programme included 15 movements in 60 minutes: 5 minutes of slow walking, 5 minutes of extension movements and 10 minutes of general warming up, 15 minutes of anaerobic exercise, 20 minutes of specific exercise and 5 minutes return to the first position. The exercises were recommended by the Tarbiat Modares Faculty of Sport and tested for pregnant women by physiotherapists. Women exercised three times a week, supervised by a midwife. The intensity of the exercise was controlled by maternal pulse rate. If the pulse rate exceeded 140 beats/minute the exercise was stopped	No intervention	Experience of any kind of low back pain, weight gain from prepregnancy to 38 weeks, pregnancy length, weight of the neonate
Gomez-Tabarez 1994[97] Spanish/ English (abstract)	**Method of randomisation:** not reported **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** negative for glucose tolerance test in 28th week of gestation; obesity: weight at least 20% above ideal weight **Exclusion criteria:** abnormities in glucose level; pre-eclampsia; gestation-induced hypertension **Number of participants:** experimental 30, control 30	**Diet:** diet for gestational diabetes; 30 kcal/kg ideal weight: 50% carbohydrates, 30% fat, 20% proteins. The total energy capacity could not be <1600 kcal and >2200 kcal	No intervention	Macrosomia, caesarean section because of LGA infant, Apgar score ≥ 7 at 5 minutes

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Guelinckx 2010[126] English	**Method of randomisation:** patients randomly assigned by using block randomisation **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** obese (BMI > 29.0 kg/m^2 according to IOM criteria); white women consecutively attending the prenatal clinic before 15 weeks of gestation **Exclusion criteria:** pre-existing diabetes or developing GDM; multiple pregnancy; recruitment after 15 weeks of gestation; premature labour (delivery before 37 weeks of gestation); primary need for nutritional advice because of a metabolic disorder, kidney problems, Crohn's disease, allergic conditions; inadequate knowledge of the Dutch language **Number of participants:** experimental (active) 65, experimental (passive) 65, control 65	**Lifestyle intervention based on a brochure or on active education:** passive group given a brochure during the first prenatal consultation; active group received the same brochure and actively counselled by a trained nutritionist in three group sessions. A maximum of five women were brought together in these 1-hour sessions, which were scheduled at 15, 20 and 32 weeks of pregnancy The sessions provided subjects with recommendations on a balanced, healthy diet, based on the official National Dietary Recommendations (9–11% of the energy should come from proteins, 30–35% from fat and 50–55% from carbohydrates). The dietary intervention aimed to limit the intake of energy-dense foods (e.g. fast food and sweets) by substituting them with healthier alternatives (e.g. fruit), increasing consumption of low-fat dairy products and wholewheat grains and reducing consumption of saturated fatty acids. Moreover, more general topics such as energy balance, body composition, food labels and how to increase physical activity were discussed. Techniques of behavioural modification were used to give the women insight into controlling periods of emotional eating, preventing binge eating sessions, etc. Brochure was specifically designed for the study and provided advice on nutrition and physical activity and tips to limit pregnancy-related weight gain Energy intake was never restricted in any group; however, by reducing consumption of energy-dense foods, the intervention indirectly aimed to reduce total energy intake. In case of weight gain above IOM recommendations, patients were advised to limit the intake of energy-dense foods Nutritional data were obtained from 7-day dietary records A physical activity score was calculated for each trimester of the pregnancy using the Baecke questionnaire	No intervention	Pregnancy-induced hypertension, gestational weight gain in accordance with IOM, gestational weight gain > 11.2 kg, weight gain from prepregnancy to 38 weeks, chronic hypertension, pre-eclampsia, induction of labour, caesarean section, birthweight > 4000 g, total physical activity score, gestational weight gain, gestational age, birthweight, infant length
Haakstad 2009[112] English (abstract)	**Method of randomisation:** not reported **Allocation concealment:** not reported **Blinding:** not reported	**Inclusion criteria:** sedentary, primiparous women; mean age 30.7 (± 4.0) years **Number of participants:** experimental 52, control 53	**Physical activity:** 12-week aerobic dance exercise programme during pregnancy The exercise programme followed the ACOG exercise prescription and consisted of supervised aerobic dance and strength training for 60 minutes, performed at least twice a week for a minimum of 12 weeks	No intervention	Exceeding IOM recommendations, weight gain

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Hopkins 2010[113] English	**Method of randomisation:** not reported **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** healthy nulliparous women; between 20 and 40 years of age; singleton pregnancy; <20 weeks of gestation **Exclusion criteria:** alcohol consumption or tobacco use at recruitment; a personal or family history of type 2 diabetes mellitus; development of any medical condition for which participation in an exercise programme was contraindicated by ACOG (e.g. pre-eclampsia, fetal growth restriction, preterm birth) **Number of participants:** experimental 49, control 49	**Physical activity:** aerobic exercise training in the second half of pregnancy The aerobic exercise programme was home based, using stationary cycling, and was individually prescribed for a maximum of five sessions of 40 minutes a week. Exercise programmes aimed to achieve a moderate exercise intensity of approximately 65% of predicted aerobic capacity (VO_{2max}) The study protocol recommended that regular exercise was maintained until at least 36 weeks of gestation. After this time participants were encouraged to maintain as close to their prescribed exercise programme as possible until delivery (subject to capacity). During a fortnightly supervised exercise session, maternal heart rate and blood pressure responses were monitored, and exercise prescription was updated to maintain the prescribed exercise intensity. Compliance with the exercise programme was assessed by self-reported exercise diaries and downloadable heart rate monitors (Polar S625, Polar, Kempele, Finland). The required workload was estimated using linear regression of oxygen uptake and workload obtained from aerobic fitness testing, with standard equations used to calculate energy expenditure for all exercise sessions. Weekly energy expenditure, exercise duration (minutes) and exercise intensity (in metabolic equivalents) were averaged for each phase of the exercise programme: familiarisation (20–27 weeks), maintenance (28–35 weeks) and subject to capacity (36–40 weeks). Compliance was reported as the percentage of prescribed weekly exercise duration completed	No intervention	Body weight at baseline, 19 weeks and 35 weeks, BMI, gestational age, crown–heel length, head circumference, neonatal BMI, ponderal index, birthweight

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Hui 2006[127] English	**Method of randomisation:** not reported **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** < 26 weeks of gestation; no pre-existing diabetes **Exclusion criteria:** medical, obstetric, skeletal or muscular disorders that could contraindicate physical exercise during pregnancy **Number of participants:** overall 52; completed treatment: experimental 24, control 21	**Lifestyle, diet and physical activity:** community-based exercise/dietary intervention programme; group exercise sessions and home-based exercise Participants in the AI (additional information) group were instructed in group exercise sessions and home-based exercises. Recommended activities included walking, swimming, mild aerobics, stretching and strength exercises (e.g. lifting a 500-g food can with each hand).Weekly group sessions were held in an air-conditioned gymnasium in a community centre in the urban core provided by the government of the city of Winnipeg. Floor aerobics, stretching and strength exercises in group sessions (~ 45 minutes/session) were led by professional trainers. Student assistants taught participants to correctly use a pedometer, self-monitor their heart rate and record daily physical activities in a diary before or after the sessions. Exercise three to five times a week for 30–45 minutes per session was recommended for participants in the AI group. Video exercise instruction was produced in both VHS and DVD formats and provided to participants to assist with home-based exercise. Information about daily physical activity, including a self-recorded activity diary, were collected and analysed by student research assistants Dieticians provided a personalised plan for participants, including recommended changes in food choice, frequency, portion size and pattern of intake, if required (after assessment of normal 1-week food intake)	**No intervention (standard care, SC):** physical activity was recommended for participants in the SC group, but they were not instructed in the group exercise sessions or home-based exercises. An information package of materials from Health Canada was provided containing dietary recommendations for a healthy pregnancy	Excessive weight gain, GDM, need for birthweight-related procedures, macrosomia, weight gain from 26 weeks to delivery, weight of newborn, pregnancy duration, physical activity level

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Jackson 2010[17] English	**Method of randomisation:** computer-generated randomisation **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** English-speaking women; ≥ 18 years; < 26 weeks of gestation **Number of participants:** experimental 158, control 163	**Lifestyle:** Video Doctor teaching and counselling session about nutrition, exercise and weight gain Video Doctor is a computer program delivered on laptop computers in the clinic setting. It conducts in-depth behavioural risk assessments, delivers tailored counselling messages and produces printed output for both the patient and the clinician. An actor-portrayed Video Doctor appears and offers education on exercise, nutrition and weight gain based on principles of motivational interviewing. The Video Doctor engages subjects in a confidential, 'face-to-face' discussion in which the Video Doctor actor expresses reflexive understanding of the subject's concerns, shows compassion for the subject and provides non-judgemental counselling. The Video Doctor simulates an ideal conversation with a health-care provider and has been highly acceptable to diverse samples of patients. Using a library of digital video clips, extensive branching logic and participant input the computer programme matches counselling video clips to the participant's BMI, eating and exercise habits, and readiness to change. At the conclusion of each session the programme prints a cueing sheet for the clinician that offers a summary of the patient's risk profile and suggests counselling statements. an educational worksheet that contains information presented by the Video Doctor and includes questions for self-reflection is printed for the patient to keep. In summary, the intervention consists of three parts: Video Doctor counselling session, cueing sheet for the clinician and educational worksheet for the patient The intervention group received dietary counselling focused on increasing intake of fruits and vegetables and whole grains, increasing consumption of healthful versus unhealthful fats and decreasing consumption of sugary foods. The Video Doctor emphasised dietary and exercise behaviour changes over weight gain. The Video Doctor portion required 10–15 minutes to complete. The participant then proceeded to her prenatal care appointment and returned briefly to the research assistant to report whether nutrition, exercise or weight had been discussed and to obtain the computer-generated educational worksheet specific to the patient's risk profile	No intervention	Weight gain from before 26 weeks to delivery

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
			Both intervention and control participants were invited back for a follow-up assessment at least 4 weeks after the baseline session consisting of the same diet and exercise questions. Intervention participants received a brief 'booster' Video Doctor counselling session after the follow-up questionnaire had been completed, including feedback reflecting changes made since baseline and an updated cueing sheet and educational worksheet		
Jeffries 2009[128] English	**Method of randomisation:** randomisation sequence obtained using a computer random number generator **Allocation concealment:** number cards allocating women to either the intervention or control group were placed in opaque, sequentially numbered envelopes **Blinding:** patients	**Inclusion criteria:** women from a tertiary obstetric hospital in Melbourne, Australia **Exclusion criteria:** >14 weeks' gestation at first appointment; non-English speaking; <18 or >45 years of age; multiple pregnancy; type 1 or 2 diabetes mellitus **Number of participants:** experimental 148, control 138	**Advisory:** women advised of their optimal gestational weight gain Women allocated to the intervention group were given personalised weight measurement card, advised of their optimal gestational weight gain (based on their BMI at the time of recruitment and the IOM guidelines) and instructed to record their weight at 16, 20, 24, 28, 30, 32 and 34 weeks' gestation Weight measurements during pregnancy were carried out on either the participants' own scales at home or the scales at the hospital, according to patient preference The control group was weighed at recruitment and at 36 weeks' gestation, but was not given instructions about regular weight measurement	No intervention	Gaining more weight than in IOM guidelines, birthweight <10th percentile, birthweight >90th percentile, preterm delivery, instrumental delivery, caesarean delivery, pre-eclampsia, pregnancy-induced hypertension, GDM, Apgar score <7 at 5 minutes, hypoglycaemia, shoulder dystocia, weeks' gestation at delivery, birthweight, weight gain per week, total weight gain from 11 weeks to delivery

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Khaledan 2010[114] Persian/English	**Method of randomisation:** not reported **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** single pregnancy; intact amniotic membranes **Exclusion criteria:** any contraindications for exercise, heart disease associated with significant haemodynamic changes, chronic pulmonary disease, cervical insufficiency or correction of cervical insufficiency; multiple pregnancy; permanent vaginal bleeding in second and third trimester of pregnancy; placenta praevia after 26 weeks of pregnancy; risk of preterm delivery in the current pregnancy; rupture of fetal membranes; presence of hypertension during pregnancy; severe anaemia; unchecked arrhythmia in the mother; chronic inflammation of the airways; type 1 diabetes mellitus with poor control; extreme morbid obesity; very low maternal weight; history of completely sedentary lifestyle; fetal growth restriction in current pregnancy; skeletal and structural limitations; seizure disorders; uncontrolled hyperthyroidism; heavy smoking **Number of participants:** experimental 20, control 24	**Physical activity:** specific aerobic exercise Three sessions of 30–45 minutes a week for 8 weeks. The first 15 minutes of stretching was carried out to make muscles and joints soft and flexible. The aerobic stage rally was performed to continue with the rhythm so that the person takes a walk so slowly in a second leg on the ground. This step lasted 5 minutes in the first session and then in each session 1 minute was added to the time and in eighteenth session the time was reached to 15 minutes; it then remained constant for the rest of the sessions. The intensity of exercise was based on 60% of the maximal heart rate, calculated by 220 – age × 60/100 All participants received diet information based on food pyramid guidelines recommended by the American Agricultural Department plus iron and folic acid tablets	No intervention	Caesarean section, failure of labour, mother's weight after 2 months of receiving the intervention from 28 to 36 weeks of pregnancy, neonatal weight, gestational age at delivery
Khoury 2005[98] English	**Method of randomisation:** the randomisation list was generated from a table of random numbers drawn up by one of the investigators (who had no contact with the pregnant women) **Allocation concealment:** sealed, consecutively numbered opaque envelopes **Blinding:** investigators/ clinicians and outcome assessors	**Inclusion criteria:** non-smoking (previous smokers had to have quit ≥ 5 years before inclusion); white; single healthy fetus; age 21–38 years; BMI of 19–32 kg/m^2; no previous pregnancy complications; first, second or third pregnancy; not vegetarian or following a Mediterranean-type diet or immigrants to Norway from non-Western countries **Exclusion criteria:** high-risk pregnancy caused by diabetes mellitus, endocrine disease, chronic hypertension, drug abuse, history of thromboembolic disease or significant gastrointestinal, cardiac, pulmonary or haematological disease; women with complications during a previous pregnancy including neonatal death, stillbirth or preterm delivery, or with a history of habitual abortion (more than three previous spontaneous abortions); women who experienced ongoing hyperemesis gravidarum or bleeding after gestational week 12 in the current pregnancy **Number of participants:** experimental 141, control 149	**Diet/dietary advice:** cholesterol-lowering diet from gestational week 17–20 to birth	**No intervention:** control group was asked to consume their usual diet based on Norwegian foodstuffs and not to introduce more oils or low-fat meat and dairy products than usual; energy intake aimed at a weight gain of 8–14 kg, as in the intervention group	Preterm delivery, preterm stillbirth, intrauterine growth restriction, hypertensive complications, fetal distress, pre-eclampsia, birthweight, gestational age at delivery

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Kulpa 1987[129] English	**Method of randomisation:** not reported **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** age 18–34 years; non-smoker; ≤ 15% of their ideal body weight; ≥ 10 metabolic equivalents of 3.5 ml/kg/minute of oxygen consumption performance on the treadmill; no known medical problems; no high-risk obstetric complications according to criteria of *Williams Obstetrics*; interest in recreational sports **Exclusion criteria:** spontaneous aborters; non-complying subjects; dropouts **Number of participants:** overall 141; completed treatment: experimental 38, control 47	Exercise (no particular aerobic exercise) and nutritional counselling	No intervention	Premature rupture of membranes, post-dates pregnancy, chorioamnionitis, meconium-stained amniotic fluid, oxytocin induction or augmentation of labour, use of forceps, uterine atony, total weight gain from prepregnancy to delivery
Landon 2009[99] English	**Method of randomisation:** women were randomly assigned by the co-ordinating centre with the use of the simple urn method, stratified by clinical centre **Allocation concealment:** not reported. **Blinding:** no blinding used	**Inclusion criteria:** between 24 weeks 0 days and 30 weeks 6 days of gestation; blood glucose concentration between 135 and 200 mg/dl (between 7.5 and 11.1 mmol/l) 1 hour after a 50 g glucose loading test; mild GDM defined as a fasting glucose level of < 95 mg/dl (5.3 mmol/l) and two or three timed glucose measurements that exceeded established thresholds: 1-hour, 180 mg/dl (10.0 mmol/l); 2-hour, 155 mg/dl (8.6 mmol/l); and 3-hour, 140 mg/dl (7.8 mmol/l) **Exclusion criteria:** pre-existing diabetes mellitus; fasting glucose level of ≥ 95 mg/dl on the diagnostic oral glucose tolerance test; abnormal result on a glucose screening test before 24 weeks of gestation; previous GDM; history of stillbirth; multifetal gestation; asthma or chronic hypertension; taking corticosteroids; known fetal anomaly; if imminent or preterm delivery was likely because of maternal disease or fetal condition **Number of participants:** experimental 485, control 473	**Diet:** formal nutritional counselling and diet therapy along with insulin if required	No intervention	Hypoglycaemia, hyperbilirubinaemia, birth trauma, birthweight > 4000 g, LGA infants, preterm delivery, SGA infants, admission to NICU, intravenous glucose treatment, respiratory distress syndrome, induction of labour, caesarean delivery, shoulder dystocia, pre-eclampsia, gestational age at birth, birthweight (g), fat mass (g), BMI at delivery, weight gain (kg) from 29 weeks to delivery

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Lee 1996[115] English	**Method of randomisation:** random number table **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** nulliparous; singleton pregnancy; booked at St Thomas' Hospital, London, UK **Exclusion criteria:** pregnancy exclusion factors: diabetes, weight of <50 kg or >90 kg, history of more than one spontaneous abortion, spinal or leg injuries, cervical suture in situ, use of drugs of addiction (including cigarettes but excluding alcohol in moderation); exclusion factors developing during pregnancy: insulin-dependent GDM, abruptio placentae, pregnancy-included hypertension, anaemia of <9 g/dl of haemoglobin, discovery of multiple pregnancy, threatened abortion, placenta praevia, intrauterine growth retardation, preterm labour, breech presentation at 40 weeks; smoking **Number of participants:** experimental 182, control 188	**Physical activity:** planned programme of aerobic exercise for 1 hour three times a week Exercises were designed to allow women to perform at moderate intensity (about 60–70% of age-related maximum heart rate). Classes were run by aerobic teachers trained in exercise during pregnancy. Resting and exercise pulse rates were recorded manually and with electronic pulse watches Local venues, travel expenses and exercise shoes were provided	No intervention	Caesarean section, vaginal delivery, postnatal incontinence, postnatal physical pain and discomfort, perceived positive physical outcome related to exercise, requests for postnatal exercise classes, perceived positive social outcome related to exercise, requests for maternity services, miscellaneous comments
Marquez-Sterling 2000[116] English	**Method of randomisation:** not reported **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** completed a medical questionnaire; provided a sonogram of the fetus; classified as low risk by physician; sedentary; not exercised on a regular basis for at least 1 year before conception **Number of participants:** experimental 10, control 10	**Physical activity:** aggressive exercise programme The training programme consisted of a series of 1-hour sessions held three times a week for 15 weeks. Subjects were taught to use their heart rate monitors so that they could adhere to their target heart rates during each training session. Each session started with a 5-minute warm-up on the stationary bicycle ergonometer or treadmill after which subjects were introduced to a combination of rowing, stationary cycling and walk-jogging as part of the aerobic portion of their training After the acclimation period a rhythmic calisthenics class, which was a modification of the Fitness Canada programme, and a step class were added to the aerobic workout. After 6 weeks the StairMaster was included as part of the aerobic workout and alternated with other equipment. On brisk nights the aerobic programme was modified and brisk walks were performed instead to add diversity to the aerobic programme. These were carried out using quick marching steps, long deliberate strides, leg kicks and knee kicks. All exercise sessions ended with standing and floor-supported stretches and were conducted by certified personnel	No intervention	Caesarean section, weight gain from prepregnancy to delivery, skinfold thickness, infant birthweight, Apgar score at 5 minutes

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Ney 1982[100] English	**Method of randomisation:** not reported Allocation method: not reported **Blinding:** no blinding used	**Inclusion criteria:** type 1 or type 2 diabetes mellitus **Number of participants:** experimental 11, control 9	**Diet:** high-carbohydrate, high-fibre, low-fat (HCF) diet All patients were hospitalised in the University of California San Diego School of Medicine General Clinical Research Centre at 10–30 weeks' gestation for an 8-day baseline evaluation and for metabolic studies and intensive dietary education During the initial 24-hour study each patient received her usual dose of insulin and a 2000-kcal control meal pattern with a standardised nutrient distribution, including three meals at 8:00, 12:00 and 17:00) and three between-meal snacks (at 10:00, 15:00 and 22:00)	No intervention (diet commonly prescribed for pregnancy)	Weight gain from prepregnancy to delivery, gestational age, birthweight
Ong 2009[117] English	**Method of randomisation:** not reported **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** singleton pregnancy; normal 18-week anatomy scan; no evidence of cardiovascular disease or pre-existent diabetes **Number of participants:** experimental 6, control 6	**Physical activity:** home-based supervised exercise programme consisting of three sessions a week of stationary cycling beginning at week 18 of gestation Exercise training was performed on an upright stationary cycle ergometer (Marquee Series, Healthstream) that each participant kept in her home for the duration of the intervention. Each session involved a 10-minute warm-up followed by one or two 15-minute bouts of cycling (with rest periods if necessary) at an intensity of 50–60% of maximum heart rate. As the weeks progressed the exercise intensity was increased to 60–70% of maximum heart rate and the duration was increased to 40–45 minutes. Sessions ended with a 10-minute cool-down period of easy pedalling	No intervention	Weight gain in kg from 18 to 28 weeks
Polley 2002[130] English	**Method of randomisation:** not reported **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** pregnancy before 20 weeks' gestation **Exclusion criteria:** underweight women (BMI $< 19.8\ kg/m^2$ based on self-reported weight and height at the last menstrual period); women younger than 18 years; first prenatal visit >12 weeks' gestation; high-risk pregnancy (i.e. drug abuse, chronic health problems, previous complications during pregnancy or current multiple gestation) **Number of participants:** experimental 61, control 59	**Stepped care behavioural intervention:** education and feedback about weight gain during pregnancy, stressing modest exercise and healthy, low-fat eating	No intervention	Exceeded, within or below IOM recommendations at some point during pregnancy, low birthweight (<2500 g), macrosomia, preterm delivery, caesarean delivery, pre-eclampsia, maternal hypertension, GDM, total weight gain from prepregnancy to last prenatal visit before delivery, post-partum weight loss at 8 weeks, net weight retention, birthweight, weeks' gestation at delivery

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Prevedel 2003[118] Portuguese (Brazilian)	**Method of randomisation:** women were randomly selected (model randomised) **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** primiparous or adolescents, with singleton pregnancy; absence of medical or obstetric disease; gestational age 16–20 weeks **Exclusion criteria:** more than three absences a month at hydrotherapy sessions were considered as withdrawal; prenatal care and childbirth out of service; development of medical or obstetric complications **Number of participants:** experimental 29, control 31	**Physical activity:** moderate-intensity hydrotherapy programme The hydrotherapy programme was delivered by the physiotherapist in the company of the obstetrician in subgroups of up to 10 pregnant women. The programme was carried out with moderate intensity for 1 hour three times a week in a covered and heated swimming pool (between 28ºC and 32ºC). The sessions comprised five phases of aquatic exercise, taking into consideration the recommendations of ACOG: stretching, heating, resistance, localised exercises and relaxation with breathing exercises During the sessions of hydrotherapy heart rate was monitored by frequency-grip to control the intensity of the exercise	No intervention	Preterm birth, adequate weight, LGA, body weight at baseline, 16–20 weeks and close to delivery (36–40 weeks), lean mass, total fat, relative fat (%), birthweight
Rae 2000[101] English	**Method of randomisation:** women were allocated at random by draw of opaque numbered envelopes **Blinding:** patients and investigators/clinicians	GDM women only **Inclusion criteria:** gestation ≤ 35 weeks and 6 days; > 110% of ideal body weight for height (adjusted for expected pregnancy weight gain and using a BMI of 25 kg/m^2 as equal to 100% of ideal body weight); oral glucose tolerance test with fasting plasma glucose > 5.4 mmol/l and/or 2-hour plasma glucose > 7.9 mmol/l **Number of participants:** experimental 67, control 58	**Diet:** energy restriction (30% – moderate) The intervention comprised instruction in a moderately energy-restricted diabetic diet providing between 6800 and 7600 kJ (1590–1776 kcal). This represents 70% of the recommended dietary intake for pregnant women (National Health and Medical Research Council of Australia) To monitor diet compliance, 3-day food diaries were kept by participants at three time periods after recruitment, and were later analysed using System for Online Dietary Analysis (SODA version 5B, 1991, developed by Computer Models, Cottesloe, Western Australia) The decision to commence insulin therapy was made by medical staff who were blinded to the group allocation of each participant All women were seen by the research dietitian at each antenatal visit	No intervention [diabetic diet that was not energy restricted, providing approximately 8600–9500 kJ (2010–2220 kcal) a day]	Pre-eclampsia, induction of labour, vaginal delivery, assisted delivery, elective lower uterine segment caesarean section, non-elective lower uterine segment caesarean section, shoulder dystocia, infants ≥ 4000 g, infants ≥ 90th centile (birthweight), hypoglycaemia, weight change from treatment to delivery, weight lost from treatment to delivery, weight change from prepregnancy to delivery, gestation at delivery, mean birthweight, estimated birthweight ratio, skinfold thickness (neonatal)

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Santos 2005[119] English	**Method of randomisation:** randomised following a blocked sequence generated from a random number table by a statistician not participating in other aspects of the study **Allocation concealment:** numbered, opaque envelopes **Blinding:** outcome assessors	**Inclusion criteria:** healthy, non-smoking pregnant women; age ≥ 20 years; gestational age < 20 weeks; BMI between 26 and 31 kg/m^2 (corresponding to a prepregnancy BMI of 25–30 kg/m^2) **Exclusion criteria:** compliance to the run-in period protocol; hypertension; diabetes mellitus; conditions considered to contraindicate exercise such as preterm labour, an incompetent cervix, high-order multiple gestation (more than three) and uncontrolled thyroid disease **Number of participants:** experimental 46, control 46	**Physical activity:** supervised, gymnasium-style physical activity programme of aerobic exercise The intervention consisted of an unblinded programme of supervised physical exercise of 60 minutes' duration performed three times a week. Each session consisted of 5–10 minutes of warm-up, 30 minutes of heart rate-monitored aerobic activity, 10–15 minutes of exercise involving upper and lower limbs and 10 minutes of stretching and relaxation. Aerobic activities were always performed at between 50% and 60% of the maximum predicted heart rate, never exceeding 140 beats/minute. The exercises followed the recommendations concerning physical activity practice during pregnancy of the American College of Sports Medicine and ACOG. Aerobic exercises included walking, pedalling a bicycle ergometer and aerobic gymnastics. Upper extremity resistance exercises were performed with hand-held dumbbells (up to 1 kg), rods and tennis balls. For the legs, body weight resistance exercises such as squats and lunges were performed	The control group participated in once-weekly sessions that included relaxation (respiratory exercises and light stretching but no aerobic or weight-resistance exercises) and focus group discussions concerning maternity. Control participants were neither encouraged to exercise nor discouraged from exercising	Low birthweight, prematurity delivery, weight gain of mother from 18 to 30 weeks, birthweight, Apgar score
Sedaghati 2007[120] English	**Method of randomisation:** not reported **Allocation concealment:** not reported **Blinding:** no blinding used	**Inclusion criteria:** attendance at prenatal clinics in Qom province, Islamic Republic of Iran **Exclusion criteria:** any absolute and relative contraindications to aerobic exercise during pregnancy; history of exercise before pregnancy; history of orthopaedic disease or surgery; missing three sessions of the exercise programme **Number of participants:** experimental 50, control 50	**Physical exercise:** special pregnancy exercise in preventing or reducing low back pain Exercise programmes included a 15-minute warm-up and cool down plus 30 minutes cycling in the range of 55–65% of maximal heart rate with respect to age The warm-up consisted of 5 minutes of extension movements and 5 minutes slow cycling and the cool down (return to the first condition) consisted of 5 minutes of extension movements (nonsense, probably mistake in publication). The cycling exercise was defined as 30 minutes of cycling (three sessions a week at moderate intensity). The exercises were prescribed by a physical training specialist and were offered to the pregnant women after evaluation of the required criteria During the running of the whole programme supervision was carried out by a midwife	No intervention	Weight gain from 20–22 weeks to delivery, pregnancy length, low back pain

Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Thornton 2009[102] English	**Method of randomisation:** envelopes were prepared and sequentially numbered. A card indicating the assigned group was placed in the envelope and the envelope was sealed. A random number table was used to assign each consecutively numbered envelope to either the study or the control group in blocks of 10 **Allocation concealment:** numbered and sealed envelopes; not known if they were opaque **Blinding:** no blinding used	Obese women **Inclusion criteria:** pregnant with a single fetus; between 12 and 28 weeks of gestation; BMI $\geq 30\,kg/m^2$ **Exclusion criteria:** pre-existing diabetes; hypertension; chronic renal disease **Number of participants:** experimental 124, control 133	Diet intervention based on a balanced nutritional regiment The study group was placed on an 18–24 kcal/kg balanced nutritional regimen consisting of 40% carbohydrates, 30% protein and 30% fat. No patient received a diet of <2000 calories. All women in the study group were asked to record in a diary all of the foods and beverages consumed each day. Participants in both groups were encouraged to engage in 30 minutes of walking a day	No intervention	GDM, pre-eclampsia, gestational hypertension, post-partum haemorrhage, preterm delivery, labour induction, caesarean delivery, macrosomic infant, Apgar score (<7 at 5 minutes), infant birthweight, gestational age at delivery, weight gain from 20–22 weeks to delivery, weight loss difference post partum
Wolff 2008[103] English	**Method of randomisation:** computerised randomisation **Allocation concealment:** not reported **Blinding:** investigators/ clinicians	**Inclusion criteria:** non-diabetic; Caucasian; BMI $\geq 30\,kg/m^2$; early pregnancy (15 ± 3 weeks of gestation) **Exclusion criteria:** smoking; age <18 or >45 years; multiple pregnancy; medical complications known to affect fetal growth adversely; contraindication to limitation of weight gain **Number of participants:** experimental 28, control 38	Dietary consultations (healthy diet, restriction of energy intake) The intervention group received 10 consultations of 1 hour each with a trained dietitian during the pregnancy. Women were instructed to eat a healthy diet according to the official Danish dietary recommendations [fat intake: maximum 30 energy per cent (E%); protein intake: 15–20 E%; carbohydrate intake: 50–55 E%] Energy intake was restricted based on individually estimated energy requirements and estimated energetic cost of fetal growth [energy requirement = basal metabolic rate $\times$ 1.4 (physical activity level factor of $1.2 + 0.2$ added to cover energetic cost of fetal growth)]	No intervention	GDM, pregnancy-induced hypertension, pre-eclampsia, caesarean delivery, gain in body mass from 15 to 36 weeks, birthweight, infant length, head circumference, abdominal circumference

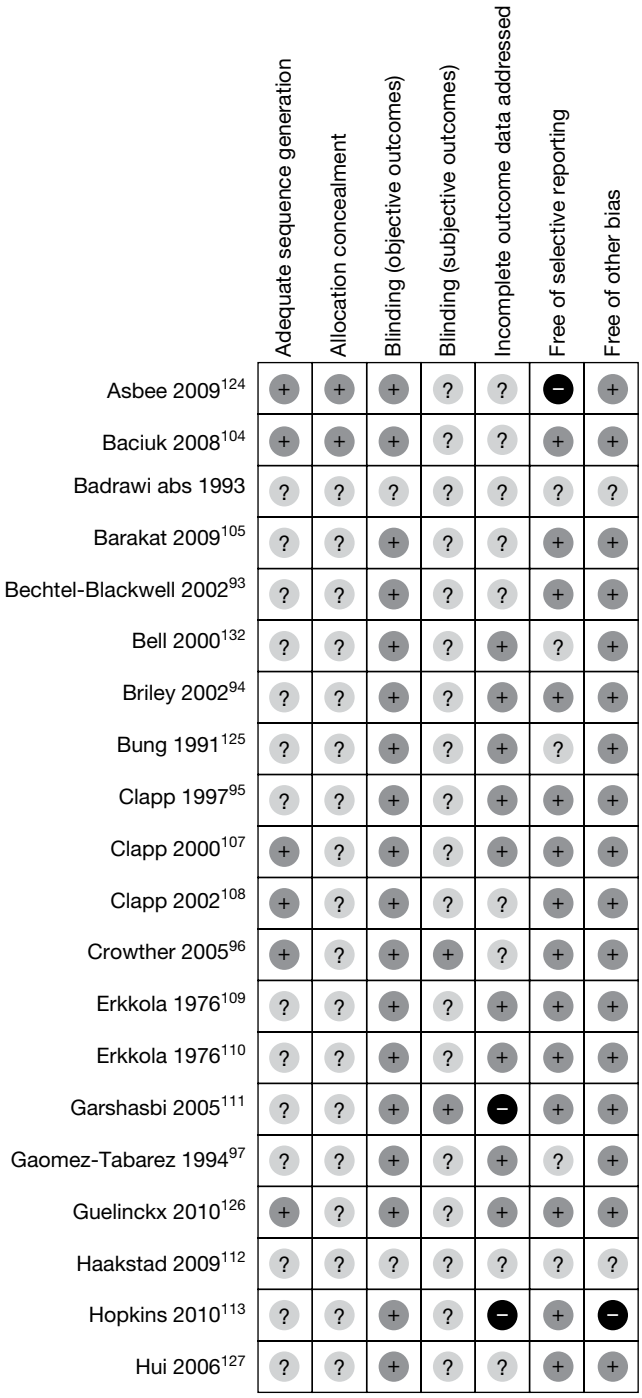
Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Yeo 2000[121] English	**Method of randomisation:** not reported **Allocation concealment:** not reported **Blinding:** not reported	**Inclusion criteria:** at least 18 years old; high risk of gestational hypertensive disorders **Exclusion criteria:** diabetes mellitus; renal disease; multiple pregnancies; extremely vigorous exercisers [more than three times a week at a level above Rating of Perceived Exertion (RPE; a widely accepted subjective measure of exercise intensity) 14 for >30 minutes per session] **Number of participants:** experimental 8, control 8	Exercise at RPE level 13 The exercise group visited the laboratory three times a week to perform 30 minutes of exercise at RPE level 13, considered a moderate level of exercise A motorised treadmill and bicycle ergometer were alternated. Exercise started with a 5-minute warm-up using the branching protocol, followed by 30 minutes steady state (RPE 13), finishing with a 10-minute cool-down	No intervention	Mean per cent body fat of mother
Yeo 2008[122] English	**Method of randomisation:** simple randomisation **Allocation concealment:** not reported **Blinding:** outcomes assessors	**Inclusion criteria:** pre-eclampsia during a previous pregnancy; lower than average cardiovascular fitness level (i.e. peak oxygen consumption ≤50th percentile); sedentary lifestyle **Exclusion criteria:** chronic hypertension; pregestational diabetes mellitus; medical or physical condition that prohibits daily regular exercise; recommendation of a primary care provider not to participate; inability to communicate reasonably with research staff (language; mental state) **Number of participants:** experimental (stretching) 41, control (walking) 38	The stretching exercise programme consisted of 40 minutes of stretching exercises five times a week without increasing the heart rate >10% of the resting heart rate. The stretch movements consisted of slow muscle movements that had neither aerobic nor muscle resistance components. Movements were selected from maternity nursing textbooks and the maternity guidebooks distributed at the data collection clinics. A videotape of the movements was developed for the study. Subjects followed the videotaped movement at each session to control the movement and the duration. Subjects wore a portable heart rate monitor to keep the heart rate within the specified range	Walking exercise was defined as 40 minutes of walking five times a week at moderate intensity. This programme was consistent with the recommendations of the Surgeon General for healthy people and ACOG for healthy pregnant women. Moderate-intensity cardiovascular exercise was defined by: (1) heart rate between 55% and 69% of maximum heart rate (HR_{max}); (2) oxygen uptake (VO_2) between 50% and 74% of peak VO_2; and (3) RPE of either 12 or 13	Pre-eclampsia, gestational hypertension, birthweight

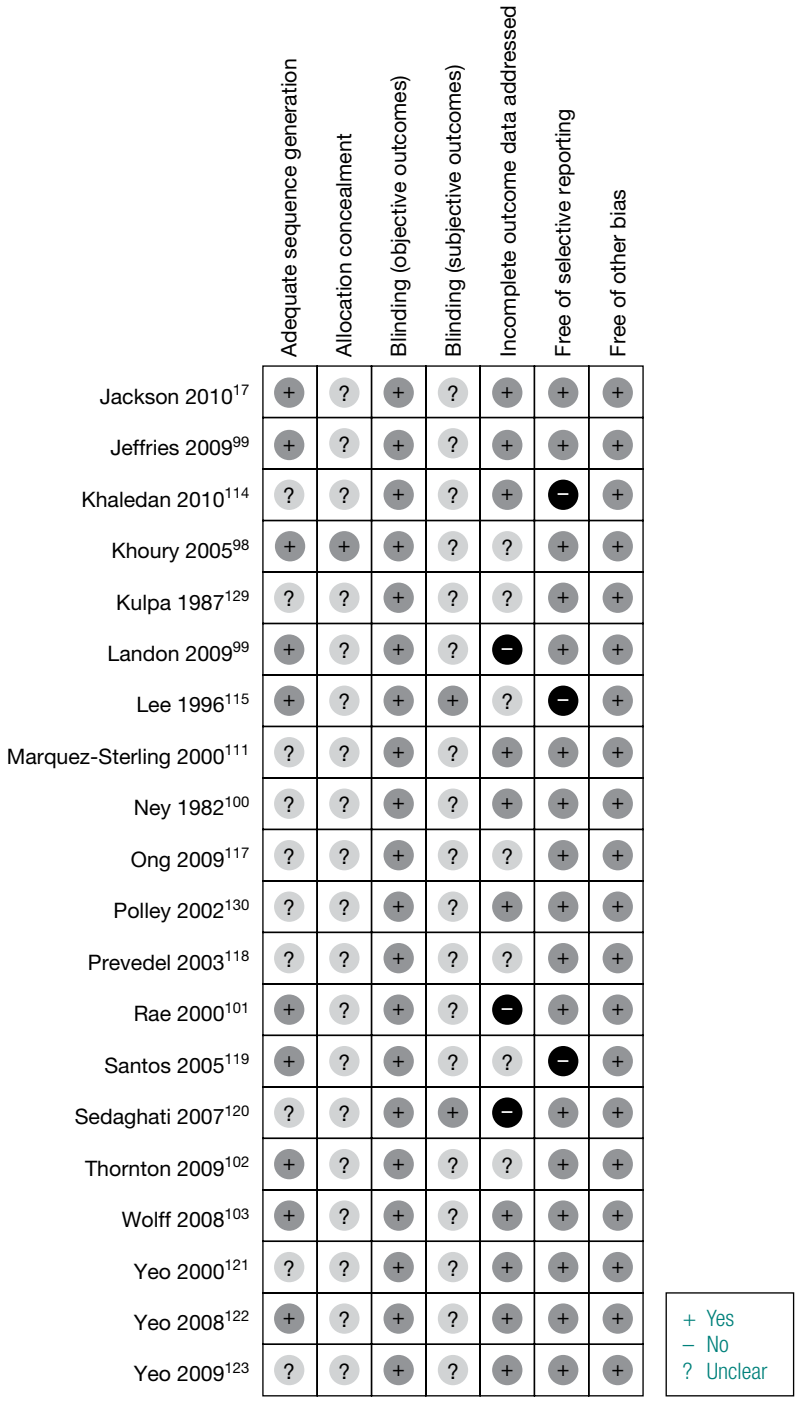
Study, year, language	Methods	Participants	Interventions	Control	Outcomes
Yeo 2009[123] English	**Method of randomisation:** women were randomised to two groups using a pre-generated allocation schedule **Allocation concealment:** sealed envelopes to withhold knowledge of future assignments from both the women and the researchers **Blinding:** no blinding used	**Inclusion criteria:** < 14 weeks' gestation; lower than average cardiovascular fitness level or peak oxygen consumption ≤ 50th percentile of women in same age group; sedentary lifestyle/estimated energy expenditure for daily physical activity during the index pregnancy of < 840 kcal/week **Exclusion criteria:** chronic hypertension; pregestational diabetes (at the time of recruitment); medical/physical condition prohibiting daily regular exercise; recommendation of primary care provider not to participate; inability to communicate (language, mental status) **Number of participants:** experimental (stretching) 60, control (walking) 64	The stretching programme consisted of slow muscle movements that had neither aerobic nor muscle resistance components. A 40-minute videotape of the stretching movements was given to each stretching participant so that she could follow movement sequences at a prespecified pace Once randomised, participants individually visited the exercise laboratory three times in the 18th week of gestation. During these visits a staff exercise specialist trained and supervised participants in their assigned exercises Stretchers were trained in stretching manoeuvres and were also taught the warning signs indicating that they should either stop or not start exercise to ensure maternal and fetal safety. Participants were instructed to exercise two more times on their own at home for the required five times a week. In the 19th week of gestation participants exercised twice at the exercise laboratory under the supervision of an exercise specialist and three times on their own at home. From then on they visited the exercise laboratory once a week for supervised exercise by a trained staff member and completed the other four exercise sessions on their own at home Participants received a weekly exercise log; they were asked to check off the date and time after each exercise session. At the end of each week they submitted the form filled out for the previous week and received a new form for the next week. Stretchers recorded the number of completed stretching sessions. The total number of sessions for each week was entered as the frequency of exercise performed	Walkers were trained to walk at the prescribed target heart rate and at RPE 12 or 13 and were taught the warning signs indicating that they should either stop or not start exercise to ensure maternal and fetal safety The walkers brought in their heart rate monitors to weekly laboratory visits and heart rate data during each exercise session were downloaded to determine the length of exercise and the proportion of exercise within the target heart rate. In order to monitor their daily physical activity during the intervention all participants wore a pedometer daily from when they woke up until bedtime	Weight gain from prepregnancy to 37 weeks

Hi-Lo, high-low; Lo-Hi, low-high; Mod-Mod, moderate.

Appendix 4

Risk of bias in randomised controlled trials included in the effectiveness review


Adequate sequence generation
Allocation concealment
Blinding (objective outcomes)
Blinding (subjective outcomes)
Incomplete outcome data addressed
Free of selective reporting
Free of other bias
Asbee 2009[124]
Baciuk 2008[104]
Badrawi abs 1993
Barakat 2009[105]
Bechtel-Blackwell 2002[93]
Bell 2000[132]
Briley 2002[94]
Bung 1991[125]
Clapp 1997[95]
Clapp 2000[107]
Clapp 2002[108]
Crowther 2005[96]
Erkkola 1976[109]
Erkkola 1976[110]
Garshasbi 2005[111]
Gaomez-Tabarez 1994[97]
Guelinckx 2010[126]
Haakstad 2009[112]
Hopkins 2010[113]
Hui 2006[127]



Appendix 5

Quality assessment of individual non-randomised studies evaluating the effectiveness of weight management interventions in pregnancy

Intervention based on a mixed approach

Study	Blinding	Incomplete outcome data	Selective outcome reporting	Selection bias and risk of confounders
Casanueva 1994[48]	Not used (–)	No loss to follow-up (++)	Unclear	Baseline differences (–)
Claesson 2008[49]	Not used (–)	No (–)	Unclear	No differences (++)
Gray-Donald 2000[54]	Not used (–)	No (–)	Yes (+)	No differences (++)
Kinnunen 2007[57]	Not used (–)	Yes (28/132 lost to follow-up, intention-to-treat analysis not performed) (+)	Unclear	Baseline differences, adjustment made in the analysis (++)

+, medium risk of bias; ++, low risk of bias; –, high risk of bias.

Intervention based mainly on dietary intervention

Study	Blinding	Incomplete outcome data	Selective outcome reporting	Selection bias and risk of confounders
Borberg 1980[45]	Not used (–)	No loss to follow-up (++)	Unclear	No differences (++)
Campbell 1975[46]	Not used (–)	No (–)	Yes (+)	No differences, patients matched (++)
Campbell 1983[47]	Not used (–)	No (–)	Yes (+)	No differences, patients matched (++)
El Hiday 1992[53]	Not used (–)	No loss to follow-up (++)	No (–)	No differences (++)
Moses 2006[58]	Not used (–)	8/62 lost to follow-up, intention-to-treat analysis performed (++)	Yes (+)	Baseline differences, adjustment made in the analysis (++)

+, medium risk of bias; ++, low risk of bias; –, high risk of bias.

Physical activity-based intervention

Study	Blinding	Incomplete outcome data	Selective outcome reporting	Selection bias and risk of confounders
Artal 2007[44]	Not used (–)	No (–)	Yes (+)	Baseline differences (–)
Clapp 1995[51]	Not used (–)	No loss to follow-up (++)	Yes (+)	Baseline differences (–)
Collings 1983[52]	Not used (–)	No (–)	Yes (+)	No differences (++)
Hall 1987[55]	Not used (–)	No loss to follow-up (++)	Yes (+)	Unclear
Kardel 1998[56]	Not used (–)	No loss to follow-up (++)	Yes (+)	Baseline differences (–)
Narendran 2005[59]	Not used (–)	No loss to follow-up (++)	Yes (+)	No differences, patients matched (++)

+, medium risk of bias; ++, low risk of bias; –, high risk of bias.

Appendix 6

Quality assessment of the observational studies evaluating the effectiveness of weight management interventions in pregnancy

Cohort studies

Study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts	Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow-up of cohorts	Overall score (max. 9)
Bell 1995[60]	+	+	–	+	–	–	+	–	++++
Bungum 2000[61]	–	+	–	–	+	–	+	–	+++
Clapp 1984[62]	+	+	+	–	++	+	+	–	+++++++
Clapp 1990[63]	+	–	+	+	–	+	+	–	+++++
Clapp 1990[64]	+	+	+	+	–	+	+	–	++++++
Cogswell 1999[65]	+	+	–	–	++	–	+	–	+++++
Conway 1999[66]	+	+	+	–	–	–	+	+	+++++
Dale 1982[67]	–	–	+	+	–	+	+	–	++++
Dempsey 2004[69]	+	+	+	+	++	+	+	+	+++++++++
de Rooij 2007[68]	+	+	–	–	+	+	–	+	+++++
Hatch 1993[70]	+	+	+	–	–	+	–	–	++++
Horns 1996[71]	+	+	+	+	–	+	+	+	+++++++
Jackson 1995[72]	+	+	–	–	–	+	+	+	+++++
Knudsen 2008[73]	+	+	–	+	++	+	+	+	++++++++
Lenders 1994[74]	+	+	+	+	+	+	+	+	++++++++
Lenders 1997[75]	+	+	+	+	+	+	+	+	++++++++
Lumey 2009[76]	+	–	–	–	++	+	+	+	++++++
Magann 2002[77]	–	+	+	+	+	–	+	+	++++++
Melzer 2010[78]	+	+	+	–	–	+	–	–	++++
Mottola 2010[79]	+	–	+	–	–	–	+	+	++++
Neugebauer 1999[80]	–	+	–	–	+	+	+	+	+++++
Olson 2004[81]	+	–	+	–	+	–	–	+	++++
Perichart 2009[82]	–	–	–	–	–	+	+	+	+++
Piravej 2001[83]	+	+	+	–	–	+	+	–	+++++
Shirazian 2010[84]	+	+	+	+	+	+	+	–	+++++++
Stein 2007[85]	+	–	–	–	++	+	+	+	++++++

Case–control studies

Study	Is case definition adequate?	Representativeness of the cases	Selection of controls	Definition of controls	Comparability of cases and controls	Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-response rate	Overall score (max. 9)
Berkowitz 1983[86]	+	+	+	–	+	–	+	+	++++++
Dempsey 2004[87]	–	+	+	+	+	–	+	–	+++++
Dye 1997[88]	+	+	+	–	+	–	+	–	+++++
Gregory 1987[89]	+	+	+	–	+	+	+	–	++++++
Oken 2006[90]	+	+	+	+	++	–	+	–	+++++++
Sorensen 2003[91]	+	–	+	+	+	+	+	–	++++++

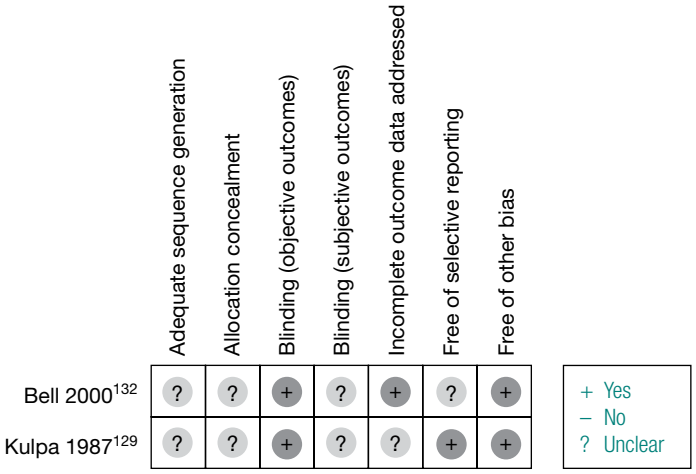
Appendix 7

Clinical characteristics of the randomised controlled trials included in the review of adverse effects

Study	Methods	No. of patients	Population	Intervention/ Comparator
Bell 2000[132]	**Randomisation:** not reported **Allocation concealment:** not reported **Blinding:** not used	61	Women already intending to exercise during pregnancy	**Intervention:** physical exercise more than five times a week **Comparator:** exercise three or less times a week
Kulpa 1987[129]	**Randomisation:** not reported **Allocation concealment:** not reported **Blinding:** not used	141	Pregnant recreational athletes aged 18–49 years	**Intervention:** exercise (no particular aerobic exercise) and nutritional counselling **Comparator:** no intervention

Appendix 8

Risk of bias summary of the randomised controlled trials included in the review of adverse effects



Appendix 9

Quality assessment of the observational studies evaluating the adverse effects of weight management interventions in pregnancy

Cohort studies

Study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts	Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow-up of cohorts	Overall score (max. 9)
Clapp 1990[63]	+	–	+	+	–	+	+	–	+++++
Clapp 1990[64]	+	+	+	+	–	+	+	–	++++++
Dale 1982[67]	–	–	+	+	–	+	+	–	++++
de Rooij 2006[134]	+	+	–	–	+	+	–	+	+++++
de Rooij 2007[68]	+	+	–	–	+	+	–	+	+++++
Hatch 1993[70]	+	+	+	–	–	+	–	–	++++
Knudsen 2008[73]	+	+	–	+	+	+	+	+	++++++++
Lenders 1994[74]	+	+	+	+	+	+	+	+	++++++++
Lenders 1997[75]	+	+	+	+	+	+	+	+	++++++++
Lumey 2009[76]	+	–	–	–	++	+	+	+	++++++
Magann 2002[77]	–	+	+	+	+	–	+	+	++++++
Neugebauer 1999[80]	–	+	–	–	+	+	+	+	+++++
Painter 2008[135]	+	+	–	–	+	–	–	+	++++
Ravelli 1976[136]	+	–	–	–	–	+	+	+	++++
Ravelli 1998[137]	+	+	–	–	+	+	–	+	+++++
Roseboom 2000[138]	+	+	–	–	+	+	+	+	++++++
Roseboom 2000[139]	+	+	–	–	+	+	–	+	+++++
Stanner 1997[141]	+	–	–	–	+	+	+	+	+++++
Stein 2007[85]	+	–	–	–	++	+	+	+	++++++

max., maximum.

Case–control studies

Study	Is case definition adequate	Representativeness of the cases	Selection of controls	Definition of controls	Comparability of cases and controls	Ascertainment of exposure	Same Method of ascertainment for cases and controls	Non-response rate	Overall score (max. 9)
Carmichael 2003[133]	+	+	+	+	+	–	+	+	+++++++
Gregory 1987[89]	+	+	+	–	+	+	+	–	++++++
Schramm 1996[140]	+	+	+	–	++	–	+	–	++++++
Vujkovic 2007[142]	+	+	+	–	+	–	+	–	+++++
Yazdy 2010[143]	+	+	+	–	+	–	+	–	+++++

max., maximum.

Appendix 10

Clinical characteristics and findings of the observational studies evaluating the adverse effects of weight management interventions in pregnancy

Outcome	Study	*N*	Intervention/exposure	*n*/*N*	Control group	*n*/N	OR or HR (95% CI)	Comments
NTD	Carmichael 2003[133]	1077	Infants/fetuses diagnosed with NTD		Infants/fetuses with no defects			Diet: different types (during first trimester of pregnancy)
	Case–control study		Diet to lose weight	29/538	Diet to lose weight	14/539	OR 2.1 (1.1 to 4.1)[a]	
			Fasting diet	17/538	Fasting diet	3/539	OR 5.8 (1.7 to 20.0)[a]	
			Other special diet	17/538	Other special diet	3/539	OR 1.0 (0.3 to 3.1)[a]	
			Eating disorder	18/538	Eating disorder	11/539	OR 1.7 (0.8 to 3.6)[a]	
			Any special diet or eating disorder	61/538	Any special diet or eating disorder	31/539	OR 2.1 (1.3 to 3.3)[a]	
			Binge eating (self-reported dieting behaviour for any time during 3 months before pregnancy or during pregnancy)	36/538	Binge eating (self-reported dieting behaviour for any time during 3 months before pregnancy or during pregnancy)	44/539	OR 0.8 (0.5 to 1.3)[a]	
NTD	Yazdy 2010[147]	1394	Infants with NTD		Infants with no major congenital anomalies			
	Case–control study		Glycemic index low < 60	522/698	Glycemic index low < 60	594/696	OR 2.0 (1.5 to 2.6)[a]	
			Glycemic index high ≥ 60	176/698	Glycemic index high ≥ 60	102/696	OR 1.5 (1.1 to 2.0)[b]	
			Glycemic load low < 205	668/698	Glycemic load low < 205	683/696	OR 2.4 (1.2 to 4.6)[a]	
			Glycemic load high ≥ 205	30/698	Glycemic load high ≥ 205	13/696	OR 1.8 (0.8 to 4.0)[b]	
		Subgroup BMI ≥ 30 kg/m^2 (100)	Glycemic index low < 60	23/36	Glycemic index low < 60	53/64	OR 2.7 (1.1 to 7.0)[a]	
			Glycemic index high ≥ 60	13/36	Glycemic index high ≥ 60	11/64	OR 2.0 (0.6 to 7.3)[b]	
			Glycemic load low < 205	32/36	Glycemic load low < 205	59/64	OR 1.5 (0.4 to 5.9)[a]	
			Glycemic load high ≥ 205	4/36	Glycemic load high ≥ 205	5/64	OR 0.9 (0.2 to 4.7)[b]	
		Subgroup BMI < 30kg/m^2 (816)	Glycemic index low < 60	138/185	Glycemic index low < 60	540/631	OR 2.0 (1.4 to 3.0)[a]	
			Glycemic index high ≥ 60	47/185	Glycemic index high ≥ 60	91/631	OR 1.7 (1.1 to 2.7)[b]	
			Glycemic load low < 205	177/185	Glycemic load low < 205	623/631	OR 3.8 (1.4 to 10.5)[a]	
			Glycemic load high ≥ 205	8/185	Glycemic load high ≥ 205	8/631	OR 3.3 (1.0 to 10.6)[b]	
Cord abnormalities	Magann 2002[77]	750	Exercise: different levels		No exercise	18/217		$p = 0.051$
	Cohort study		Light	15/222			OR 0.80 (0.39 to 1.63)[a]	
			Moderate	7/73			OR 1.17 (0.47 to 2.93)[a]	
			Heavy	9/238			OR 0.43 (0.19 to 0.99)[a]	

Outcome	Study	*N*	Intervention/exposure	*n*/*N*	Control group	*n*/N	OR or HR (95% CI)	Comments
Coronary heart disease (adult)	Roseboom 2000[138] Cohort study	736	Diet: famine		Unexposed to famine:			
			Exposed in late gestation	3/120	Conceived after	6/232	Exposed late gestation vs not exposed prenatally: OR 0.8 (0.2 to 2.8)	
			Exposed in mid-gestation	1/108	Born before	8/208	Exposed mid-gestation: OR 3.0 (0.0 to 2.2)	
			Exposed in early gestation	6/68			Exposed early: OR 3.0 (1.1 to 8.0)	
	de Rooij 2006[134] Cohort study	694	Diet: famine		Unexposed to famine:		Exposed generally vs not exposed prenatally: OR 0.79 (0.42 to 1.49)[a]	
			Exposed in late gestation	7/120	Conceived after	14/197	Exposed late: OR 0.82 (0.35 to 1.92)[a]	
			Exposed in mid-gestation	4/100	Born before	15/215	Exposed mid: OR 0.55 (0.19 to 1.60)[a]	
			Exposed in early gestation	5/62			Exposed early: OR 1.16 (0.43 to 3.11)[a]	
Metabolic syndrome (adult)	de Rooij 2007[68] Cohort study	783	Diet: famine		Unexposed to famine:		General: OR 1.2 (0.9 to 1.7)	
			Exposed in late gestation	54/141	Conceived after	64/214	Exposed late: OR 1.4 (0.9 to 2.1)	
			Exposed in mid-gestation	34/116	Born before	71/238	Exposed mid: OR not available	
			Exposed in early gestation	28/74			Exposed early: OR 1.4 (0.6 to 1.5)[a]	
	de Rooij 2006[134] Cohort study	694	Diet: famine		Unexposed to famine:		Exposed generally vs not exposed prenatally: OR 1.09 (0.78 to 1.51)[a]	Metabolic syndrome definition according to NCEP (National Cholesterol Educational Programme)
			Exposed in late gestation	40/120	Conceived after	59/197	Exposed late: OR 1.16 (0.75 to 1.79)[a]	
			Exposed in mid-gestation	28/100	Born before	65/215	Exposed mid: OR 0.90 (0.56 to 1.47)[a]	
			Exposed in early gestation	22/62			Exposed early: OR 1.28 (0.73 to 2.24)[a]	

Outcome	Study	*N*	Intervention/exposure	*n*/*N*	Control group	*n*/N	OR or HR (95% CI)	Comments
Hypertension (adult)	Lumey 2009[76] Cohort study	638	Diet: famine	224/344	Unexposed to famine (hospital control subjects)	168/294	OR 1.40 (1.02 to 1.93)[a]	$p=0.03$ Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or prior diagnosis with medication
Breast cancer	Painter 2006[135]	475	Diet: famine		Unexposed to famine:		HR (all exposed) 2.6 (0.9 to 7.7)[a]	$p<0.005$ (Cox regression)
	Cohort study		Exposed in late gestation	3/82	Conceived after	1/126	HR 2.6 (0.9 to 7.7)[b]	Adjusted for maternal cancer status
			Exposed in mid-gestation	3/77	Born before	4/144	HR 2.5 (0.8 to 7.4)[b]	Adjusted for birthweight
			Exposed in early gestation	4/46			HR 4.0 (1.1 to 14.5)[b]	Adjusted for BMI
Cleft lip or palate or both	Vujkovic 2007[142] Case–control study	381	Diet: Western vs prudent		Diet: Western vs prudent			Adjusted for periconception maternal folic acid intake and/or multivitamin intake
			Western (by tertile)		Western (by tertile)		T1: ref. T2: OR 1.3 (0.8 to 2.2)[a] T3: OR 1.9 (1.2 to 3.1)[a]	The Western diet case group consisted of 12 cleft palate-only mothers in T1, 7 mothers in T2 and 13 mothers in T3
			T1 (127)	58/203	T1 (127)	69/178	T2: OR 1.2 (0.7 to 2.1)[b] T3: OR 1.7 (1.0 to 3.0)[b]	
			T2 (127)	67/203	T2 (127)	60/178	T2: OR 1.2 (0.8 to 2.1)[b] T3: OR 1.8 (1.0 to 2.9)[b]	In the prudent dietary pattern, 6 cases were present in T1, 12 cases in T2 and 14 cases in T3
			T3 (127)	78/203	T3 (127)	49/178		
			Prudent (by tertile)		Prudent (by tertile)		T1: ref. T2: OR 0.9 (0.5 to 1.4)[a] T3: OR 1.1 (0.7 to 1.8)[a]	Tertiles were calculated by summing of intake food groups weighted by their factor loadings. The factor score for each pattern was calculated by adding up the intakes of the food groups weighted by the factor loadings
			T1 (127)	68/203	T1 (127)	59/178	T2: OR 0.8 (0.5 to 1.4)[b] T3: OR 1.3 (0.8 to 1.8)[b]	
			T2 (127)	64/203	T2 (127)	63/178	T2: OR 0.7 (0.5 to 1.2)[b] T3: OR 1.0 (0.6 to 1.7)[b]	
			T3 (127)	71/203	T3 (127)	56/178	T1: ref. T2: OR 1.3 (0.8 to 2.2)[a] T3: OR 1.9 (1.2 to 3.1)[a]	T1: lowest tertile of the daily pattern scores; T2: middle tertile of the daily pattern scores; T3: highest tertile of the daily pattern scores

Outcome	Study	*N*	Intervention/exposure	*n*/*N*	Control group	*n*/N	OR or HR (95% CI)	Comments
Antisocial personality disorder	Neugebauer 1999[80] Cohort study	76,630	Diet: famine western Holland					Adjusted for social class (manual laborers including farmers and non-manual laborers
			By trimester		Unexposed to famine	50/45,007		
			First, second or third	26/14,310			OR 1.6 (1.02 to 2.6)	
							OR 2.0 (1.2 to 3.3)[b]	
			First and/or second	20/9252			OR 2.0 (1.2 to 3.5)	
							OR 2.5 (1.5 to 4.2)[b]	
			First only	6/2443			OR 2.2 (0.95 to 5.0)	
							OR 2.9 (1.2 to 6.7)[b]	
			First and second only	6/2223			OR 2.4 (1.04 to 5.7)	
							OR 3.0 (1.3 to 7.0)[b]	
			Second only	9/4586			OR 1.8 (0.9 to 3.6)	
							OR 2.1 (1.03 to 4.4)[b]	
			Third only	5/5058			OR 0.9 (0.4 to 2.2)	
							OR 1.1 (0.4 to 2.7)[b]	
			By severity		Unexposed to famine	50/45,007		
			Severely exposed	26/14,310			OR 1.9 (1.02 to 2.6)	
							OR 2.0 (1.2 to 3.3)[b]	
			Moderately exposed	10/9615			OR 0.9 (0.6 to 1.9)	
							OR 0.7 (0.3 to 1.6)[b]	
Dyslipidaemia (adult)	Lumey 2009[76] Cohort study	638	Diet: famine	96/344	Unexposed to famine (hospital control subjects)	85/294	OR 0.95 (0.61 to 1.34)[a]	$p=0.39$ Ratio of total cholesterol to high-density lipoprotein cholesterol >5.0 or use of cholesterol-lowering medication
Obesity (adults)	Ravelli 1976[136] Cohort study	307,700	Diet: famine (by trimester)		Unexposed to famine (by trimester)			Obesity was defined as a value of weight for height ≥120% of the standard
			Third	51/6200	Third	148/11,200	OR 0.62 (0.45 to 0.85)[a]	$p<0.005$
			Second and third	126/7500	Second and third	286/17,600	OR 1.03 (0.84 to 1.28)[a]	Not significant
			First and second	119/4300	First and second	230/15,900	OR 1.94 (1.55 to 2.43)[a]	$p<0.0005$
			First	41/2500	First	162/10,500	OR 1.06 (0.75 to 1.50)[a]	Not significant

Outcome	Study	*N*	Intervention/exposure	*n*/*N*	Control group	*n*/N	OR or HR (95% CI)	Comments
IGT or type 2 diabetes mellitus (adults)	Stanner 1997[141] Cohort study	357	Diet: famine		Unexposed to famine			Diabetes mellitus and IGT were classified according to World Health Organization criteria
			Known diabetes	4/169	Known diabetes	7/188	OR 0.63 (0.18 to 2.18)[a]	
			Newly diagnosed diabetes	3/169	Newly diagnosed diabetes	5/188	OR 0.66 (0.16 to 2.81)[a]	
			IGT	16/169	IGT	16/188	OR 1.12 (0.54 to 2.32)[a]	
	Ravelli 1998[137] Cohort study	702	Diet: famine		Unexposed to famine		General OR 1.19 (0.79 to 1.79)[a]	
			Exposed in late gestation	24/116	Conceived after	33/221		
			Exposed in mid-gestation	14/100	Born before	30/202		
			Exposed in early gestation	10/63				
Artificial rupture of membranes	Clapp 1990[64] Cohort study	131	Physical activity: exercise regularly at or above 50% of preconceptional level throughout pregnancy	20/87	Discontinued regular exercise regimen before the end of the first trimester	22/44	OR 0.33 (0.14 to 0.65)[a]	$p=0.01$
Stimulation for abnormal labour pattern	Clapp 1990[64] Cohort study	131	Physical activity: exercise regularly at or above 50% of preconceptional level throughout pregnancy	11/87	Discontinued regular exercise regimen before the end of the first trimester	9/44	OR 0.56 (0.21 to 1.48)[a]	
Meconium in fluid	Clapp 1990[64] Cohort study	131	Physical activity: exercise regularly at or above 50% of preconceptional level throughout pregnancy	12/87	Discontinued regular exercise regimen before the end of the first trimester	11/44	OR 0.48 (0.19 to 1.20)[a]	$p=0.01$
Abnormal heart rate	Clapp 1990[64] Cohort study	131	Physical activity: exercise regularly at or above 50% of preconceptional level throughout pregnancy	12/87	Discontinued regular exercise regimen before the end of the first trimester	11/44	OR 0.48 (0.19 to 1.20)[a]	
Nuchal cord	Clapp 1990[64] Cohort study	131	Physical activity: exercise regularly at or above 50% of preconceptional level throughout pregnancy	23/87	Discontinued regular exercise regimen before the end of the first trimester	24/44	OR 0.30 (0.14 to 0.64)[a]	$p=0.01$
Threatened abortion	Dale 1982[67] Cohort study	33	Physical activity: running	1/21	Not active women: not participating in any type of exercise programme	1/11	OR 0.50 (0.03 to 8.85)[a]	

Outcome	Study	*N*	Intervention/exposure	*n*/*N*	Control group	*n*/N	OR or HR (95% CI)	Comments
Chorioamnionitis secondary to prolonged rupture of membranes	Dale 1982[67] Cohort study	33	Physical activity: running	0/21	Not active women: not participating in any type of exercise programme	1/11	OR 0.16 (0.01 to 4.35)[a]	
Failure to progress with oxytocin augmentation	Dale 1982[67] Cohort study	33	Physical activity: running	3/21	Not active women: not participating in any type of exercise programme	3/11	OR 0.44 (0.07 to 2.70)[a]	
Anaemia (mother)	Dale 1982[67] Cohort study	33	Physical activity: running	3/21	Not active women: not participating in any type of exercise programme	2/11	OR 0.75 (0.11 to 5.30)[a]	
Anaemia	Magann 2002[77] Cohort study	750	Exercise: different levels		No exercise	*n* = 217 12.91 ± 0.87		*p* = 0.442
			Light	*n* = 222 12.78 ± 0.94			OR –0.13 (–0.30 to 0.04)[a]	
			Moderate	*n* = 73 12.98 ± 0.79			OR 0.07 (–0.15 to 0.29)[a]	
			Heavy	*n* = 238 13.0 ± 2.19			OR 0.09 (–0.21 to 0.39)[a]	

Outcome	Study	*N*	Intervention/exposure	*n*/*N*	Control group	*n*/N	OR or HR (95% CI)	Comments
Asphyxia/ meconium staining/fetal distress	Dale 1982[67] Cohort study	33	Physical activity: running	0/21	Not active women: not participating in any type of exercise programme	4/11	OR 0.04 (0.00 to 0.81)[a]	
Sepsis	Dale 1982[67] Cohort study	33	Physical activity: running	0/21	Not active women: not participating in any type of exercise programme	1/11	OR 0.16 (0.01 to 4.35)[a]	

HR, hazard ratio; IGT, impaired glucose tolerance.
a Unadjusted value.
b Adjusted value.

Appendix 11

Delphi ranking of maternal and fetal weight management outcomes according to their importance in the management of maternal weight in pregnancy

	First round		Second round	
Outcomes	**Median**	**IQR**	**Median**	**IQR**
Maternal outcomes				
Weight gain in pregnancy	6	3	6	1.25
Post-partum weight retention	6	2.5	6	1.25
Interpregnancy weight gain	7	3	7	1.25
GDM[a]	8	1	8	0.25
Pre-eclampsia/pregnancy-induced hypertension[a]	8	1.5	8	2
Post-partum haemorrhage	7	2	7	0.25
Prolonged labour	7	2	6	1
Preterm delivery	7	2.5	7	2
Induction of labour[a]	7	1.5	8	1.25
Prelabour rupture of membranes	6	3.5	6	1.25
Caesarean section	8	1	7	1
Instrumental delivery	7	1	7	1.25
Perineal trauma	7	2.5	6.5	1
Puerperal pyrexia (≥ 38°C)	6	2	5	1
Miscarriage	5	2	6	1.5
Need for resuscitation at delivery	7	2	7	0.25
Antepartum haemorrhage	6	2.5	6	1
Thromboembolism[a]	8	2	8	1.25
Admission to HDU/ITU[a]	8	2	8	1
Anaemia	6	4	5	3
Infections	6	2.5	6	2
Postnatal infections	6	2.5	6	2.25
Postnatal depression	6	2	6	2.25
Anxiety	5	1.5	5	0.5
Quality of life	6	2	6	1.25
Physical activity	6	2	6	0.25
Dietary behaviour	7	3	7	0.25
Body fat (%)	6	2	6	2.25
Back pain[b]			6	2
Breast feeding[b]			5	2.25
Threatened abortion[b]			3.5	2
Failed instrumental delivery[b]			7	2
Coronary artery disease[b]			6	3.25
Non-infective respiratory distress[b]			5.5	2.25

Outcomes	First round		Second round	
	Median	IQR	Median	IQR
Fetal outcomes				
SGA[a]	8	2	8	1.25
LGA	7	2	7	1.25
Skinfold thickness	6	2	6	1
Fetal fat mass (%)	6	0.5	6	1.25
Abdominal circumference	6	0.5	6	1.25
Head circumference	5	1.5	5	0.25
Ponderal index ($g/cm^3 \times 100$)	6	1.5	6	2
Neonate length/crown–heel length	5	1.5	5	0.25
Head-to-abdomen ratio	5	2	5	1
Birthweight-related outcomes, e.g. BMI	6	2	6	2
Hypoglycaemia	7	1	7	1
Hyperbilirubinaemia	6	1	6	2
Intrauterine death[a]	8	2	8.5	1
Respiratory distress syndrome	7	1.5	7	1
Admission to NICU[a]	8	1	8	1
Shoulder dystocia[a]	8	1	8	1
One or more perinatal complication[a]	7	2	8	1
Birth trauma[a]	8	2	8	0.5
NTD	6	2	6	2
Cleft lip or palate or both	6	2.5	6	1.25
Other congenital abnormalities	7	2	6.5	1.25
Apgar score	6	2	6	1
CTG abnormalities	6	2	5.5	1.25
Abnormal cord pH	7	2	7	2
Long-term neurological sequelae	8	3	8	2.25
Cord abnormalities[b]			5	2.25
Long-term metabolic sequelae[b]			7.5	1.25

CTG, cardiotocographic.
1–3, of limited importance to patient care; 4–6, important but not critical to patient care; 7–9, critical to patient care.
a Included in the final list of obstetric and outcomes.
b Outcomes suggested by the panellists and included for ranking in the second round.

Appendix 12

Grading the quality of randomised evidence for the primary and clinically important outcomes for the effectiveness of weight management interventions in pregnancy

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Dietary and lifestyle interventions	Control	Relative (95% CI)	Absolute	Quality	Importance
Gestational weight gain (kg) (better indicated by lower values)												
30	Randomised trials	Serious[a,b,c]	No serious inconsistency	No serious indirectness	No serious imprecision	None	2309	2286	–	MD 0.94 lower (1.57 to 0.3 lower)	⊕⊕⊕⊖ Moderate	Important
Birthweight (kg) (better indicated by lower values)												
28	Randomised trials	Serious[a,b,d]	No serious inconsistency	No serious indirectness	No serious imprecision	None	2302	2271	–	MD 0.07 lower (0.14 to 0.01 lower)	⊕⊕⊕⊖ Moderate	Important
LGA												
12	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious[e]	No serious imprecision	None	155/1527 (10.2%)	234/1494 (15.7%)	RR 0.73 (0.54 to 0.99)	42 fewer per 1000 (from 2 fewer to 72 fewer)	⊕⊕⊕⊖ Moderate	Critical
SGA												
8	Randomised trials	No serious limitations[f]	No serious inconsistency	No serious indirectness	No serious imprecision	None	103/1456 (7.1%)	103/1445 (7.1%)	RR 0.99 (0.76 to 1.29)	1 fewer per 1000 (from 17 fewer to 21 more)	⊕⊕⊕⊕ High	Critical
Pre-eclampsia												
10	Randomised trials	No serious limitations[f]	Serious[g]	Serious[h]	No serious imprecision	None	115/1543 (7.5%)	157/1529 (10.3%)	RR 0.74 (0.59 to 0.92)	27 fewer per 1000 (from 8 fewer to 42 fewer)	⊕⊕⊖⊖ Low	Critical
Gestational hypertension												
6	Randomised trials	No serious limitations	Serious[i]	No serious indirectness	Serious	None	41/403 (10.2%)	52/388 (13.4%)	RR 0.77 (0.54 to 1.1)	31 fewer per 1000 (from 62 fewer to 13 more)	⊕⊕⊖⊖ Low	Critical

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Dietary and lifestyle interventions	Control	Relative (95% CI)	Absolute	Quality	Importance
GDM												
5	Randomised trials	No serious limitations[f]	No serious inconsistency	No serious indirectness	Serious[j]	Reporting bias[k]	27/344 (7.8%)	37/331 (11.2%)	RR 0.71 (0.44 to 1.13)	32 fewer per 1000 (from 63 fewer to 15 more)	⊕⊕⊖⊖ Low	Critical
Preterm birth												
11	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious[e]	No serious imprecision	None	70/1115 (6.3%)	89/1083 (8.2%)	RR 0.76 (0.56 to 1.02)	20 fewer per 1000 (from 36 fewer to 2 more)	⊕⊕⊕⊖ Moderate	Critical
Caesarean section												
14	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious[e]	No serious imprecision	Reporting bias[k]	505/1666 (30.3%)	538/1646 (32.7%)	RR 0.93 (85 to 1.03)	23 fewer per 1000 (from 49 fewer to 10 more)	⊕⊕⊖⊖ Low	Critical
Induction of labour												
5	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious[e]	No serious imprecision	None	394/1187 (33.2%)	347/1175 (29.5%)	RR 1.12 (1 to 1.26)	35 more per 1000 (from 0 more to 77 more)	⊕⊕⊕⊖ Moderate	Critical
Post-partum haemorrhage												
2	Randomised trials	No serious limitations	No serious inconsistency	Serious[e]	No serious imprecision	Reporting bias[l]	32/606 (5.3%)	37/626 (5.9%)	RR 0.80 (0.57 to 1.42)	6 fewer per 1000 (from 25 fewer to 25 more)	⊕⊕⊖⊖ Low	Critical
Intrauterine death												
2	Randomised trials	No serious limitations[f]	No serious inconsistency	No serious indirectness	Serious	None	0/647 (0%)	6/673 (0.9%)	RR 0.15 (0.02 to 1.2)	8 fewer per 1000 (from 9 fewer to 2 more)	⊕⊕⊕⊖ Moderate	Critical

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Dietary and lifestyle interventions	Control	Relative (95% CI)	Absolute	Quality	Importance
Admission to NICU												
2[m]	Randomised trials	No serious limitations[a,b]	Serious[g]	Very serious[e]	Serious[j]	None	400/983 (40.7%)	374/979 (38.2%)	RR 0.98 (0.66 to 1.47)	8 fewer per 1000 (from 130 fewer to 180 more)	⊕⊖⊖⊖ Very low	Critical
Shoulder dystocia												
4	Randomised trials	No serious limitations	No serious inconsistency	Serious[e]	No serious imprecision	None	15/1173 (1.3%)	38/1144 (3.3%)	RR 0.39 (0.22 to 0.7)	20 fewer per 1000 (from 10 fewer to 26 fewer)	⊕⊕⊕⊖ Moderate	Critical
Birth trauma												
2[m]	Randomised trials	No serious limitations[f]	No serious inconsistency	Serious[e]	Serious	None	3/982 (0.3%)	9/979 (0.9%)	RR 0.36 (0.11 to 1.23)	6 fewer per 1000 (from 8 fewer to 2 more)	⊕⊕⊖⊖ Low	Critical
Neonatal hypoglycaemia												
5	Randomised trials	No serious limitations	No serious inconsistency	Serious[e]	Serious[j]	Reporting bias[k]	124/1087 (11.4%)	109/1059 (10.3%)	RR 1.07 (0.85 to 1.35)	7 more per 1000 (from 36 fewer to 36 fewer)	⊕⊖⊖⊖ Very low	Critical

a Poor information about allocation concealment, which was assessed as not strongly significant.
b Poor information about blinding of subjective outcomes, which was assessed as not strongly significant.
c High risk of bias regarding incompleteness of outcome data addressed and selective reporting.
d High risk of bias regarding incompleteness of outcome data addressed.
e Women with GDM.
f Allocation concealment not clear but not considered to be necessary for downgrading.
g Qualitative difference in the summary estimate.
h Significant subgroup effect observed for women with GDM.
i Heterogeneity: $I^2 = 48\%$.
j Wide CI crossing line of no effect.
k Slight skew in funnel plot for given outcome.
l Difficult to interpret as only two studies.
m Evidence for only one group of interventions.

Appendix 13

Grading the quality of evidence for the primary and clinically important outcomes for the effectiveness of dietary interventions in pregnancy

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Diet and nutrition counselling	Control	Relative (95% CI)	Absolute	Quality	Importance
Gestational weight gain (kg) (better indicated by lower values)												
9	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious	No serious imprecision	None	1221	1215	–	MD 3.36 lower (4.73 to 1.99 lower)	⊕⊕⊕⊖ Moderate	Important
Birthweight (kg) (better indicated by lower values)												
9	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious[c]	Serious[d]	Reporting bias[e]	1365	1372	–	MD 0.07 lower (0.21 lower to 0.07 higher)	⊕⊖⊖⊖ Very low	Important
LGA												
5	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious[c]	No serious imprecision	Reporting bias[e]	134/1196 (11.2%)	203/1182 (17.2%)	RR 0.78 (0.51 to 1.19)	38 fewer per 1000 (from 84 fewer to 33 more)	⊕⊕⊖⊖ Low	Critical
SGA												
3	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious[c]	No serious imprecision[d]	None	80/1124 (7.1%)	79/1128 (7%)	RR 1.02 (0.75 to 1.37)	1 more per 1000 (from 18 fewer to 26 more)	⊕⊕⊕⊖ Moderate	Critical
Pre-eclampsia												
6	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious[c]	No serious imprecision	None	99/1309 (7.6%)	150/1315 (11.4%)	RR 0.67 (0.53 to 0.85)	38 fewer per 1000 (from 17 fewer to 54 fewer)	⊕⊕⊕⊖ Moderate	Critical
Gestational hypertension												
2	Randomised trials	No serious limitations[a,b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	4/139 (2.9%)	14/143 (9.8%)	RR 0.3 (0.1 to 0.88)	69 fewer per 1000 (from 12 fewer to 88 fewer)	⊕⊕⊕⊕ High	Critical

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Diet and nutrition counselling	Control	Relative (95% CI)	Absolute	Quality	Importance
GDM												
2	Randomised trials	No serious limitations[a,b]	No serious inconsistency	No serious indirectness	Serious[f]	Reporting bias[g]	11/139 (7.9%)	22/146 (15.1%)	RR 0.52 (0.27 to 1.03)	72 fewer per 1000 (from 110 fewer to 5 more)	⊕⊕⊖⊖ Low	Critical
Preterm delivery												
4	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious[c]	No serious imprecision	Reporting bias[g]	49/744 (6.6%)	70/730 (9.6%)	RR 0.68 (0.48 to 96)	31 fewer per 1000 (from 50 fewer to 9110 more)	⊕⊕⊖⊖ Low	Critical
Caesarean section												
5	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious[c]	No serious imprecision	None[e]	387/1135 (34.1%)	416/1138 (36.6%)	RR 0.93 (0.84 to 1.04)	26 fewer per 1000 (from 58 fewer to 15 more)	⊕⊕⊕⊖ Moderate	Critical
Induction of labour												
4	Randomised trials	No serious limitations[a,b]	No serious inconsistency[h]	Serious[c]	No serious imprecision	Reporting bias[g]	370/1145 (32.3%)	326/1132 (28.8%)	RR 1.12 (0.99 to 1.27)	35 more per 1000 (from 3 fewer to 78 more)	⊕⊕⊖⊖ Low	Critical
Post-partum haemorrhage												
2	Randomised trials	No serious limitations	No serious inconsistency	Serious[c]	No serious imprecision	Reporting bias[i]	32/606 (5.3%)	37/626 (5.9%)	RR 0.80 (0.57 to 1.42)	6 fewer per 1000 (from 26 fewer to 25 more)	⊕⊕⊖⊖ Low	Critical
Intrauterine death												
2	Randomised trials	No serious limitations[a]	No serious inconsistency	Serious	Serious[d]	None	0/647 (0%)	6/673 (0.9%)	RR 0.15 (0.02 to 1.2)	8 fewer per 1000 (from 9 fewer to 2 more)	⊕⊕⊖⊖ Low	Critical

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Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Diet and nutrition counselling	Control	Relative (95% CI)	Absolute	Quality	Importance
Admission to NICU												
2	Randomised trials	No serious limitations[a,b]	Serious[j]	Serious[c]	Serious[d]	None	400/983 (40.7%)	374/979 (38.2%)	RR 0.98 (0.66 to 1.47)	8 fewer per 1000 (from 130 fewer to 180 more)	⊕⊖⊖⊖ Very low	Critical
Shoulder dystocia												
3	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious	No serious imprecision	None	14/1049 (1.3%)	37/1033 (3.6%)	RR 0.38 (0.21 to 0.69)	22 fewer per 1000 (from 11 fewer to 28 fewer)	⊕⊕⊕⊖ Moderate	Critical
Birth trauma												
2	Randomised trials	No serious limitations[a]	No serious inconsistency	Serious	Serious[d]	None	3/982 (0.3%)	9/979 (0.9%)	RR 0.36 (0.11 to 1.23)	6 fewer per 1000 (from 8 fewer to 2 more)	⊕⊕⊖⊖ Low	Critical
Neonatal hypoglycaemia												
3	Randomised trials	No serious limitations	No serious inconsistency	Serious[c]	No serious imprecision	Reporting bias[i]	119/946 (12.6%)	107/931 (11.5%)	RR 1.05 (0.83 to 1.33)	12 more per 1000 (from 38 more to 20 fewer)	⊕⊕⊖⊖ Low	Critical

a Poor information about allocation concealment, which was assessed as not strongly significant.
b Poor information about blinding of subjective outcomes, which was assessed as not strongly significant.
c Women with GDM.
d Wide CI.
e Slight skew in funnel plot for given outcome.
f Non-significant RR result, with large disproportion between study groups.
g Meaningful skew in funnel plot graph.
h High heterogeneity (>50%), which can be explained by the diversity in the health of the study populations.
i Difficult to interpret as only two studies.
j Qualitative difference in effect.

Appendix 14

Grading the quality of evidence for the primary and clinically important outcomes for the effectiveness of physical activity interventions in pregnancy

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Physical activity and counselling about physical activity	Control	Relative (95% CI)	Absolute	Quality	Importance
Gestational weight gain (kg) (better indicated by lower values)												
15	Randomised trials	Serious[a,b,c]	No serious inconsistency	No serious indirectness	No serious imprecision	Reporting bias[d]	582	583	–	MD 0.07 lower (1.08 lower to 0.93 higher)	⨁⨁⨀⨀ Low	Important
Birthweight (kg) (better indicated by lower values)												
15	Randomised trials	Very serious[a,b,e]	No serious inconsistency	No serious indirectness	Serious[f]	None	673	654	–	MD 0.09 lower (0.18 lower to 0 higher)	⨁⨀⨀⨀ Very low	Important
LGA												
2	Randomised trials	No serious limitations[a,b]	No serious inconsistency	No serious indirectness	Very serious[f]	None	3/94 (3.2%)	9/89 (10.1%)	RR 0.37 (0.06 to 2.3)	64 fewer per 1000 (from 95 fewer to 131 more)	⨁⨁⨀⨀ Low	Critical
SGA												
3	Randomised trials	Serious[a,b,g,h]	No serious inconsistency	No serious indirectness	No serious imprecision[f]	None	9/151 (6.0%)	7/153 (4.6%)	RR 1.31 (0.5 to 3.42)	14 more per 1000 (from 23 fewer to 111 more)	⨁⨁⨁⨀ Moderate	Critical
Pre-eclampsia												
1	Randomised trials	No serious limitations[a,b]	No serious inconsistency	No serious indirectness	Serious[i]	None	6/41 (14.6%)	1/38 (2.6%)	RR 5.56 (0.7 to 44.09)	120 more per 1000 (from 8 fewer to 1134 more)	⨁⨁⨁⨀ Moderate	Critical
Gestational hypertension												
1	Randomised trials	No serious limitations[a,b,g]	No serious inconsistency	No serious indirectness	Serious[f]	None	9/41 (22.0%)	15/38 (39.5%)	RR 0.56 (0.28 to 1.12)	174 fewer per 1000 (from 284 fewer to 47 more)	⨁⨁⨁⨀ Moderate	Critical

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Physical activity and counselling about physical activity	Control	Relative (95% CI)	Absolute	Quality	Importance
GDM												
1	Observational studies[j]	No serious limitations	No serious inconsistency	No serious indirectness	Very serious[f]	None	23/615 (3.7%)	19/294 (6.5%)	OR 0.58 (0.32 to 1.06)	26 fewer per 1000 (from 43 fewer to 4 more)	⊕⊖⊖⊖ Very low	Critical
Preterm delivery												
4	Randomised trials	[a,b]	No serious inconsistency	No serious indirectness	Serious[f]	None	9/173 (5.2%)	8/172 (4.7%)	RR 1.12 (0.44 to 2.85)	6 more per 1000 (from 26 fewer to 86 more)		Critical
Caesarean section												
4	Randomised trials	No serious limitations[a,b]	No serious inconsistency	No serious indirectness	[f]	None	52/234 (22.2%)	60/241 (24.9%)	RR 0.92 (0.68 to 1.24)	20 fewer per 1000 (from 80 fewer to 60 more)		Critical
Induction of labour: not reported												
0	–	–	–	–	–	None	0/0 (0%)	0/0 (0%)	–	0 fewer per 1000 (from 0 fewer to 0 fewer)		Critical
Post-partum haemorrhage: not reported												
0	–	–	–	–	–	None	0/0 (0%)	0/0 (0%)	–	–		Critical
Intrauterine death												
1	Observational studies[k]	No serious limitations[l]	No serious inconsistency	No serious indirectness	Serious[f]	None	2/169 (1.2%)	3/166 (1.8%)	RR 0.65 (0.11 to 3.68)	6 fewer per 1000 (from 16 fewer to 48 more)	⊕⊖⊖⊖ Very low	Critical

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Physical activity and counselling about physical activity	Control	Relative (95% CI)	Absolute	Quality	Importance
Admission to NICU: not reported												
0	–	–	–	–	–	None	0/0 (0%)	0/0 (0%)	–	–		Critical
Shoulder dystocia: not reported												
0	–	–	–	–	–	None	0/0 (0%)	0/0 (0%)	–	–		Critical
Birth trauma: not reported												
0	–	–	–	–	–	None	0/0 (0%)	0/0 (0%)	–	–		Critical
Neonatal hypoglycaemia: not reported												
0	–	–	–	–	–	None	0/0 (0%)	0/0 (0%)	–	–		Critical

a Poor information about allocation concealment, which was assessed as not strongly significant.
b Poor information about blinding of subjective outcomes, which was assessed as not strongly significant.
c High risk of bias regarding incompleteness of outcome data addressed and selective reporting.
d Strong skew in funnel plot graph.
e High risk of bias regarding incompleteness of outcome data addressed, selective reporting and other bias.
f Wide CI crossing line of no effect.
g Poor information about random sequence generation, which was assessed as not strongly significant.
h High risk of selective reporting in Santos 2005[119] study.
i Non-significant RR result, with large disproportion between study groups.
j Outcome assessed in few studies; for GRADE the study of the highest quality has been chosen (cohort study: Dempsey 2004[69]).
k Non-randomised study with control group: Narendran 2005.[59]
l Study of moderate quality: inadequate sequence generation, no blinding, no loss to follow-up and no differences in matching patients in the two groups.

Appendix 15

Grading the quality of evidence for the primary and clinically important outcomes for the effectiveness of mixed approach interventions in pregnancy

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Mixed approach	Control	Relative (95% CI)	Absolute	Quality	Importance
Gestational weight gain (kg) (better indicated by lower values)												
6	Randomised trials	No serious limitations[a,b]	No serious inconsistency	No serious indirectness	Serious[c]	Reporting bias[d]	506	488	–	MD 0.36 lower (1.4 lower to 0.68 higher)	⨁⨁⨀⨀ Low	Important
Birthweight (kg) (better indicated by lower values)												
5	Randomised trials	No serious limitations[a,b]	No serious inconsistency	No serious indirectness	Serious[c]	Reporting bias[d]	264	245	–	MD 0.02 lower (0.1 lower to 0.07 higher)	⨁⨁⨀⨀ Low	Important
LGA												
5	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious[e]	No serious imprecision	None	18/237 (7.6%)	22/223 (9.9%)	RR 0.75 (0.41 to 1.38)	25 fewer per 1000 (from 58 fewer to 37 more)	⨁⨁⨁⨀ Moderate	Critical
SGA												
2	Randomised trials	No serious limitations[a,b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	14/181 (7.7%)	17/164 (10.4%)	RR 0.76 (0.39 to 1.48)	25 fewer per 1000 (from 63 fewer to 50 more)	⨁⨁⨁⨁ High	Critical
Pre-eclampisa												
3	Randomised trials	No serious limitations[a,b]	Serious[f]	No serious indirectness	Serious[c]	None	10/193 (5.2%)	6/176 (3.4%)	RR 1.48 (0.56 to 3.94)	16 more per 1000 (from 15 fewer to 100 more)	⨁⨁⨀⨀ Low	Critical
Gestational hypertension												
3	Randomised trials	No serious limitations[a,b]	Serious[f]	No serious indirectness	Serious[c]	None	28/223 (12.6%)	23/207 (11.1%)	RR 1.19 (0.74 to 1.9)	21 more per 1000 (from 29 fewer to 100 more)	⨁⨁⨀⨀ Low	Critical
GDM												
3	Randomised trials	No serious limitations[a,b]		No serious indirectness	Serious[c]	None	16/205 (7.8%)	15/185 (8.1%)	RR 0.96 (0.49 to 1.86)	3 fewer per 1000 (from 41 fewer to 70 more)	⨁⨁⨁⨀ Moderate	Critical

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Mixed approach	Control	Relative (95% CI)	Absolute	Quality	Importance
Preterm delivery												
3	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious[e]	No serious imprecision	None[d]	12/198 (6.1%)	11/181 (6.1%)	RR 1.02 (0.47 to 2.21)	1 more per 1000 (from 32 fewer to 74 more)	⊕⊕⊕⊖ Moderate	Critical
Caesarean section												
5	Randomised trials	No serious limitations[a,b]	No serious inconsistency	Serious[e]	No serious imprecision	Reporting bias[g]	66/297 (22.2%)	62/267 (23.2%)	RR 0.95 (0.7 to 1.28)	12 fewer per 1000 (from 70 fewer to 65 more)	⊕⊕⊖⊖ Low	Critical
Induction of labour												
1	Randomised trials	No serious limitations	No serious inconsistency[h]	No serious indirectness[i]	Serious[c]	None	24/42 (57.1%)	21/43 (48.8%)	RR 1.17 (0.78 to 1.75)	83 more per 1000 (from 107 fewer to 366 more)	⊕⊕⊕⊖ Moderate	Critical
Post-partum haemorrhage: not reported												
0	–	–	–	–	–	None	0/0 (0%)	0/0 (0%)	–	–		Critical
Intrauterine death: not reported												
1[k]	Observational studies	Very serious[l]	No serious inconsistency	Serious[e]	No serious impression	None	3/88 (3.4%)	3/86 (3.5%)	OR 098 (0.19 to 2.56)	1 fewer per 1000 (from 28 fewer to 50 more)	⊕⊖⊖⊖ Very low	Critical
Admission to NICU: not reported												
1[k]	Observational studies	Very serious[l]	No serious inconsistency	Serious[e]	No serious impression	None	21/88 (23.9%)	42/86 (48.8%)	OR 0.33 (0.17 to 0.63)	249 fewer per 1000 (from 113 fewer to 349 fewer)	⊕⊖⊖⊖ Very low	Critical
Shoulder dystocia												
1	Randomised trials	No serious limitations[a,b]	No serious inconsistency	No serious indirectness	Serious[c]	None	1/124 (0.8%)	1/111 (0.9%)	RR 0.9 (0.06 to 14.14)	1 fewer per 1000 (from 8 fewer to 118 more)	⊕⊕⊕⊖ Moderate	Critical

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Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Mixed approach	Control	Relative (95% CI)	Absolute	Quality	Importance
Birth trauma: not measured												
0	–	–	–	–	–	None	0/0 (0%)	0/0 (0%)	–	–		Critical
Neonatal hypoglycaemia												
2	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious[c]	Reporting bias[j]	5/141 (3.5%)	2/128 (1.6%)	RR 2.35 (0.47 to 11.76)	19 more per 1000 (from 172 more to 9 fewer)	⨁⨁⊖⊖ Low	Critical

a Poor information about allocation concealment, which was assessed as not strongly significant.
b Poor information about blinding of subjective outcomes, which was assessed as not strongly significant.
c Wide CI crossing line of no effect.
d Slight skew in funnel plot for given outcome.
e Women with GDM.
f Differences in range of interventions (intervention programme, behavioural intervention, advisory concerning adequate weight gain).
g Meaningful skew in funnel plot for given outcome.
h Single study.
i Small sample size.
j Difficult to interpret as only two studies.
k Data from observational studies Penchar 2009.[82]
l Study of low quality (Penchart 2009[82]); weakness in cohort representativeness, selection of exposed cohort, asscertainment of exopsure and cohorts comparability.

Appendix 16

Grading the quality of evidence for the adverse outcomes of diet in pregnancy

Quality assessment							Summary of findings				
							No. of patients		Effect		
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Diet	Control	OR (95% CI)	Quality	Importance
NTD											
2	Observational studies	Very serious[a]	No serious inconsistency	Serious[b]	Serious	Reporting bias[b] Strong association[c]	0/0 (0%)	0/0 (0%)	Not pooled	⨁⊖⊖⊖ Very low	Important
Coronary heart disease: long term in children as adults											
1	Observational studies	Very serious[d]	No serious inconsistency	Serious[e]	No serious imprecision	Strong association[c]	6/68 (8.8%)[f]	14/440 (3.2%)	OR 3 (1.1 to 8)	⨁⊖⊖⊖ Very low	N/A
Metabolic syndrome: long term in children as adults											
1	Observational studies	Very serious[d]	No serious inconsistency	Serious[e]	No serious imprecision	None	26/14,310 (0.2%)[g]	50/45,007 (0.1%)	OR 1.2 (0.9 to 1.7)	⨁⊖⊖⊖ Very low	Critical
Hypertension: long term in children as adults											
1	Observational studies	Very serious[h]	No serious inconsistency	Serious[e]	No serious imprecision	None	224/344 (65.1%)	168/294 (57.1%)	OR 1.4 (1.02 to 1.93)	⨁⊖⊖⊖ Very low	N/A
Cleft lip or palate or both: child											
1	Observational studies	Very serious[d]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/0 (0%)	0/0 (0%)	Not estimable	⨁⊖⊖⊖ Very low	Important
Antisocial personality disorder: long term in children as adults											
1	Observational studies	Very serious[d]	No serious inconsistency	Serious[e]	No serious imprecision	None[c]	26/14,310 (0.2%)[g]	50/45,007 (0.1%)	OR 2.0 (1.2 to 3.3)	⨁⊖⊖⊖ Very low	Critical

Quality assessment							Summary of findings				
							No. of patients		Effect		
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Diet	Control	OR (95% CI)	Quality	Importance
Dyslipidaemia: long term in children as adults											
1	Observational studies	Very serious[h]	No serious inconsistency	Serious[e]	Very serious[i]	None	96/344 (27.9%)	85/294 (28.9%)	OR 0.95 (0.61 to 1.34)	⊕⊖⊖⊖ Very low	N/A
Obesity: long term in children as adults											
1	Observational studies	Very serious[j]	No serious inconsistency	Serious[e]	No serious imprecision	None	51/6200 (0.8%)[k]	148/11,200 (1.3%)[k]	OR 0.62 (0.45 to 0.85)	⊕⊖⊖⊖ Very low	Critical
Adult obesity: long-term outcome in children											
1	Observational studies	Very serious[j]	No serious inconsistency	Serious[e]	No serious imprecision	None	119/4300 (2.8%)[l]	230/15,900 (1.4%)[l]	OR 1.94 (1.55 to 2.43)	⊕⊖⊖⊖ Very low	Critical
IGT or type 2 diabetes mellitus: long term in children as adults											
1	Observational studies	Very serious[d]	No serious inconsistency	Serious[e]	No serious imprecision	None	0/0 (0%)	0/0 (0%)	Not estimable	⊕⊖⊖⊖ Very low	Critical

IGT, impaired glucose tolerance; N/A, not available.

a Poor information about definition of controls, ascertainment of exposure and non-responce rate in Yazdy 2010 study.[143]
b No explanation was provided.
c OR > 2.
d Observational study, 5 points (9 maximum) in NOS questionnaire.
e Singleton men and women born between January 1945 and March 1946 whose mothers were exposed or not to the Dutch famine during pregnancy.
f Exposed early.
g During first, second or third trimester.
h Observational study, 6 points (9 maximum) in NOS questionnaire.
i Wide CI.
j Observational study, 4 points (9 maximum) in NOS questionnaire.
k During third trimester of pregnancy.
l During first and second trimesters of pregnancy.

Appendix 17

Grading the quality of evidence for the adverse outcomes of physical activity in pregnancy

Quality assessment							Summary of findings				
							No. of patients		Effect		
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Physical activity	Control	OR/RR (95% CI)	Quality	Importance
Cord abnormalities											
3	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	9/238 (3.8%)[b]	18/217 (8.3%)	OR 0.43 (0.19 to 0.99)	⊕⊖⊖⊖ Very low	Important
Stimulation for abnormal labour pattern											
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	11/87 (12.6%)	9/44 (20.5%)	RR 0.56 (0.21 to 1.48)	⊕⊖⊖⊖ Very low	N/A
Meconium-stained liquor											
1	Randomised trials	No serious limitations[d,e,f]	No serious inconsistency	No serious indirectness	Very serious[c]	None	4/38 (10.5%)	8/47 (17.0%)	RR 0.62 (0.2 to 1.9)	⊕⊕⊖⊖ Low	N/A
Abnormal fetal heart rate											
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	12/87 (13.8%)	11/44 (25.0%)	OR 0.48 (0.19 to 1.2)	⊕⊖⊖⊖ Very low	N/A
Nuchal cord											
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	23/87 (26.4%)	24/44 (54.5%)	OR 0.3 (0.14 to 0.64)	⊕⊖⊖⊖ Very low	N/A
Threatened abortion											
1	Observational studies	Very serious[g]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/21 (4.8%)	1/11 (9.1%)	OR 0.5 (0.03 to 8.85)	⊕⊖⊖⊖ Very low	Important

Quality assessment							Summary of findings				
							No. of patients		Effect		
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Physical activity	Control	OR/RR (95% CI)	Quality	Importance
Failure to progress with oxytocin augmentation: mother											
1	Observational studies	Very serious[g]	No serious inconsistency	No serious indirectness	Very serious[c]	None	3/21 (14.3%)	3/11 (27.3%)	OR 0.44 (0.07 to 2.7)	⊕⊖⊖⊖ Very low	N/A
Chorioamnionitis											
1	Randomised trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious imprecision	None	1/38 (2.6%)	0/47 (0%)	OR 3.69 (0.15 to 88.13)	⊕⊕⊕⊕ Low	Important
Maternal anaemia											
1	Observational studies	Very serious[g]	No serious inconsistency	No serious indirectness	Very serious[c]	None	3/21 (14.3%)	2/11 (18.2%)	OR 0.75 (0.11 to 5.3)	⊕⊖⊖⊖ Very low	Important
Maternal sepsis											
1	Observational studies	Very serious[g]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/21 (0%)	1/11 (9.1%)	OR 0.16 (0.01 to 4.35)	⊕⊖⊖⊖ Very low	N/A
Uterine atony											
1	Randomised trials	No serious limitations[d,e,f]	No serious inconsistency	No serious indirectness	Serious imprecision	None	3/38 (7.9%)	4/47 (8.5%)	RR 0.93 (0.22 to 3.89)	⊕⊕⊕⊕ Low	N/A

N/A, not available.
a Observational study, 6 points (9 max.) in NOS questionnaire.
b Exercise (heavy).
c Wide CI.
d Poor information about allocation concealment, which was assessed as not strongly significant.
e Poor information about blinding of subjective outcomes, which was assessed as not strongly significant.
f Poor information about adequate sequence generation, which was assessed as not strongly significant.
g Observational study, 4 points (9 maximum) in NOS questionnaire.

Appendix 18

Data extraction form for effectiveness of interventions for weight management in pregnancy

Part I: General

Date	(dd/mm/yy)
Reviewer ID	Study ID

Study title		
First author		
Publication year		
Source of publication		
Journal yy;vol.(issue):pp		
Language		
Publication type	❑ Journal Abstract	❑ Other (*specify*):

If included study is a comparative experimental study (randomised or non-randomised controlled trial), then go to point A in Part II

If included study is a comparative observational study (case–control, cohort), then go to point B in Part II

Part II

A) Comparative experimental studies

1. Study characteristics

Methods/methodological quality

Study design ❑ RCT ❑ NRS

RCT

Method of randomisation *Specify and assess the method:*

.....

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Allocation concealment ❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Describe.....

Blinding *Select blinded subjects:*

❑ Patients ❑ Investigators/clinicians

❑ Outcome assessors ❑ No blinding used

Assess the method:

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Information about drop-outs	❑ Precise information (number of patients and reasons) ❑ Inaccurate information ❑ Lack of information
Statistical technique used	
Intention-to-treat analysis	❑ Implemented ❑ Not implemented
What was the definition of ITT in the study?	....
Sample size calculation	
Was sensitivity analysis performed?	❑ Yes ❑ No ❑ Not applicable
How problem with missing data was resolved?	
Were missing data accounted for in the analyses?	❑ Yes ❑ No
Post hoc analysis	
Funding source	

NRS

Control group selection	*Specify and assess the method:* ..... ❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported
Allocation concealment	❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported Describe.....
Blinding	*Select blinded subjects:* ❑ Patients ❑ Investigators/clinicians ❑ Outcome assessors ❑ No blinding used *Assess the method:* ❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported
Information about drop-outs	❑ Precise information (number of patients and reasons) ❑ Inaccurate information ❑ Lack of information
Statistical technique used	
Intention-to-treat analysis	❑ Implemented ❑ Not implemented
What was the definition of ITT in the study?	....
Sample size calculation	
Was sensitivity analysis performed?	❑ Yes ❑ No ❑ Not applicable
How problem with missing data was resolved?	
Were missing data accounted for in the analyses?	❑ Yes ❑ No
Post hoc analysis	
Funding source	

Population

Trial inclusion criteria
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Trial exclusion criteria
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-
-

	Intervention group	Control group
Number of enrolled patients		
Number of patients randomised, $N_{R\ (RCT)}$ Number of patients included, $N_{(NRS)}$		
Number of patients who completed treatment, *n* (%)		
Number of patients available for follow-up, *n* (%)		
Age in years *Specify the measure*:		
Ethnicity, *n* (%)		
BMI at baseline (mean, SD) ■ Normal (25–29.9 kg/m^2) ■ Overweight (30–34.9 kg/m^2) ■ Obese (≥ 35 kg/m^2)	 ❑ Normal ..... ❑ Overweight ..... ❑ Obese	 ❑ Normal ..... ❑ Overweight ..... ❑ Obese .....
Weight at baseline (mean, SD)		
Singleton pregnancy only (if no give percentage)	Yes/no/unclear (.....)	Yes/no/unclear (.....)
Primiparas only (if no give percentage)	Yes/no/unclear (.....)	Yes/no/unclear (.....)
Gestational age (week; SD; SE)		
Other baseline characteristics		
Are the treatment groups comparable at baseline?	❑ Yes ❑ No *If 'no' please specify the reasons:*	

Intervention

Type and specifics of intervention(s) used (diet, physical activity, behavioural change, lifestyle)	
How was intervention delivered	
Intervention duration	
Intervention provider(s)	
Duration of follow-up	

Comparator	
Comparator	❑ No intervention ❑ Other intervention (specify) .....
Outcomes	
Maternal outcomes related with (more than one possible)	❑ Safety *Outcome assessment..... ❑ Delivery *Outcome assessment..... ❑ Pregnancy-related diseases *Outcome assessment..... ❑ Mental state *Outcome assessment..... ❑ Weight change *Outcome assessment..... ❑ Others *Outcome assessment……
Fetal outcomes related with (more than one possible)	❑ Safety *Outcome assessment..... ❑ Others *Outcome assessment.....
Childhood and adult outcomes in offspring (more than one possible)	❑ Childhood obesity *Outcome assessment..... ❑ Adult obesity *Outcome assessment..... ❑ Diabetes mellitus *Outcome assessment..... ❑ Coronary heart disease *Outcome assessment..... ❑ Hypertension *Outcome assessment..... ❑ Stroke *Outcome assessment..... ❑ Depression *Outcome assessment..... ❑ Death *Outcome assessment..... ❑ Other (specify) *Outcome assessment..... ❑ Not stated in study

*Outcome assessment:

1. Self-reported
2. Hospital records
3. Trained assessor
4. Other
5. Blinded
6. Unblinded

2. Results

Dichotomous data

Outcome:..... Category:..... Follow up:.....

Intervention group		Control group	
$N_R/N=$		$N_R/N=$	
N'	***n* (%)**	***N'***	***n* (%)**

Effect estimate ❑ RR ❑ OR (95% CI ❑ SE ❑ *p*)

Blinding *Select blinded subjects:*

❑ Patients ❑ Investigators/clinicians
❑ Outcome assessors ❑ No blinding used

Assess the method:

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Incomplete outcome data addressed

N', number of evaluated patients; *n*, number of patients with outcome.

Time-to-event data

Outcome:..... Category:..... Follow up:.....

Intervention group		Control group	
$N_R/N=$		$N_R/N=$	
N'	Median	*N'*	Median

Effect estimate ❑ RR ❑ OR (95% CI ❑ SE ❑ *p*)

Blinding *Select blinded subjects:*

❑ Patients ❑ Investigators/clinicians
❑ Outcome assessors ❑ No blinding used

Assess the method:

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Incomplete outcome data addressed

N', number of evaluated patients.

Continuous data

Outcome:..... Category:..... Follow up:.....

Intervention group $N_R/N=$				Control group $N_R/N=$			
N'	Mean value at baseline (❑ SD/ ❑ SE/ ❑ other)	Mean end-point value (❑ SD/ ❑ SE/ ❑ other)	Mean change from baseline (❑ SD/ ❑ SE/ ❑ other)	*N'*	Mean value at baseline (❑ SD/ ❑ SE/ ❑ other)	Mean end-point value (❑ SD/ ❑ SE/ ❑ other)	Mean change from baseline (❑ SD/ ❑ SE/ ❑ other)

Blinding

Select blinded subjects:

❑ Patients ❑ Investigators/clinicians
❑ Outcome assessors ❑ No blinding used

Assess the method:

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Incomplete outcome data addressed

N', number of evaluated patients.

Reviewers' comments

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B) Comparative observational studies

1. Study characteristics

Methods/methodological quality

Study design	❑ Case–control ❑ Cohort
Case–control	
Is case definition adequate?	❑ Independent validation Record linkage Self-reported None
Are the cases representative?	❑ All cases arising from same population or group ❑ Not known
Selection of controls	❑ Same population as cases Not known or no
Definition of controls	❑ Outcome of interest not present in history ❑ No mention of history of outcome
Comparability of cases and controls	❑ Yes No Unclear
Ascertainment of exposure to intervention	❑ Secure record ❑ Structured interview where blind to case/control status ❑ Interview not blinded to case/control status ❑ Written self-report of medical record only ❑ No description
Was the method of ascertainment of exposure for cases and controls the same?	❑ Yes No Unclear
Non-response rate	❑ Same for both groups ❑ Non-respondents described ❑ Rate different and no designation
Cohort	
Is the cohort representative	❑ Yes No Unclear
Selection of non-exposed cohort	❑ Same population as exposed cohort not known or no
Ascertainment of exposure	❑ Secure record ❑ Structured interview ❑ Written self-report ❑ No description
Demonstration that outcome of interest was not present at start of study?	❑ Yes No Unclear
Comparability of cohorts on the basis of the design or analysis	❑ Yes No Unclear
Assessment of outcome	❑ Independent or blind assessment Record linkage Self-report No description
Was follow-up long enough for outcomes to occur?	❑ Yes No Unclear *If 'yes', specify*.....
Was follow-up of cohorts adequate?	❑ Complete follow-up ❑ Subjects lost to follow-up unlikely to introduce bias, small number lost (…..%) ❑ Follow-up rate ….%, and no description of this lost ❑ No statement
Were the objectives or the hypothesis of the study stated?	❑ Yes No Unclear
Method of allocation to groups	

For patients who were not eligible for study, are the reasons why stated?	❑ Yes No
Information about drop-outs	❑ Precise information (number of patients and reasons) ❑ Inaccurate information ❑ Lack of information
Statistical technique used	
Intention-to-treat analysis	❑ Implemented Not implemented
What was the definition of ITT in the study?	....
Sample size calculation	
Was loss to follow-up taken into account in the analysis?	❑ Yes ❑ No
Comparability of groups established	❑ Yes ❑ No
Were any confounders mentioned?	❑ Yes, please describe…….. No
Were confounders accounted for in analyses?	❑ Yes ❑ No
How problem with missing data was resolved?	
Were missing data accounted for in the analyses?	❑ Yes ❑ No
Was the impact of biases assessed?	❑ Yes ❑ No ❑ Not clearly assessed
Funding source	

Population

Trial inclusion criteria	▪ ▪ ▪ ▪
Trial exclusion criteria	▪ ▪ ▪ ▪
Is target population defined?	❑ Yes ❑ No

	Intervention group	**Control group**
Number of eligible patients		
Number of included patients, *N*		
Number of patients who completed treatment, *n* (%)		
Age in years *Specify the measure*:		
Ethnicity, *n* (%)		
BMI at baseline (mean, SD) Normal (25–29.9 kg/m^2) Overweight (30–34.9 kg/m^2) Obese (≥ 35 kg/m^2)	❑ Normal ..... ❑ Overweight ..... ❑ Obese	_ Normal ..... _ Overweight ..... _ Obese .....
Weight at baseline (mean, SD)		

Singleton pregnancy only (if no give percentage)	Yes/no/unclear (.....)	Yes/no/unclear (.....)
Primiparas only (if no give percentage)	Yes/no/unclear (.....)	Yes/no/unclear (.....)
Gestational age (week; SD; SE)		
Other baseline characteristics		
Are the treatment groups comparable at baseline?	❑ Yes ❑ No *If 'no' please specify the reasons:*	
Intervention		
Type and specifics of intervention(s) used (diet, physical activity, behavioural change, lifestyle)		
How was intervention delivered		
Intervention duration		
Intervention provider(s)		
Duration of follow-up		
Comparator		
Comparator	❑ No intervention ❑ Other intervention (specify)	
Outcomes		
Maternal outcomes related with (more than one possible)	❑ Safety *Outcome assessment..... ❑ Delivery *Outcome assessment..... ❑ Pregnancy-related diseases *Outcome assessment..... ❑ Mental state *Outcome assessment..... ❑ Weight change *Outcome assessment..... ❑ Others *Outcome assessment.....	
Fetal outcomes related with (more than one possible)	❑ Safety *Outcome assessment..... ❑ Others *Outcome assessment.....	

Childhood and adult outcomes in offspring (more than one possible)	❑ Childhood obesity *Outcome assessment..... ❑ Adult obesity *Outcome assessment..... ❑ Diabetes mellitus *Outcome assessment..... ❑ Coronary heart disease *Outcome assessment..... ❑ Hypertension *Outcome assessment..... ❑ Stroke *Outcome assessment..... ❑ Depression *Outcome assessment..... ❑ Death *Outcome assessment..... ❑ Other (specify) *Outcome assessment..... ❑ Not stated in study

Outcome assessment:

1. Self-reported
2. Hospital records
3. Trained assessor
4. Other
5. Blinded
6. Unblinded

2. Results

Dichotomous data

Outcome:..... Category:..... Follow up:.....

Intervention group		Control group	
$N_R/N=$		$N_R/N=$	
N'	***n* (%)**	***N'***	***n* (%)**

Effect estimate ❑ RR ❑ OR (95% CI ❑ SE ❑ *p*)

Blinding

Select blinded subjects:

❑ Patients ❑ Investigators/clinicians
❑ Outcome assessors ❑ No blinding used

Assess the method:

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Incomplete outcome data addressed

N', number of evaluated patients; *n*, number of patients with outcome.

Time-to-event data

Outcome:..... Category:..... Follow up:.....

Intervention group

N_R/N=

N Median

Control group

N_R/N=

N Median

Effect estimate ❑ RR ❑ OR (95% CI ❑ SE ❑ *p*)

Blinding

Select blinded subjects:

❑ Patients ❑ Investigators/clinicians
❑ Outcome assessors ❑ No blinding used

Assess the method:

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Incomplete outcome data addressed

N, number of evaluated patients.

Continuous data

Outcome:..... Category:..... Follow up:.....

Intervention group

N_R/N=

N	Mean value at baseline (❑ SD/ ❑ SE/ ❑ other)	Mean end-point value (❑ SD/ ❑ SE/ ❑ other)	Mean change from baseline (❑ SD/ ❑ SE/ ❑ other)

Control group

N_R/N=

N	Mean value at baseline (❑ SD/ ❑ SE/ ❑ other)	Mean end-point value (❑ SD/ ❑ SE/ ❑ other)	Mean change from baseline (❑ SD/ ❑ SE/ ❑ other)

Blinding

Select blinded subjects:

❑ Patients ❑ Investigators/clinicians
❑ Outcome assessors ❑ No blinding used

Assess the method:

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Incomplete outcome data addressed

N, number of evaluated patients.

Reviewers' comments

Appendix 19

Data extraction form for adverse effects of weight management interventions in pregnancy

Part I: General

Date	(dd/mm/yy)
Reviewer ID	Study ID

Study title	
First author	
Publication year	
Source of publication	
Journal yy;vol.(issue):pp	
Language	
Publication type	❑ Journal Abstract ❑ Other (*specify*):

If included study is a comparative experimental study (randomised or non-randomised controlled trial), then go to point A in Part II

If included study is a comparative observational study (case–control or cohort), then go to point B in Part II

If included study is a non-comparative study, then go to point C in Part II

Part II

A) Comparative experimental studies

1. Study characteristics

Methods/methodological quality

Study design	❑ RCT ❑ NRS

RCT

Population indirectness	❑ Very ❑ Serious ❑ Not serious ❑ Difficult to assess
Was the eligible population representative of the source? Were important groups under-represented?	Describe ....
Method of randomisation	*Specify and assess the method:* ..... ❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported
Allocation concealment	❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported Describe.....

Blinding	*Select blinded subjects:* ❑ Patients ❑ Investigators/clinicians ❑ Outcome assessors ❑ No blinding used *assess the method:* ❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported
Information about drop-outs	❑ Precise information (number of patients and reasons) ❑ Inaccurate information ❑ Lack of information
Rate of loss to follow-up	
Patients lost to follow-up analysed for adverse events	
Was the follow-up adequate to ascertain adverse effects?	❑ Yes ❑ No ❑ Unclear *If 'yes', specify*.....
Statistical technique used	
Was adequate statistical analysis of potential confounders performed?	❑ Yes ❑ No ❑ Unclear
Intention-to-treat analysis	❑ Implemented ❑ Not implemented
What was the definition of ITT in the study?	....
Sample size calculation	
Was sensitivity analysis performed?	❑ Yes ❑ No ❑ Not applicable
How problem with missing data was resolved?	
Were missing data accounted for in the analyses?	❑ Yes ❑ No
Post hoc analysis	
Funding source	
NRS	
Population indirectness	❑ Very ❑ Serious ❑ Not serious ❑ Difficult to assess
Was the eligible population representative of the source? Were important groups under-represented?	Describe ....
Control group selection	*Specify and assess the method:* ..... ❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported
Allocation concealment	❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported Describe.....
Blinding	*Select blinded subjects:* ❑ Patients ❑ Investigators/clinicians ❑ Outcome assessors ❑ No blinding used *Assess the method:* ❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported
Information about drop-outs	❑ Precise information (number of patients and reasons) ❑ Inaccurate information ❑ Lack of information
Rate of loss to follow-up	

Patients lost to follow-up analysed for adverse events	
Was the follow-up adequate to ascertain adverse effects?	❑ Yes ❑ No ❑ Unclear *If 'yes', specify*.....
Statistical technique used	
Was adequate statistical analysis of potential confounders performed?	❑ Yes ❑ No ❑ Unclear
Intention-to-treat analysis	❑ Implemented ❑ Not implemented
What was the definition of ITT in the study?	....
Sample size calculation	
Was sensitivity analysis performed?	❑ Yes ❑ No ❑ Not applicable
How problem with missing data was resolved?	
Were missing data accounted for in the analyses?	❑ Yes ❑ No
Post hoc analysis	
Funding source	
Population	
Trial inclusion criteria	▪ ▪ ▪ ▪
Trial exclusion criteria	▪ ▪ ▪ ▪

	Intervention group	**Control group**
Number of enrolled patients		
Number of patients randomised, $N_{R\ (RCT)}$		
Number of patients included, $N_{(NRS)}$		
Number of patients who completed treatment, *n* (%)		
Number of patients available for follow-up, *n* (%)		
Age in years *Specify the measure*:		
Ethnicity, *n* (%)		
BMI at baseline (mean, SD)		
▪ Normal (18.5–24.9 kg/m^2)	❑ Normal	❑ Normal .....
▪ Overweight (25–29.9 kg/m^2)	❑ Overweight	❑ Overweight .....
▪ Obese (≥ 30 kg/m^2)	❑ Obese	❑ Obese .....
Weight at baseline (mean, SD)		
Singleton pregnancy only (if no give percentage)	Yes/no/unclear (.....)	Yes/no/unclear (.....)

Primiparas only (if no give percentage)	Yes/no/unclear (.....)	Yes/no/unclear (.....)
Gestational age (week; SD; SE)		
Other baseline characteristics		
Are the treatment groups comparable at baseline?	❑ Yes ❑ No *If 'no' please specify the reasons:*	
Intervention		
Type of dietary or lifestyle intervention with description		
How was intervention delivered		
Intervention duration		
Intervention provider		
Duration of follow-up		
Comparator		
Comparator	❑ No intervention ❑ Other intervention (specify)	
Outcomes (harms)		
Definition of outcomes	❑ Any published definition ❑ No definition	
Adequacy of data source	❑ Reliable ❑ Non-reliable	
Approach to ascertain the cause of harm	❑ Adequate ❑ Non-adequate	
Proportion of cases with attributable cause of harm established	❑ ……..(%) ❑ Unclassified	
Adverse effects occurred in	❑ Mother ❑ Fetus/baby/child ❑ Both	
Outcomes (adverse effects) related with	❑ Weight change in pregnancy ❑ Dietary intervention type ❑ Not clear ❑ Others (specify)……	
Maternal outcomes (adverse effects)	▪ *Outcome assessment…… ▪ *Outcome assessment…… ▪ *Outcome assessment……	

Child outcomes (adverse effects)	■ *Outcome assessment…… ■ *Outcome assessment…… ■ *Outcome assessment……

*Outcome assessment:

1. Self-reported
2. Hospital records
3. Trained assessor
4. Other
5. Blinded
6. Unblinded

2. Results

Dichotomous data

Outcome:..... Category:..... Follow up:.....

Intervention group		Control group	
$N_R/N=$		$N_R/N=$	
N'	***n* (%)**	***N'***	***n* (%)**

Effect estimate ❑ RR ❑ OR (95% CI ❑ SE ❑ *p*)

Blinding

Select blinded subjects:

❑ Patients ❑ Investigators/clinicians
❑ Outcome assessors ❑ No blinding used

Assess the method:

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Incomplete outcome data addressed

N', number of evaluated patients; *n*, number of patients with outcome.

Time-to-event data

Outcome:..... Category:..... Follow up:.....

Intervention group

N_R/N=

N' Median

Control group

N_R/N=

N' Median

Effect estimate ❑ RR ❑ OR (95% CI ❑ SE ❑ *p*)

Blinding

Select blinded subjects:

❑ Patients ❑ Investigators/clinicians
❑ Outcome assessors ❑ No blinding used

Assess the method:

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Incomplete outcome data addressed

N', number of evaluated patients.

Continuous data

Outcome:..... Category:..... Follow up:.....

Intervention group

N_R/N=

N'	Mean value at baseline (❑ SD/ ❑ SE/ ❑ other)	Mean end-point value (❑ SD/ ❑ SE/ ❑ other)	Mean change from baseline (❑ SD/ ❑ SE/ ❑ other)

Control group

N_R/N=

N'	Mean value at baseline (❑ SD/ ❑ SE/ ❑ other)	Mean end-point value (❑ SD/ ❑ SE/ ❑ other)	Mean change from baseline (❑ SD/ ❑ SE/ ❑ other)

Blinding

Select blinded subjects:

❑ Patients ❑ Investigators/clinicians
❑ Outcome assessors ❑ No blinding used

Assess the method:

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Incomplete outcome data addressed

N', number of evaluated patients.

Reviewers' comments

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B) Comparative observational studies

1. Study characteristics

Methods/methodological quality

Study design ❑ Case–control ❑ Cohort

Case–control

Population indirectness ❑ Very ❑ Serious ❑ Not serious ❑ Difficult to assess

Was the eligible population representative of the source? Were important groups under-represented? Describe .....

Is case definition adequate? ❑ Independent validation ❑ Record linkage ❑ Self-reported ❑ None

Are the cases representative? ❑ All cases arising from same population or group ❑ Not known

Selection of controls ❑ Same population as cases ❑ Not known or no

Definition of controls ❑ Outcome of interest not present in history
❑ No mention of history of outcome

Comparability of cases and controls ❑ Yes ❑ No ❑ Unclear

Ascertainment of exposure to intervention ❑ Secure record
❑ Structured interview where blind to case/control status
❑ Interview not blinded to case/control status
❑ Written self-report of medical record only
❑ No description

Was the method of ascertainment of exposure for cases and controls the same? ❑ Yes ❑ No ❑ Unclear

Non-response rate ❑ Same for both groups
❑ Non-respondents described
❑ Rate different and no designation

Cohort

Population indirectness ❑ Very ❑ Serious ❑ Not serious ❑ Difficult to assess

Was the eligible population representative of the source? Were important groups under-represented? Describe .....

Is the cohort representative ❑ Yes ❑ No ❑ Unclear

Selection of non-exposed cohort ❑ Same population as exposed cohort ❑ Not known or no

Ascertainment of exposure ❑ Secure record
❑ Structured interview
❑ Written self-report
❑ No description

Demonstration that outcome of interest wasn't present at start of study? ❑ Yes ❑ No ❑ Unclear

Assessment of outcome Independent or blind assessment Record linkage Self-report No description

Was follow-up long enough for outcomes to occur? ❑ Yes ❑ No ❑ Unclear
If 'yes', specify.....

Was follow-up of cohorts adequate? ❑ Complete follow-up
❑ Subjects lost to follow-up unlikely to introduce bias, small number lost (.....%)
❑ Follow-up rate ....%, and no description of this lost
❑ No statement

Are the objectives or the hypothesis of the study stated?	❑ Yes ❑ No ❑ Unclear
Method of allocation to groups	
For patients who were not eligible for study, are the reasons why stated?	❑ Yes ❑ No
Information about drop-outs	❑ Precise information (number of patients and reasons) ❑ Inaccurate information ❑ Lack of information
Statistical technique used	
Sample size calculation	
Was loss to follow-up taken into account in the analysis?	❑ Yes ❑ No
Were any confounders mentioned?	❑ Yes, please describe…….. ❑ No
Were confounders accounted for in analyses?	❑ Yes ❑ No
Were missing data accounted for in the analyses?	❑ Yes ❑ No
Was the impact of biases assessed?	❑ Yes ❑ No ❑ Not clearly assessed
Funding source	
Population	
Trial inclusion criteria	■ ■ ■ ■
Trial exclusion criteria	■ ■ ■ ■
Is target population defined?	❑ Yes ❑ No

	Intervention group	**Control group**
Number of eligible patients		
Number of included patients, *N*		
Number of patients who completed treatment, *n* (%)		
Age in years *Specify the measure*: ……		
Ethnicity, *n* (%)		
BMI at baseline (mean, SD)		
■ Normal (18.5–24.9 kg/m^2)	❑ Normal …….	❑ Normal …….
■ Overweight (25–29.9 kg/m^2)	❑ Overweight …….	❑ Overweight …….
■ Obese (≥ 30 kg/m^2)	❑ Obese …….	❑ Obese …….
Weight at baseline (mean, SD)		
Singleton pregnancy only (if no give percentage)	Yes/no/unclear (…..)	Yes/no/unclear (…..)
Primiparas only (if no give percentage)	Yes/no/unclear (…..)	Yes/no/unclear (…..)

Gestational age (week; SD; SE)	
Other baseline characteristics	
Are the treatment groups comparable at baseline?	❑ Yes ❑ No *If 'no' please specify the reasons:* ....
Intervention	
Type of dietary intervention with description	
How was intervention delivered	
Intervention duration	
Intervention provider	
Duration of follow-up	
Comparator	
Comparator	❑ No intervention ❑ Other intervention (specify) .....
Outcomes (harms)	
Adverse effects occurred in	❑ Mother ❑ Fetus/baby/child ❑ Both
Outcomes (adverse effects) related with	❑ Weight change in pregnancy ❑ Dietary intervention type ❑ Not clear ❑ Others (specify).....
Maternal outcomes (adverse effects)	▪ *Outcome assessment..... ▪ *Outcome assessment..... ▪ *Outcome assessment.....
Child outcomes (adverse effects)	▪ *Outcome assessment..... ▪ *Outcome assessment..... ▪ *Outcome assessment.....
Definition of outcomes	❑ Any published definition ❑ No definition
Adequacy of data source	❑ Reliable ❑ Non-reliable
Approach to ascertain the cause of harm	❑ Adequate ❑ Non-adequate
Proportion of cases with attributable cause of harm established	❑ ……..(%) ❑ Unclassified

*Outcome assessment:

1. Self-reported
2. Hospital records
3. Trained assessor
4. Other
5. Blinded
6. Unblinded

2. Results

Dichotomous data

Outcome:..... Category:..... Follow up:.....

Intervention group		Control group	
N_R/N=		N_R/N=	
N'	***n* (%)**	***N'***	***n* (%)**

Effect estimate ❑ RR ❑ OR (95% CI ❑ SE ❑ *p*)

Blinding *Select blinded subjects:*

❑ Patients ❑ Investigators/clinicians
❑ Outcome assessors ❑ No blinding used

Assess the method:

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Incomplete outcome data addressed

N', number of evaluated patients; *n*, number of patients with outcome.

Time-to-event data

Outcome:..... Category:..... Follow up:.....

Intervention group		Control group	
N_R/N=		N_R/N=	
N'	Median	*N'*	Median

Effect estimate ❑ RR ❑ OR (95% CI ❑ SE ❑ *p*)

Blinding *Select blinded subjects:*

❑ Patients ❑ Investigators/clinicians
❑ Outcome assessors ❑ No blinding used

Assess the method:

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Incomplete outcome data addressed

N', number of evaluated patients.

Continuous data

Outcome:..... Category:..... Follow up:.....

Intervention group $N_R/N=$				Control group $N_R/N=$			
N'	Mean value at baseline (❑ SD/ ❑ SE/ ❑ other)	Mean end-point value (❑ SD/ ❑ SE/ ❑ other)	Mean change from baseline (❑ SD/ ❑ SE/ ❑ other)	*N'*	Mean value at baseline (❑ SD/ ❑ SE/ ❑ other)	Mean end-point value (❑ SD/ ❑ SE/ ❑ other)	Mean change from baseline (❑ SD/ ❑ SE/ ❑ other)

Blinding

Select blinded subjects:

❑ Patients ❑ Investigators/clinicians
❑ Outcome assessors ❑ No blinding used

Assess the method:

❑ Adequate ❑ Inadequate ❑ Unclear ❑ Not reported

Incomplete outcome data addressed

N', number of evaluated patients.

Reviewers' comments

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C) Non-comparative studies

Quality assessment according to checklist from *Methods for the Development of NICE Public Health Guidance (second edition)*

Type of study, methodology description

.....

.....

.....

Population

Trial inclusion criteria

Trial exclusion criteria

Number of enrolled patients

Number of patients who completed treatment, *n* (%)

Number of patients available for follow-up, *n* (%)

Age in years

Specify the measure:

.....

Other baseline characteristics

Treatment

Type of treatment used (technique, no. of sessions)

Treatment duration

Duration of follow-up

Outcomes

Definition and unit of measurement

Reviewers' comments

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Appendix 20

Review protocol

1. Existing reviews

In preparing this proposal, we have conducted a scoping search in the major electronic databases MEDLINE, EMBASE and The Cochrane library to collate citations of individual research studies and systematic reviews on effectiveness and harm of various dietary interventions on weight change in pregnancy. Although there are 3 reviews in this area they have not included all the relevant studies on effectiveness and harm of dietary interventions. The existing Cochrane review on the adverse effect of weight loss or dietary intervention on mother and fetus provides some data but has not included all relevant studies. The review needs updating and quality assessment of included studies to generate firm inferences. This scoping exercise has identified the following reviews in *Table 1* which are not up to date or have limitations in quality. Furthermore the reviews on harm are infrequent. Thus there is a need for new reviews.

2. Objectives:

Our project will follow the key steps involved in health technology assessment of treatment and will meet the commissioned brief by fulfilling the following objectives:

(a) **Effectiveness of dietary interventions on maternal and fetal outcomes:** To determine the effectiveness of various dietary interventions that prevent or treat obesity on
   - maternal outcomes in pregnancy, puerperium and long term
   - fetal, neonatal and long term outcome in children

(b) **Effectiveness of dietary interventions in pregnancy on maternal weight:** To determine the effectiveness of various dietary interventions in pregnant women on
   - weight change in pregnancy and afterwards in obese (BMI 30 or more) and overweight (BMI 25 to 29.9) pregnant women
   - prevention of excessive weight gain in pregnancy and afterwards in women with normal weight (BMI 18.5 to 24.9)

(c) **Harm of dietary interventions in pregnancy:** To evaluate the potential short term and long term adverse effects in mother and baby due to
   - weight change in pregnancy in a) obese and overweight women b) normal weight women
   - the type of dietary intervention in a) obese and overweight women b) normal weight women.

3. Research Methods

Systematic reviews of effectiveness and harm of interventions will be carried out using review methodology that has been used by the applicants in their previous systematic reviews. It is in line with the recommendations of the NHS Centre for Reviews and Dissemination and the Cochrane Collaboration including those of the Cochrane Adverse Methods Subgroup. The investigation will be carried out simultaneously executing the systematic reviews of effectiveness

TABLE 1 Reviews and primary studies on dietary interventions to reduce or prevent obesity in pregnant women: Scoping literature search

Review	Last updated	Primary studies included	Population	Type of intervention	Method of delivery of intervention
Dodd	2008	Polley (RCT)	Overweight and obese	Dietary and lifestyle	Stepped care behavioural intervention
		Rae (RCT)	Obese women with gestational diabetes	Diet with energy restriction	Provision of dietary information
		Gray-Donald	Normal weight, overweight and obese	Dietary and lifestyle	Nutritionist counselling
					Modelling
					Skill training
					Self monitoring
					Leaflets
					Radio
					Supermarket tours
					Cooking demonstration
					Individual counselling
					Exercise or walking group
Birdsall	2008	Claesson	Obese	Diet	Weekly motivational talk
					Aquarobics
		Bechtel-Blackwell	Adolescent pregnancy	Healthy diet	20 minute talk by health worker
		Polley (RCT)	Normal weight, overweight and obese	Healthy diet and exercise	Stepped care behavioural intervention
		Olson	Normal weight, overweight and obese	Healthy diet	Health check book
					Newsletters
					Incentives
		Kinnunen	Normal weight, overweight and obese	Regular meals	Advice by public health nurse
				5 portions fruit and vegetables	
				High fibre	
				Restricting high sugar snacks	
Cochrane	2003	Campbell	Increased weight gain and obese	Low energy diet	
		Campbell	Obese	Low energy diet	
		Badrawi	Obese	Balanced low energy diet	

and harm. Our strategy for these will be based on a prospective protocol, which is briefly outlined below. We will carry out: review of existing reviews; update of out-of-date review; and reviews of topics not reviewed in the literature.

The GRADE methodology will guide us when assessing the quality of the evidence and summarising the results. We have previously used the GRADE methodology in our reviews. The mission of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) group is to help resolve the confusion among the different systems of rating evidence and recommendations and increase transparency within individual evidence syntheses. While the GRADE system has originally been developed for making recommendations, it is now also used for only assessing the quality of the evidence and the outcomes for patients. In that sense, the Cochrane collaboration has now adopted the GRADE-methodology by adding summary of finding tables to its Cochrane reviews.

We plan to explore the need for a health economic evaluation, including decision analytical modelling, of the various dietary and lifestyle interventions on various clinically relevant outcomes. The outputs of our reviews would help us populate a decision-tree, which may be necessary to examine the competitive merits of various strategies.

We will address the following structured question in our project defining population, interventions and comparison and study designs as shown in *Table 2*.

The major maternal and fetal outcomes to be reviewed have been standardised through the GLOBE project. We shall identify evidence on additional relevant outcomes for mother and fetus /child and rank them according to their importance for decision making: critical for decision making, important (but not critical) for decision making and not important for decision making. The ranking will be done by Delphi methodology.This step is crucial in order to potentially identify knowledge gaps on critical / important outcomes that have not been investigated so far.

4. Systematic review of effectiveness of interventions

Study identification and selection

For this HTA project, a database of published and unpublished literature will be assembled from searches using a comprehensive search strategy, as well as hand searching, contacting commercial weight management organisations and consultation with experts in the area. We will communicate with major centres of obesity research and the first author of each selected study published in the last five years, with enquiry for any published or unpublished relevant studies not included on our list. Language restrictions will not be applied to electronic searches.

The following databases will be searched: MEDLINE, EMBASE, BIOSIS, LILACS, Pascal, Science Citation Index, Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment Database (HTA). In addition, information on studies in

TABLE 2 Structured questions for systematic review of interventions for preventing or reducing obesity in pregnancy

Outcome	**Maternal outcomes**
	Pregnancy related outcomes (standardised through GLOBE project): pre eclampsia; gestational diabetes mellitus; gestational hypertension; premature rupture of membranes; caesarean section, postpartum haemorrhage; sepsis; maternal death
	Other relevant outcomes: cardiac arrest; abruption; stroke; psychiatric problems; complications of labour and delivery; instrumental delivery; induction of labour; need for hospitalisation, day care unit visits, use of intensive care; depression; self esteem, change in diet and exercise
	Maternal weight gain/change: Change in maternal weight (absolute gain/loss in weight, percentage of weight gained/reduced in comparison to pre intervention weight); fat content measurement (body mass index, skin fold thickness, ponderal index, fat free mass); fat distribution measures (waist hip ratio, waist size) in pregnancy
	Fetal outcomes
	Fetal outcomes (standardised through GLOBE project): Macrosomia stillbirths; fetal abnormalities including neural tube defects, congenital heart disease; perinatal death; intrauterine growth restriction; prematurity; abnormal Apgar; neonatal respiratory distress; shoulder dystocia
	Other relevant fetal outcomes: abnormal pH at birth or antenatal; hypoxic ischemic encephalopathy; long term effect, learning disabilities, developmental and special needs after discharge; need for neonatal intensive care admission, mechanical ventilation and duration of hospital stay
	Childhood and adult outcomes in offspring
	Childhood obesity; adult obesity, diabetes mellitus; coronary heart disease; hypertension; stroke; depression; death
	Adverse events
	Clinically significant adverse outcomes in mother and child due to a) dietary intervention b) weight change in pregnancy
	Most common adverse effects that lead to pregnant women discontinuing the intervention

progress, from commercial providers like Weight Watchers, Slimming world and unpublished research or research reported in the grey literature will be sought by searching a range of relevant databases including the Inside Conferences, Systems for Information in Grey Literature (SIGLE), Dissertation Abstracts and Clinical Trials.gov. Internet searches will also be carried out using specialist search gateways (such as OMNI: http://www.omni.ac.uk/), general search engines (such as Google: http://www.google.co.uk/) and meta-search engines (such as Copernic: http://www.copernic.com/). Citations identified by the search will be selected for inclusion in the review in a two-stage process using predefined and explicit criteria regarding populations, interventions, outcomes and study design. First, a master database of the literature searches will be constructed by amalgamation of all the citations from various database sources. The citation will be scrutinised by two reviewers. Copies of full manuscripts of all citations that are likely to meet the selection criteria will be obtained. Two reviewers will then independently select the studies, which meet the predefined criteria. These criteria will be pilot tested using a sample of papers and agreement between reviewers will be measured. Disagreements will be resolved by consensus and/or arbitration involving a third reviewer.

Study quality assessment and data extraction

The quality of the selected primary randomised controlled trials (RCT's) and observational studies will be assessed based on accepted contemporary standard. Following the GRADE methodology, the quality assessment and reporting of results will be done separately for each outcome, since even within one review the quality of the evidence can vary between outcomes. We define quality of evidence as 'the extent of confidence that an estimate of effect is correct'. The GRADE system classifies quality of evidence into one of four levels: high, moderate, low and very low.

To assess the quality, we consider first of all risk of bias (internal validity), i.e. the extent to which design, methods, execution and analysis did not control for bias in assessment of effectiveness (*Table 4*). Furthermore, we explore the (in-) consistency of results (heterogeneity), (in-) directness of the evidence (to the question under consideration, including surrogate parameters), (im-) precision of the results and publication bias. Deficiencies on those criteria in the body evidence from RCTs will lower the quality of the evidence from high to moderate or low, perhaps even very low. Deficiencies in the body of evidence from non-RCTs will lower the quality of evidence from low to very low.

Individual studies will be described by study type, intervention, numbers taking part, population denominator (eg pregnant women or fetuses) and study quality. In addition to using study quality as possible explanations for differences in results (heterogeneity), the extent to which primary research met methodological standards is important per se for assessing the strength of any conclusions that are reached. Studies' findings will be extracted in duplicate using pre-designed and piloted data extraction forms, which we have already developed and used in our previously completed reviews. Any disagreements will be resolved by consensus and/or arbitration involving a third reviewer. Missing information will be obtained from investigators if it is crucial to subsequent analysis. To avoid introducing bias, unpublished information will be coded in

TABLE 3 Quality of evidence and definitions

High quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low quality	Any estimate of effect is very uncertain

TABLE 4 Criteria for assessing risk of bias

	No downgrading	Downgrading by one (possibly two) levels	Downgrading by two or three levels
1. Selection bias:	Studies with randomisation, allocation concealment, similarity of groups at baseline	RCTs with some deficiencies in randomisation e.g. lack of allocation concealment, or nonrandomised studies with either similarities at baseline or use of statistical methods to adjust for any baseline differences	Non randomised, with obvious differences at baseline, and without analytical adjustment for these differences
2. Performance bias:	Differed only in intervention, which was adhered to without contamination, groups were similar for cointerventions or statistical adjustment was made for any differences	Confounding was possible but some adjustment was made in the analysis	Intervention was not easily ascertained or groups were treated unequally other than for intervention or there was non-adherence, contamination or dissimilarities in groups and no adjustments made
3. Measurement bias:	Outcome measured equally in both groups, with adequate length of followup (i.e. at least 2 years after delivery), direct verification of outcome, with data to allow calculation of precision estimates	Inadequate length of follow up or length not given	Inadequate reporting or verification of maternal mortality or differences in measurement in both groups
4. Attrition bias:	No systematic differences in withdrawals between groups and with appropriate imputation for missing values		Incomplete follow-up data, not intention-to-treat analysis or lacking reporting on attrition

the same fashion as published information. In addition to using multiple coders to insure the reproducibility of the overview, sensitivity analyses around important or questionable judgements regarding the inclusion or exclusion of studies, the validity assessments and data extraction will be performed.

Data synthesis

We will use RevMan and Stata softwares to conduct analyses. The former will allow uniformity with Cochrane reviews and the latter will allow the data analytic flexibility that we will need to examine issues not included in the RevMan software. Separate analyses will be performed on randomised and non-randomised data. Any heterogeneity of results between studies will be statistically and graphically assessed, including use of funnel plots. We will explore causes of the heterogeneity and proceed to perform meta-analysis if appropriate. To explore causes of heterogeneity subgroup analyses will be planned a priori to see whether variations in clinical factors e.g. populations, interventions, outcomes or study quality affect the estimation of effects. Individual factors explaining heterogeneity will also be analysed using meta-regression to determine their unique contribution to the heterogeneity. Conclusions regarding the typical estimate of an effect size of the intervention will be interpreted cautiously if there is significant heterogeneity.

5. Review of adverse effect of interventions

In the proposed project addition to the search for relevant reviews and primary studies on effectiveness of interventions including those that were excluded from analysis of benefit, we will evaluate studies that specifically provide details of adverse effects due to the dietary interventions. We will conduct review of harm of interventions based on recommended methods for systematic reviews, particularly those of observational studies and adverse events including those of Cochrane adverse effects subgroup.

Study identification and selection for adverse events

We have purposefully kept the scope of the question of adverse effects of any dietary intervention on pregnant women and their children broad. This will enable us to identify a variety of adverse effects that were previously not known or recognised. The adverse outcomes to be evaluated will be in 3 groups and similar to the outcomes in the effectiveness review, they will be ranked according to their importance: critical for decision-making, important for decision making and not important.

(a) clinically significant adverse maternal outcomes in pregnancy and later due dietary interventions in (i) overweight or obese women and (ii) women with normal weight
(b) clinically significant adverse fetal, neonatal, childhood and adult outcomes in the offspring of pregnant women undergoing dietary interventions
(c) Most common adverse effects that lead to pregnant women discontinuing the intervention

We will design a separate search strategy to identify studies on harm by including adverse effects text words and indexing terms to ensure that they are not missed in the databases previously described. We will use datasets providing counts or proportions attributed to specific interventions or weight change in pregnancy leading to maternal and fetal adverse outcomes, from direct counting or from special surveys. We use the term dataset because some sources are research studies but others are direct counts or other forms of routine data collection (such as vital registration; membership of weight reduction club, web table). We will include only those datasets that represent the target population in the final analysis. In cases of partial data duplication with overlapping datasets, we will select the most recent and largest dataset.

Study quality assessment and data extraction for adverse events

Criteria used to assess study quality will follow the same concept as for assessing study quality for effectiveness: assessing risk of bias, inconsistency of results, indirectness of the evidence, imprecision and publication bias. For assessing the risk of bias in estimating adverse event rates associated with dietary intervention in pregnancy, we will take into account existing checklists for evaluation of randomised and non-randomised studies, including study design and other features associated with outcome (e.g. small for gestational age, pre term delivery etc). For the three possible designs (RCTs, observational studies with a control group, and observational studies without controls (case series)) quality assessment and presentation of results will be done separately. Additionally, information on weight change per se on mother and baby will also be extracted as these could be associated with adverse event rates or severity. The methodological quality of all eligible datasets ('risk of bias') will be assessed to investigate internal validity (the extent to which the information is probably free of bias) with the following attributes:

1. reporting of adverse maternal and fetal outcome definition to reduce bias in ascertainment of denominator data in the series (any published definition reported *Vs* no definition)
2. adequacy of data source to ascertain a capture of denominator data that is as complete as possible (use of multiple data sources, special surveys, or clinical studies *vs* routine registration enrolment in weight loss programmes, in which adequate attribution of cause of harm has been shown to be questionable for maternal and fetal outcomes, leading to substantial underreporting)
3. use of a robust approach to ascertain that the cause of harm is a representation of the underlying condition that is as true as possible (confidential enquiries, use of multiple sources of outcome vs no special efforts to confirm cause)
4. sufficiently high proportion of cases with attributable cause of harm established (< 5% unclassified).

Quality assessment will be done for each outcome. Randomised studies will start as high quality, observational studies with controls will start as low quality, and uncontrolled studies will start as very low quality. The evidence will be downgraded in the presence of methodological weaknesses and uncertainty; it can be upgraded in the presence of large effects, dose–response gradient and remaining plausible confounding which would reduce a demonstrated effect. Based on these criteria, the datasets will be classified into different quality groups.

Data synthesis for adverse events

The number of adverse events reported in pregnant women and children will be obtained for each intervention to compute a percentage of the total number of women and children in whom the occurrence of that particular adverse event or confirmation of its absence was reported. It is inappropriate to calculate adverse events rates from case studies, thus a qualitative summary will be undertaken. Quantitative adverse events rates calculations will be restricted to series of women undergoing dietary interventions and weight change as identified from RCTs and observational studies, with and without controls (case series). We shall quantify the adverse events as relative risks and 95% confidence intervals. The point estimates of proportions and their 95% CIs will be represented in forest plots to explore heterogeneity and the possibility of the differences being due to chance assessed statistically by Cochran Q test. To explore the presence of heterogeneity and its causes, regression models will be adjusted to the proportions attributed to every individual cause of maternal and fetal complications. The proportions will be transformed with the logit transformation. Explanatory variables considered in these models are: type of intervention and dataset methodological quality items.

6. Evidence Synthesis using the GRADE methodology

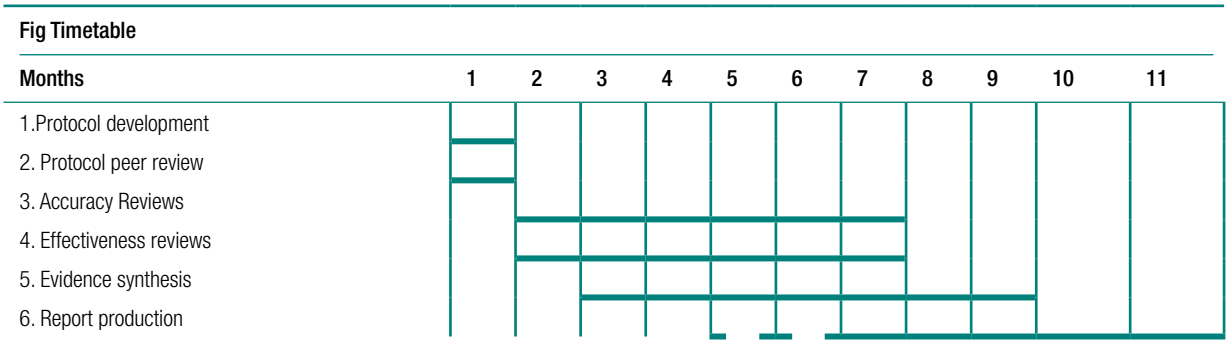
Once the systematic reviews for effectiveness and harm of dietary interventions have been undertaken, we shall prepare standardised evidence profiles using the GRADE profiling software GRADEPro. Profiles will be done for both groups (obese or overweight women and normal weight women at risk of excessive weight gain), with a separate quality assessment and summary of findings for each critical and important outcome that will allow a quick and informative summary of the evidence.

The following steps will be undertaken to come to an overall judgement: having assessed the quality of evidence for each maternal and fetal outcome, and having decided on the relative importance of the outcomes (critical or important to a decision), we will come up with a judgement on the overall quality of evidence *across the most important* outcomes, balancing net benefits and harms.

7. Project timetable

Figure shows the project timetable and milestones for the accuracy and effectiveness reviews and economic modelling.

Fig Timetable



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Feedback

The HTA programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (www.hta.ac.uk) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

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