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Ceysens G, Rouiller D, Boulvain M.
Exercise for diabetic pregnant women.
Cochrane Database of Systematic Reviews 2006, Issue 3. Art. No.: CD004225.
DOI: 10.1002/14651858.CD004225.pub2.

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[Intervention Review]

Exercise for diabetic pregnant women

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Editorial group: Cochrane Pregnancy and Childbirth Group.
Publication status and date: Edited (no change to conclusions), published in Issue 1, 2010.

Citation: Ceysens G, Rouiller D, Boulvain M. Exercise for diabetic pregnant women. *Cochrane Database of Systematic Reviews* 2006, Issue 3. Art. No.: CD004225. DOI: 10.1002/14651858.CD004225.pub2.

ABSTRACT

Background

Diabetes in pregnancy may result in unfavourable maternal and neonatal outcomes. Exercise was proposed as an additional strategy to improve glycaemic control. The effect of exercise during pregnancies complicated by diabetes needs to be assessed.

Objectives

To evaluate the effect of exercise programs, alone or in conjunction with other therapies, compared to no specific program or to other therapies, in pregnant women with diabetes on perinatal and maternal morbidity and on the frequency of prescription of insulin to control glycaemia. To compare the effectiveness of different types of exercise programs on perinatal and maternal morbidity.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 December 2005). We updated this search on 1 October 2009 and added the results to the awaiting classification section.

Selection criteria

All known randomised controlled trials evaluating the effect of exercise in diabetic pregnant women on perinatal outcome and maternal morbidity.

Data collection and analysis

We evaluated relevant studies for meeting the inclusion criteria and methodological quality. Three review authors abstracted the data. For all data analyses, we entered data based on the principle of intention to treat. We calculated relative risks and 95% confidence intervals for dichotomous data.

Main results

Four trials, involving 114 pregnant women with gestational diabetes, were included in the review. None included pregnant women with type 1 or type 2 diabetes. Women were recruited during the third trimester and the intervention was performed for about six weeks. The programs generally consisted in exercising three times a week for 20 to 45 minutes. We found no significant difference between exercise and the other regimen in all the outcomes evaluated.

Authors' conclusions

There is insufficient evidence to recommend, or advise against, diabetic pregnant women to enrol in exercise programs. Further trials, with larger sample size, involving women with gestational diabetes, and possibly type 1 and 2 diabetes, are needed to evaluate this intervention.

[Note: The six citations in the awaiting classification section of the review may alter the conclusions of the review once assessed.]

PLAIN LANGUAGE SUMMARY

Exercise for diabetic pregnant women

Insufficient information available to recommend or advise against diabetic pregnant women enrolling on exercise programs.

Exercise was proposed to improve glycaemic control in pregnant women with diabetes. Four small trials involving 114 pregnant women evaluated this intervention. None included pregnant women with type 1 or type 2 diabetes. There is insufficient evidence to recommend, or advise against, diabetic pregnant women enrolling in exercise programs. Further trials, with larger sample size, are needed.

BACKGROUND

Diabetes is a disturbance of multiple metabolic pathways, but it is the effects on carbohydrate metabolism that are most apparent. The different types of disorder of carbohydrate metabolism are all characterised by hyperglycaemia (high blood glucose level). In the short term, this can lead to coma associated with hyperglycaemia or, if there is over treatment, coma associated with hypoglycaemia (low blood glucose). Long-term complications can involve blood vessels, eyes, kidneys or the neurological system. In pregnancy, there are three types of diabetes:

1. insulin-dependent, or type 1 diabetes. This is diabetes beginning before pregnancy and is characterised by beta islet cell autoimmunity leading to destruction of the insulin producing cells in the pancreas.
2. non-insulin-dependent, or type 2 diabetes characterised by diabetes beginning before pregnancy and an inability of the pancreas to cope with a rise in insulin resistance.
3. gestational diabetes mellitus, defined as "carbohydrate intolerance with onset or first recognition during pregnancy" (Metzger 1991). Various definitions of carbohydrate intolerance exist. There is, therefore, widespread variation in the classification of gestational diabetes. Diagnosis is generally based on an abnormal oral glucose tolerance test (GTT). A GTT requires women to fast overnight before attending the hospital the following morning. Usually, four blood samples are taken. The first is taken on arrival and the woman is then given a sugary drink containing 75 g of glucose (100 g is more commonly used in the United States). The following blood samples are taken hourly (three more samples). The precise diagnostic values of the GTT are controversial (Weiss 1998) making it difficult to provide a clear definition of gestational diabetes. Values between 8 to 11 mmol/l are termed 'impaired glucose tolerance'. Current World Health Organization recommendations suggest that all abnormal glucose metabolism arising in pregnancy should be defined as gestational diabetes (Alberti 1998).

In pregnancies not complicated by diabetes, the risks and benefits of exercise are still not well-known. A Cochrane review (Kramer 2002) concluded that regular aerobic exercise appears to improve (or maintain) physical fitness but available data are insufficient to exclude important benefits and risks for the mother or infant. These conclusions may not apply in pregnant women with diabetes and the effect of exercise may differ according to type of diabetes.

Type 1 diabetes requires insulin therapy adjusted with dietary control and physical activity to achieve and maintain a normal blood glucose level. Among women with type 1 diabetes, who are not pregnant, the response to exercise is mainly influenced by the degree of diabetes control. Well-controlled diabetic women may derive benefit from regular physical activity, provided that they know how to adjust their insulin dose and carbohydrate intake (Berger 1977). Diabetic women with poor glycaemic control should avoid exercise because of the increased risk of hyperglycaemia, ketosis and worsening of vascular complications. During pregnancy, these women have an increased risk of fetal malformation, miscarriage, pre-eclampsia, late fetal death and macrosomia. Moreover, the risk of diabetic ketoacidosis is increased because of the less predictable effect of a given dose of insulin and an accelerated state of starvation. As ketoacidosis has been associated with high perinatal mortality (Lufkin 1984), exertion in type 1 diabetic pregnant women may increase the risk for the fetus.

Exercise as well as diet and weight-loss (and insulin when needed) is part of the treatment of type 2 diabetes. The effects of diet and insulin have been recently evaluated in another Cochrane review (Tuffnell 2003). The biochemical effect of exercise (in addition to diet and insulin) in type 2 non-pregnant diabetic patients is to normalize blood glucose levels (Tuomilehto 2001). This suggests that during pregnancy exercise could also reduce the risk of complications related to high blood glucose and high insulin levels, including macrosomia (big baby according to his age), birth trauma, respiratory distress, neonatal hypoglycaemia and hypocalcaemia.

Some of the perinatal complications seen in established diabetes are also found in pregnancies with gestational diabetes. Also, some of the abnormalities of insulin secretion and action that characterize type 2 diabetes have also been identified in gestational diabetes (Carpenter 1995). This suggests that regular physical exercise may normalize maternal blood glucose for pregnant women with gestational diabetes. As the first treatment of gestational diabetes is diet, the addition of exertion may, as in type 2 diabetes, prevent the administration of insulin. This benefit may be of relevance for pregnant women reluctant to start subcutaneous insulin injection, especially when considering that the gestational diabetes generally resolves spontaneously at delivery. Indirectly, as the women who suffer from gestational diabetes are at increased risk of developing type 2 diabetes in the future, exercise may also prevent this long-term complication (Manson 1991; Tuomilehto 2001).

As some doctors incorporate advice about exercise during pregnancy into their management of women with gestational diabetes (Gabbe 2004), the effect of exercise during pregnancies complicated by diabetes needs to be assessed. Although transient, gestational diabetes has a deleterious effect on birth outcome. Because of the added burden that diabetes brings to the pregnancy, every effort should be made to determine the best management strategies. Additionally, a behavioural change in life style, such as diet or exercise, may persist after delivery and help prevent or delay the development of type 2 diabetes and its long-term complications (Tuomilehto 2001).

The aim of the treatment is to reduce the complications of diabetes. As improvement in blood sugar control may not be directly related to pregnancy outcome, we will not evaluate the effect of exercise on blood sugar but on its maternal and fetal complications.

OBJECTIVES

- To evaluate the effect of exercise programs alone or in conjunction to other therapies such as diet, compared to no specific program or to other therapies, in diabetic pregnant women on perinatal and maternal morbidity and mortality.
- To evaluate the effect of exercise programs on the frequency of prescription of insulin to control glycaemia.
- To compare the effectiveness of different types of exercise programs on perinatal and maternal mortality and morbidity.

METHODS

Criteria for considering studies for this review

Types of studies

All known randomised controlled trials comparing any exercise program (as defined by trial authors) to no specific exercise program in diabetic pregnant women. Studies where the allocation was based on methods that are liable to selection bias (for example, allocation by date of birth, chart number) were not included. Comparison of interrupted time series (before and after studies) were also not included.

Types of participants

Pregnant women with diabetes. A planned subgroup analysis based on the type of diabetes (that is, type 1, type 2, or gestational diabetes mellitus) was not performed because we found no study that included women with type 1 or type 2 diabetes.

Types of interventions

Studies comparing any type of exercise program with no exercise program or other therapy. We found no studies comparing different exercise programs in pregnant women with diabetes. Type, frequency, intensity and duration of the exercise vary between studies. We have classified the various exercise programs in two categories predefined as low-level and high-level exercise programs. We have considered a cumulative duration of exercise at 50% VO2 max (maximal oxygen consumption - being a measure of oxygen consumption and therefore of aerobic exercise) of less than 180 minutes (or equivalent intensity of exercise) as a low-level intervention, and a cumulative duration equal to or more than 180 minutes (or equivalent) as a high-level intervention. This was arbitrarily decided, but we believe that as an exercise session usually lasts thirty minutes, a cumulative duration of 180 minutes would mean at least six sessions, two or three times a week so the treatment would last at least two or three weeks. Intensity, duration and timing (gestational age at the start and stopping) of the intervention were extracted from the reports and included in the 'Characteristics of included studies' table. For gestational diabetes, most women were included during the third trimester because the diagnosis was usually made at that time. Ordinary day-to-day activity such as walking or gardening was not considered as a formal exercise program. In all the studies found, diet was part of the routine care and was similar between the intervention and the control groups.

Types of outcome measures

The primary outcomes were caesarean section, perinatal death (death occurring during pregnancy or the first six days of life), admission and length of stay in neonatal intensive care unit.

Perinatal outcomes

- Macrosomia (usually defined as birthweight exceeding 4000 g or exceeding the 90th percentile)
- Small-for-gestational age (birthweight less than the 10th percentile for gestational age)
- Respiratory distress syndrome
- Congenital malformations
- Neonatal hypoglycaemia
- Hypocalcaemia
- Birth injury (shoulder dystocia, fractured clavicle, brachial plexus injury, intracranial haemorrhage)
- Hyperbilirubinaemia (usually defined as bilirubinaemia exceeding 12 or 15 mg/dl)

Pregnancy complications

- Preterm labour (less than 37 weeks of gestation)
- Hydramnios
- Oligamnios
- Pre-eclampsia (a disease characterized by the association of hypertension, proteinuria and oedema during pregnancy)
- Hypertension
- Diabetic ketoacidosis
- Instrumental delivery and caesarean section
- Maternal mortality

Maternal morbidity

- Postoperative infection
- Transfusion
- Admission to intensive care unit
- Use of insulin
- Women's views on their care

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (31 December 2005). We updated this search on 1 October 2009 and added the results to Studies awaiting classification.

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

We did not apply any language restrictions.

Data collection and analysis

Selection of studies

Trials under consideration were evaluated according to the inclusion criteria without consideration of their results. Any disagreements were resolved by discussion.

Data extraction and management

We have independently extracted information from the included studies. Any discrepancies were resolved by discussion. Wherever possible, missing data were sought from the authors.

Assessment of risk of bias in included studies

Three review authors reviewed relevant studies for methodological quality.

(1) Selection bias (randomisation and allocation concealment)

We have assigned a quality score for each trial, using the following criteria:
(A) adequate concealment of allocation: such as telephone randomisation, consecutively numbered sealed opaque envelopes;
(B) unclear whether adequate concealment of allocation: such as list or table used, sealed envelopes, or study does not report any concealment approach;
(C) inadequate concealment of allocation: such as open list of random number tables, use of case record numbers, dates of birth or days of the week.

(2) Attrition bias (loss of participants, for example, withdrawals, dropouts, protocol deviations)

We will assess completeness to follow up using the following criteria:
(A) less than 5% loss of participants;
(B) 5% to 9.9% loss of participants;
(C) 10% to 19.9% loss of participants;
(D) more than 20% loss of participants.

(3) Performance bias (blinding of participants, researchers and outcome assessment)

We will assess blinding using the following criteria:

1. blinding of participants (yes/no/unclear);
2. blinding of caregiver (yes/no/unclear);
3. blinding of outcome assessment (yes/no/unclear).

Measures of treatment effect

We have carried out statistical analysis using the Review Manager software (RevMan 2003). We used fixed-effect meta-analysis for combining data in the absence of significant heterogeneity if trials were sufficiently similar. If heterogeneity had been found this would have been explored by sensitivity analysis followed by random-effects if required.

Dichotomous data: we have presented results as summary relative risk with 95% confidence intervals.
Continuous data: we have used the weighted mean difference if outcomes are measured in the same way between trials. We used the standardised mean difference to combine trials that measured the same outcome, but used different methods.

Dealing with missing data

We analysed data on all participants with available data in the group to which they were allocated, regardless of whether or not they received the allocated intervention. If in the original reports participants were not analysed in the group to which they were randomised, and there was sufficient information in the trial report, we planned to restore them to the correct group.

Assessment of heterogeneity

We have applied tests of heterogeneity between trials, when appropriate, using the I-squared statistic. When we identified high levels of heterogeneity among the trials, (exceeding 50%), we explored it, when appropriate, by prespecified subgroup analysis and planned to perform sensitivity analysis. A random-effects meta-analysis was used as an overall summary as considered appropriate.

Subgroup analysis and investigation of heterogeneity

We planned to carry out the following subgroup analyses:

- type of diabetes;
- type of exercise program.

Only women with gestational diabetes were included. We found no study that included women with type 1 or type 2 diabetes.
As all trials were of small size, the analysis has small power to detect any difference in the effect of exercise programs.

Sensitivity analysis

We planned to carry out sensitivity analysis to explore the effect of trial quality assessed by concealment of allocation, by excluding studies with clearly inadequate allocation of concealment (rated C). As all four studies were rated B (unclear) and no one rated C, we did not perform a sensitivity analysis.

RESULTS

Description of studies

Included studies

Four trials involving 114 women with gestational diabetes were included in the review. None of the trials included women with type 1 or type 2 diabetes mellitus. Jovanovic 1989 included 10 women in the exercise group and nine in the control group; Bung 1991 17 women in each group, Avery 1997 15 women in the experimental group and 14 women in the control group, and Brankston 2004 16 women in each group. *See* Characteristics of included studies for details.

All trials included pregnant women with gestational diabetes mellitus. Women were recruited during the third trimester of pregnancy and the intervention was performed for about six weeks. The programs consisted of exercising three to four times weekly on a cycle ergometer at 70% VO2 max for 30 minutes (Avery 1997), in cycling for 45 minutes three times weekly at 50% VO2 max (Bung 1991), 20 minutes training on an arm ergometer three times a week (Jovanovic 1989) and 30 minutes circuit type resistance training three times a week (Brankston 2004). As all studies proposed high-level exercise programs, according to our classification, we found no study of low-level intensity. We cannot therefore compare the effect of high-level and low-level intensity programs. In all

studies, women in both intervention and control group were on diet therapy.

Many of the outcomes prespecified for this review, especially those related to the newborn, were not reported by the authors of three of the four trials (Avery 1997; Brankston 2004; Jovanovic 1989). Brankston 2004 reported only the percentage of women receiving insulin therapy, but we are waiting for additional data. Bung 1991 reported most of those outcomes, but the study is of small size. As all trials were of small size, the analysis has small power to detect any difference in the effect of exercise programs.

(Six reports from an updated search in October 2009 have been added to Studies awaiting classification)

Excluded studies

Three trials were excluded (Chen 1997; Garcia-Paterson 2001; Lesser 1996). *See* Characteristics of excluded studies for details.

Risk of bias in included studies

Avery 1997 used randomisation based on a table of random numbers arranged in blocks. No information regarding method of randomisation is given in Bung 1991. Jovanovic 1989, randomised by drawing a number one or two referring to the allocation group. In all three trials, no details on the method of concealment of allocation was given.

Bung 1991 had a large number of exclusions, four (19%) in the exercise group and three (15%) in the insulin group. Brankston 2004 included 38 women, but six women from the exercise group were excluded because of hypertension (3) or no compliance to the intervention (3). The reported analysis includes 32 women (information on the six women excluded was sought from the authors, to be able to perform an intent-to-treat analysis). There were apparently no exclusions in the other studies.

The nature of the intervention did not allow blinding of the women and, probably, also blinding of the physicians.

Effects of interventions

Four trials involving 114 women with gestational diabetes were included in the review. None of the trials included women with type 1 or type 2 diabetes mellitus.

The outcomes prespecified for this review that were not reported in any of the studies are not listed in the comparison and data section. The outcome 'use of insulin therapy' was only reported by Avery 1997 and Brankston 2004, where the difference between the two groups was not significant (relative risk 0.98; 95% confidence interval 0.51 to 1.87). No woman required insulin therapy in the study by Jovanovic 1989. In Bung 1991, exercise was compared to insulin treatment; therefore, this study was included in a separate analysis (diet + exercise versus diet + insulin).

The occurrence of macrosomia was defined in two of the trials as birthweight greater than 4000 g (Avery 1997; Bung 1991). No information was given in the third trial (Jovanovic 1989).

We found no significant difference between exercise and no exercise and between exercise and insulin in all the outcomes evaluated.

DISCUSSION

Many of the outcomes prespecified were not evaluated in three of the four trials (Avery 1997; Brankston 2004; Jovanovic 1989). Limited information is available regarding neonatal outcomes. Most were only evaluated in one trial (Bung 1991), giving a small sample for the analysis. We are waiting for additional data from Brankston 2004. As, in Bung 1991 insulin was an intervention and not an outcome, we analysed the results separately. We acknowledge that the outcomes we sought to evaluate are infrequent and so the power of the only study that reported them is limited. But these outcomes are those we try to prevent when treating pregnant women with diabetes; it is thus important to evaluate the effects of exercise on these clinically relevant outcomes. Only one report described the methods used for concealment of allocation (Brankston 2004).

Only women with gestational diabetes were included. We found no study that included women with type 1 or type 2 diabetes. The effect of exercise may be similar in women with type 2 and gestational diabetes, but may be different in women with type 1 diabetes. Exercise in pregnant women with type 1 diabetes may be harmful because of the increased risk of ketoacidosis, thus it may not be safe to initiate a trial in that subgroup of pregnant women. It would be important that further studies of larger sample size involving pregnant women with type 2 and gestational diabetes be initiated, given that some clinicians include exercise in their management of women with gestational diabetes without evidence that this is beneficial.

AUTHORS' CONCLUSIONS

Implications for practice

There is insufficient evidence to recommend, or advise against, diabetic pregnant women enrolling in exercise programs. Even if exercise is not beneficial during pregnancy, this change in life style may persist after delivery and may help prevent the onset of type 2 diabetes and its long-term complications. Therefore, women may enrol in exercise programs, if they wish to do so.

Implications for research

Further trials with larger sample sizes involving women with gestational diabetes, and possibly type 2 diabetes, are needed to evaluate this intervention. A useful, relevant and relatively frequent outcome measure may be 'use of insulin'. Researchers, however, must be aware of a potential bias in the prescription of insulin, given the impossibility to blind caregivers as to the group allocation in this context.

[Note: The six citations in the awaiting classification section of the review may alter the conclusions of the review once assessed.]

ACKNOWLEDGEMENTS

As part of the pre-publication editorial process, this review has been commented on by three peers (an editor and two referees who are external to the editorial team), one or more members of the Pregnancy and Childbirth Group's international panel of consumers and the Group's Statistical Adviser.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Avery 1997

Methods	Randomisation: table of random numbers arranged in blocks. Concealment of allocation: no details.
Participants	29 women at 34 weeks' gestation, or less, with gestational diabetes mellitus.
Interventions	Experimental (n = 15): 30 min exercise 3-4 x/week + supervised exercise on cycle ergometer at 70% VO2 max 2 x/week + unsupervised 30 min exercise by cycling or walking at same exercise intensity. Control (n = 14): usual physical activity. Women in both groups were given dietary advice.
Outcomes	Women: hypertension, caesarean section, use of insulin therapy, mean haemoglobin A1C at four weeks. Babies: gestational age at delivery, premature delivery, stillbirth, neonatal death, macrosomia, birth-weight, 5 minute Apgar < 7.
Notes	Classified as high-level exercise program (the cumulative time of exercise at minimum 50% VO2max exceed 180 minutes).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Brankston 2004

Methods	Randomisation: table of random numbers. Concealment of allocation: opaque sealed envelopes.
Participants	38 women at 26 to 32 weeks' gestation, with gestational diabetes mellitus.
Interventions	Experimental (n = 16): 3 sessions of a circuit of 8 exercises repeated until felt "somewhat hard". Control (n = 16): asked not to start a specific exercise program. Women in both groups were given dietary advice.
Outcomes	Use of insulin therapy.
Notes	Additional information requested.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Bung 1991

Methods	No details on the method of randomisation nor on the method of concealment of allocation.
Participants	34 pregnant women, at less than 33 weeks of gestation, with gestational diabetes mellitus.
Interventions	Experimental group n = 17: diet (30 kcal/kg/day) and cycling for 45 minutes, three times a week, at 50% VO2 max (17 women). Control group n = 17: diet (30 kcal/kg/day) and insulin therapy (17 women).
Outcomes	Gestational age at delivery, premature delivery, stillbirth, neonatal death, macrosomia, birthweight, small for date, respiratory distress syndrome, congenital malformation, 5 minute Apgar < 7, neonatal hypoglycaemia, preterm labour, induction of labour, caesarean section, instrumental delivery, use of insulin therapy.
Notes	Bung 1993 is just another citation to the included study (Bung 1991) and the outcomes were related to glycemic control rather than clinical outcomes. Classified as high-level exercise program (the cumulative time of exercise at minimum 50% VO2max exceed 180 minutes).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Jovanovic 1989

Methods	Randomisation by drawing a number (1 or 2). No details on the method of concealment of allocation.
Participants	19 pregnant women with gestational diabetes mellitus.

Jovanovic 1989 *(Continued)*

Interventions	Experimental group n = 10: 6 week program of dietary therapy of 24 to 30 kcal/kg/day (40% carbohydrates, 20% protein and 40% fat) and 20 minutes training on an arm ergometer, three times a week (10 women). Control group (n = 9): same diet but no exercise.
Outcomes	Gestational age at delivery, premature delivery, stillbirth, neonatal death, birthweight, use of insulin therapy, response to the glucose challenge test (plasma glucose level 1 hour after 50 g oral glucose) after the training program, fasting plasma glucose after the training program.
Notes	Classified as high-level exercise program (the cumulative time of exercise at minimum 50% VO2max exceed 180 minutes).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

min: minutes
RCT: randomised controlled trial
VO2max: maximal oxygen consumption

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Chen 1997	9 women; 4 with exercise and 5 without. No clinical outcome is reported, only the area under the glucose curve.
Garcia-Paterson 2001	20 women; cross-over trial comparing glucose measurements during one day with light post-prandial exercise with those of one day without exercise; no clinical outcome reported, not possible anyway with this design.
Lesser 1996	The study evaluates the effect of a single exercise session (30 minutes cycling at 60% VO2 max) on fasting glycaemia and insulin concentration and glycaemic and insulin excursion following a mixed nutrient meal in women with gestational diabetes secondary to a postexertional increase in insulin sensitivity. The authors did not evaluate the effect of chronic exercise on any of the outcomes we specified.

VO2 max: maximal oxygen consumption

DATA AND ANALYSES

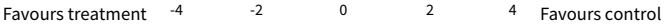
Comparison 1. Exercise and diet versus diet alone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Gestational age at delivery	1	29	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-1.07, 0.47]
2 Preterm delivery (< 37 weeks)	2	48	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Use of insulin therapy	3	80	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.51, 1.87]
4 Caesarean section	1	29	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.22, 3.88]
5 Birthweight at delivery	2	48	Mean Difference (IV, Random, 95% CI)	1.41 [-349.63, 352.45]
6 Macrosomia (> 4000 g)	1	29	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.22, 3.88]
7 Apgar < 7 at 5 minutes	1	29	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Stillbirth	2	48	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

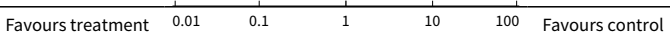
Analysis 1.1. Comparison 1 Exercise and diet versus diet alone, Outcome 1 Gestational age at delivery.

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Avery 1997	15	39.4 (1.2)	14	39.7 (0.9)		100%	-0.3[-1.07,0.47]
Total * **	**15**		**14**			**100%**	**-0.3[-1.07,0.47]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.76(P=0.44)							



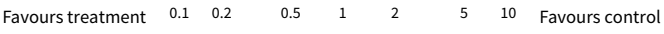
Analysis 1.2. Comparison 1 Exercise and diet versus diet alone, Outcome 2 Preterm delivery (< 37 weeks).

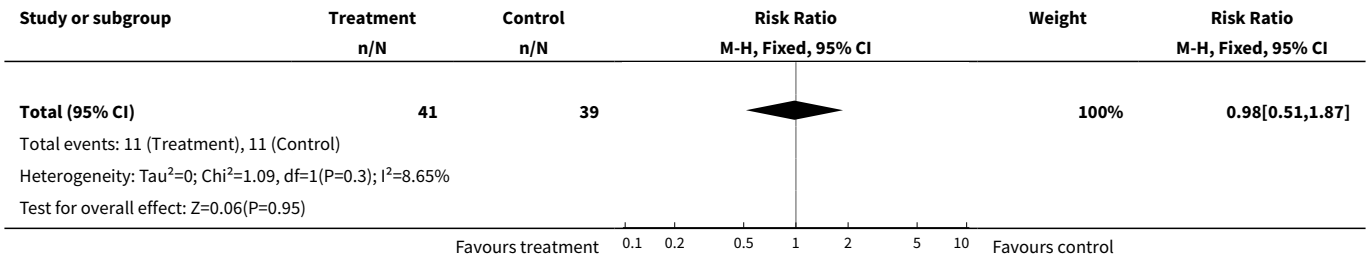
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Avery 1997	0/15	0/14			Not estimable
Jovanovic 1989	0/10	0/9			Not estimable
Total (95% CI)	**25**	**23**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



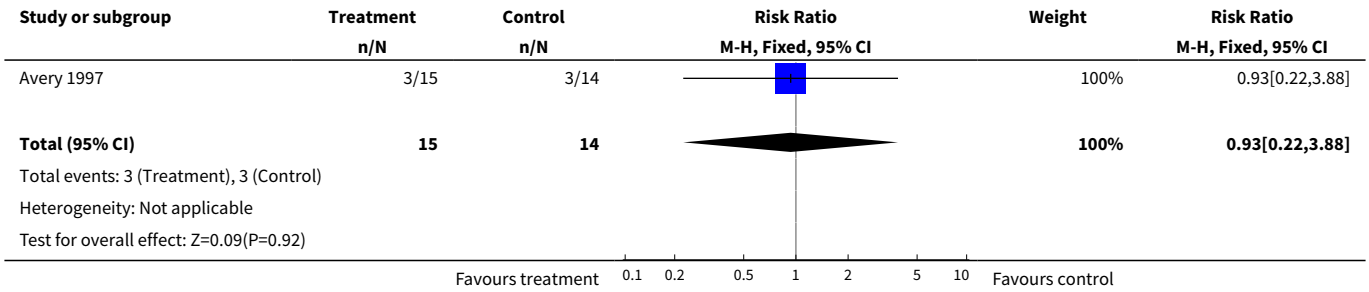
Analysis 1.3. Comparison 1 Exercise and diet versus diet alone, Outcome 3 Use of insulin therapy.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Avery 1997	4/15	2/14		18.69%	1.87[0.4,8.65]
Brankston 2004	7/16	9/16		81.31%	0.78[0.38,1.57]
Jovanovic 1989	0/10	0/9			Not estimable

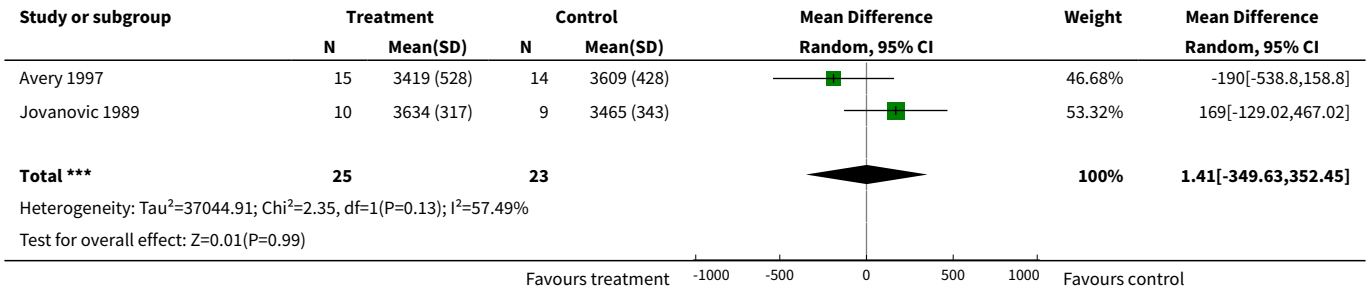




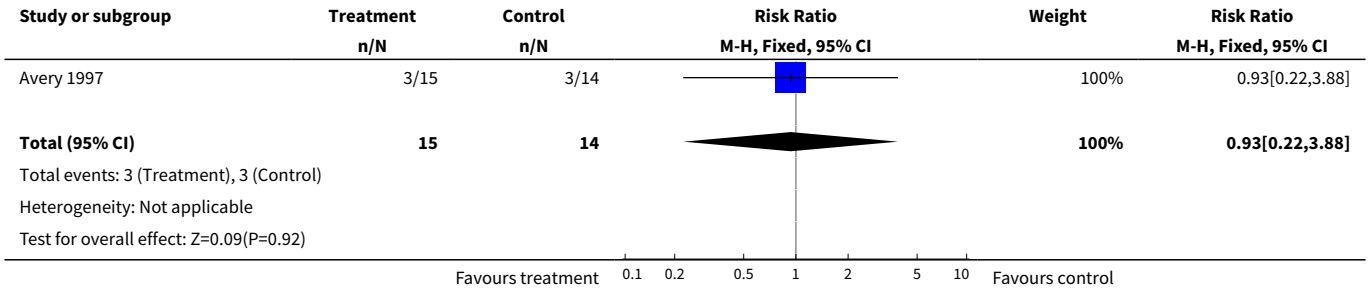
Analysis 1.4. Comparison 1 Exercise and diet versus diet alone, Outcome 4 Caesarean section.



Analysis 1.5. Comparison 1 Exercise and diet versus diet alone, Outcome 5 Birthweight at delivery.

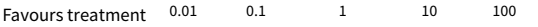


Analysis 1.6. Comparison 1 Exercise and diet versus diet alone, Outcome 6 Macrosomia (> 4000 g).



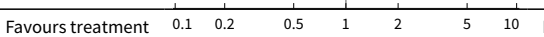
Analysis 1.7. Comparison 1 Exercise and diet versus diet alone, Outcome 7 Apgar < 7 at 5 minutes.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Avery 1997	0/15	0/14			Not estimable
Total (95% CI)	**15**	**14**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



Analysis 1.8. Comparison 1 Exercise and diet versus diet alone, Outcome 8 Stillbirth.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Avery 1997	0/15	0/14			Not estimable
Jovanovic 1989	0/10	0/9			Not estimable
Total (95% CI)	**25**	**23**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

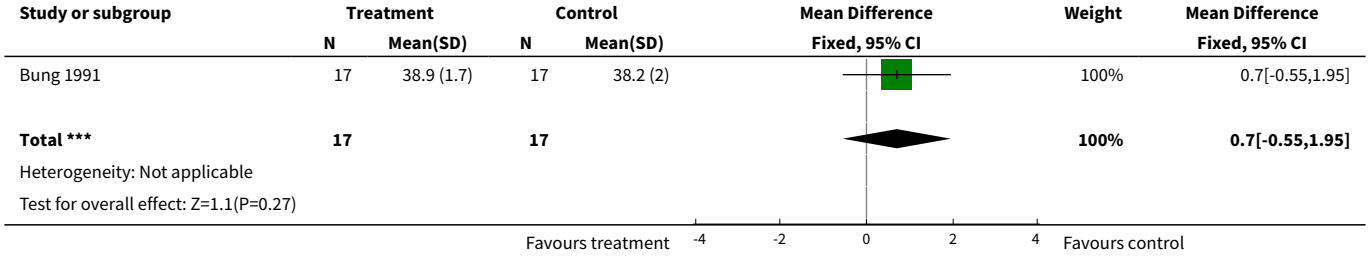


Comparison 2. Diet + exercise versus diet + insulin (not prespecified)

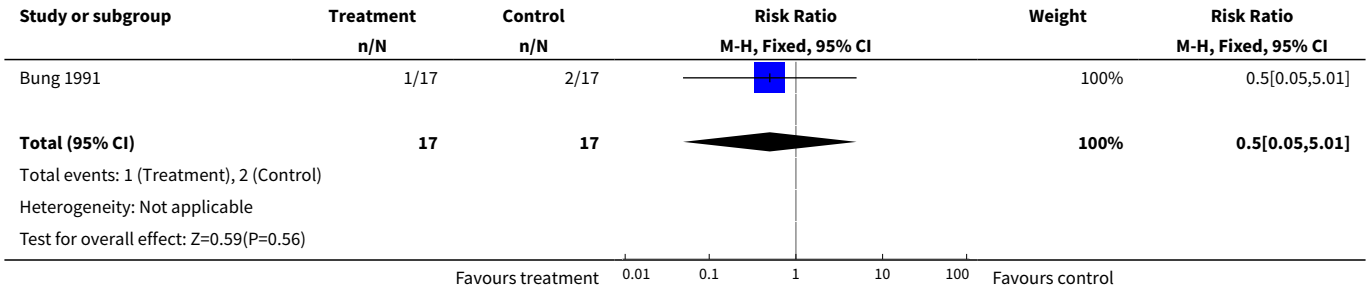
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Gestational age at delivery	1	34	Mean Difference (IV, Fixed, 95% CI)	0.70 [-0.55, 1.95]
2 Preterm delivery (< 37 weeks)	1	34	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.05, 5.01]
3 Preterm labour	1	34	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.16, 6.30]
4 Induction of labour	1	34	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.05, 5.01]
5 Caesarean section	1	34	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.13, 3.50]
6 Instrumental delivery	1	34	Risk Ratio (M-H, Fixed, 95% CI)	0.2 [0.01, 3.88]
7 Birthweight at delivery	1	34	Mean Difference (IV, Fixed, 95% CI)	-113.0 [-461.40, 235.40]
8 Macrosomia (> 4000 g)	1	34	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.11, 2.38]
9 Small-for-gestational age	1	34	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Neonatal hypoglycaemia	1	34	Risk Ratio (M-H, Fixed, 95% CI)	2.0 [0.20, 20.04]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
11 Apgar < 7 at 5 minutes	1	34	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 7.65]
12 Stillbirth	1	34	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Congenital malformation	1	34	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 7.65]

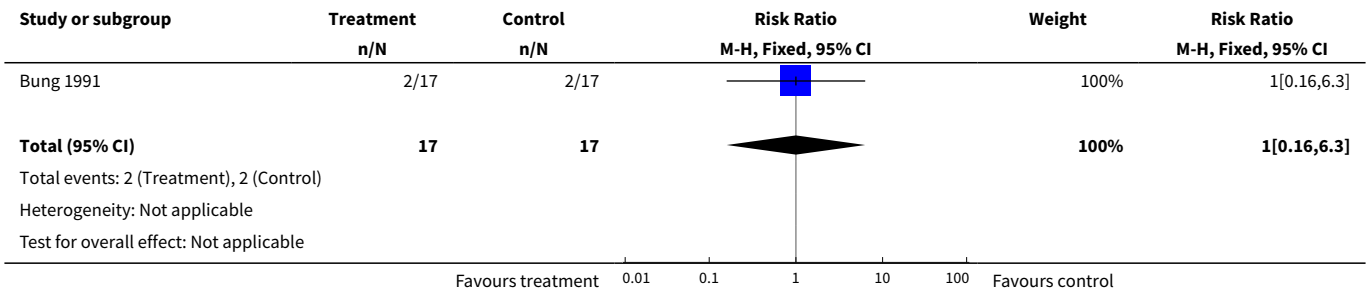
Analysis 2.1. Comparison 2 Diet + exercise versus diet + insulin (not prespecified), Outcome 1 Gestational age at delivery.



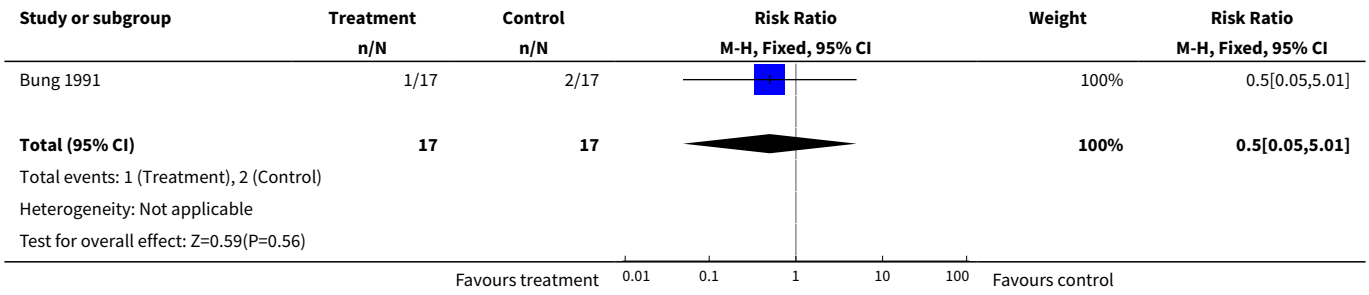
Analysis 2.2. Comparison 2 Diet + exercise versus diet + insulin (not prespecified), Outcome 2 Preterm delivery (< 37 weeks).



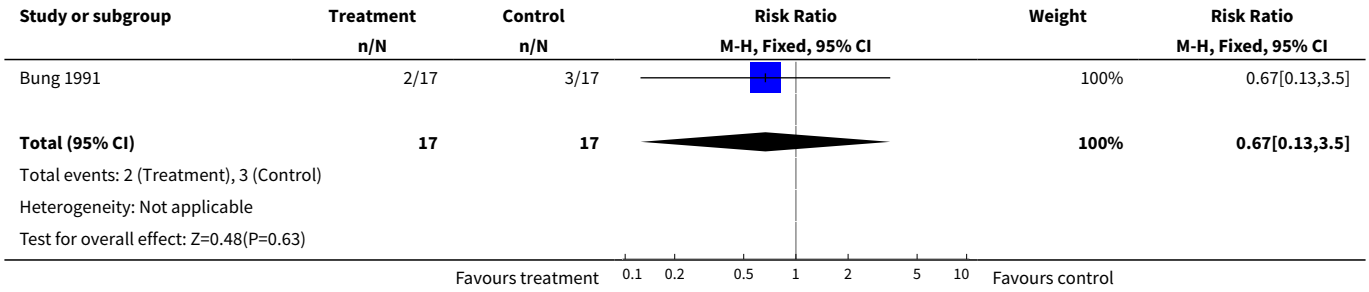
Analysis 2.3. Comparison 2 Diet + exercise versus diet + insulin (not prespecified), Outcome 3 Preterm labour.



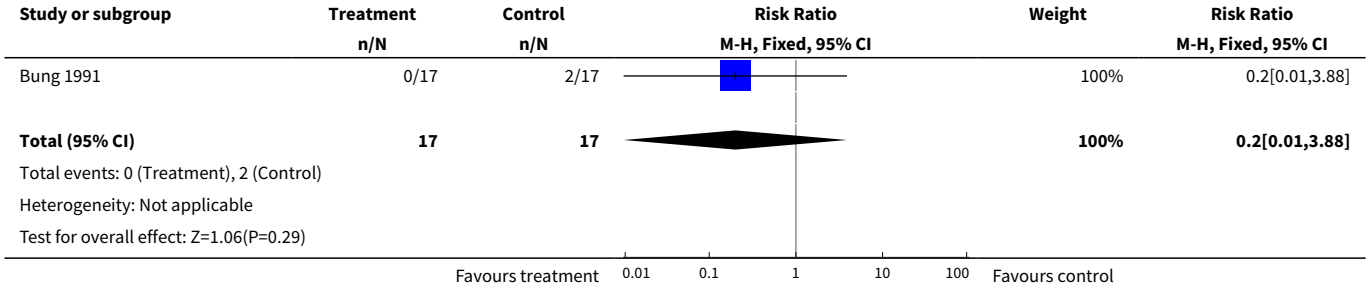
Analysis 2.4. Comparison 2 Diet + exercise versus diet + insulin (not prespecified), Outcome 4 Induction of labour.



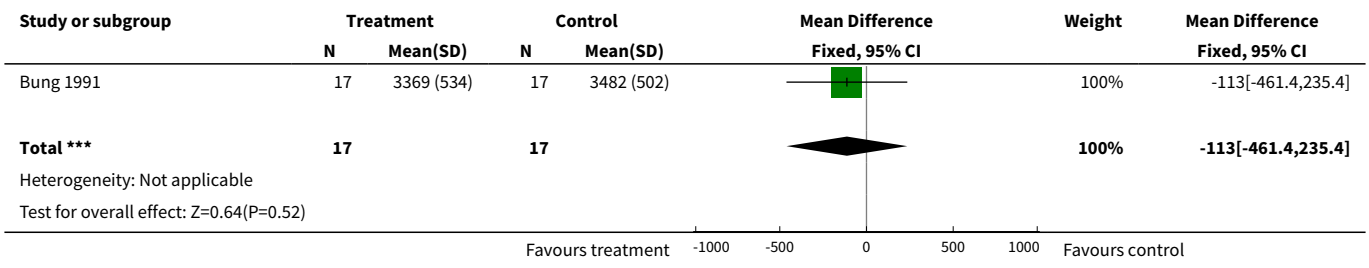
Analysis 2.5. Comparison 2 Diet + exercise versus diet + insulin (not prespecified), Outcome 5 Caesarean section.



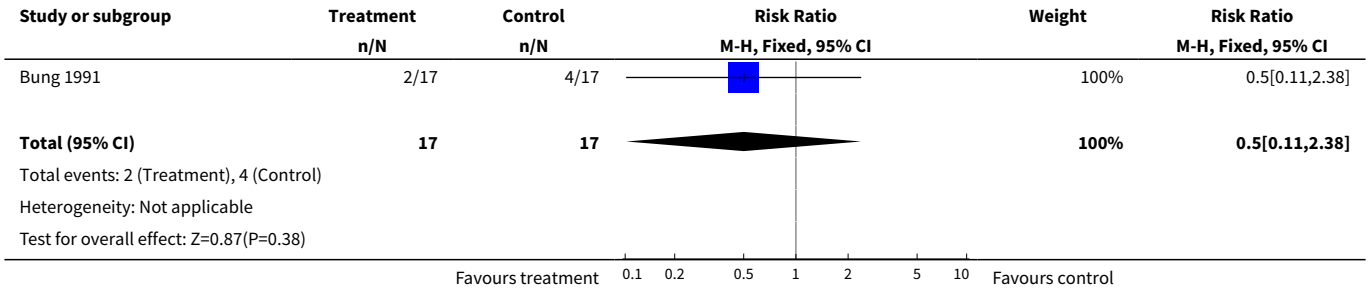
Analysis 2.6. Comparison 2 Diet + exercise versus diet + insulin (not prespecified), Outcome 6 Instrumental delivery.



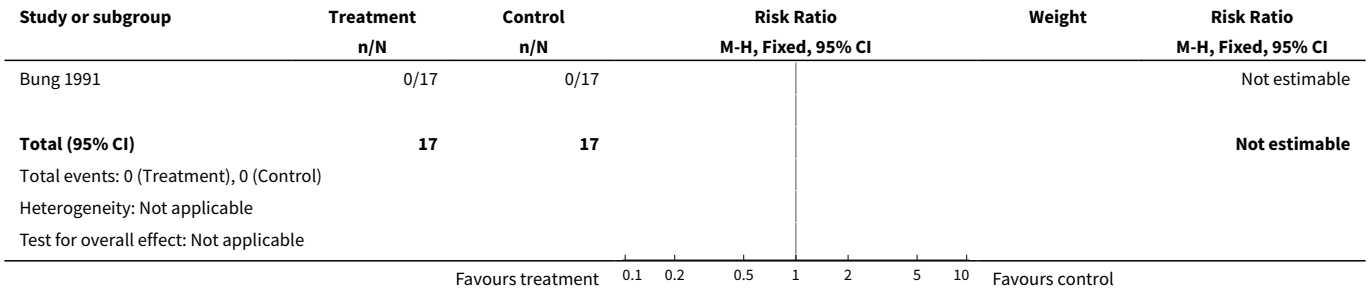
Analysis 2.7. Comparison 2 Diet + exercise versus diet + insulin (not prespecified), Outcome 7 Birthweight at delivery.



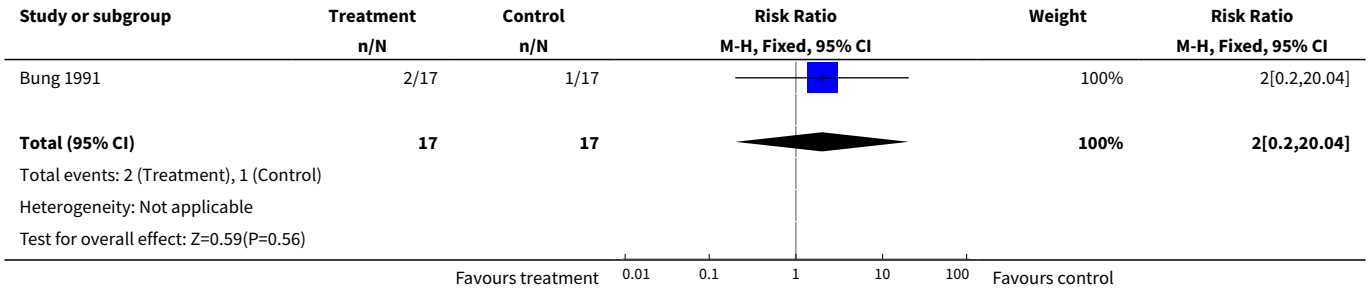
Analysis 2.8. Comparison 2 Diet + exercise versus diet + insulin (not prespecified), Outcome 8 Macrosomia (> 4000 g).



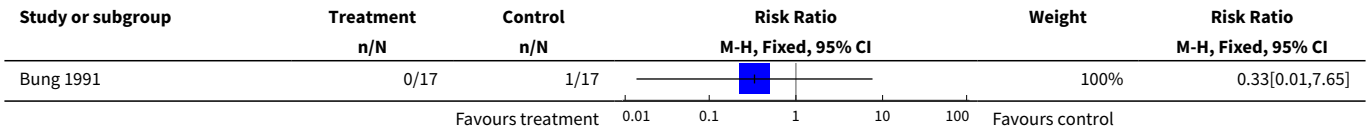
Analysis 2.9. Comparison 2 Diet + exercise versus diet + insulin (not prespecified), Outcome 9 Small-for-gestational age.

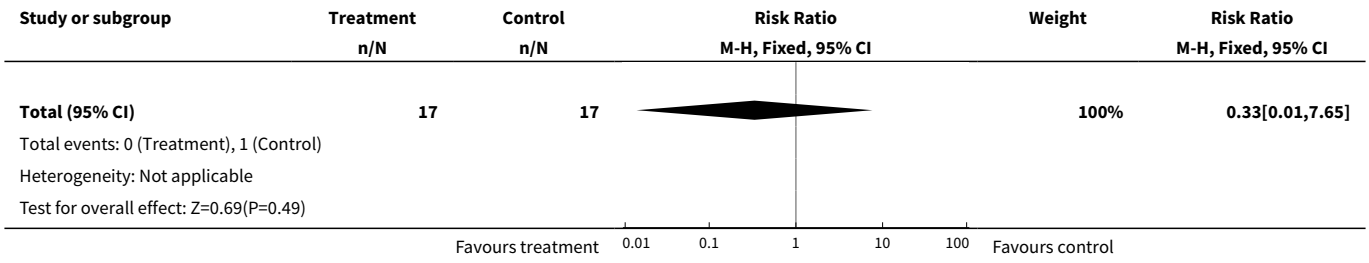


Analysis 2.10. Comparison 2 Diet + exercise versus diet + insulin (not prespecified), Outcome 10 Neonatal hypoglycaemia.

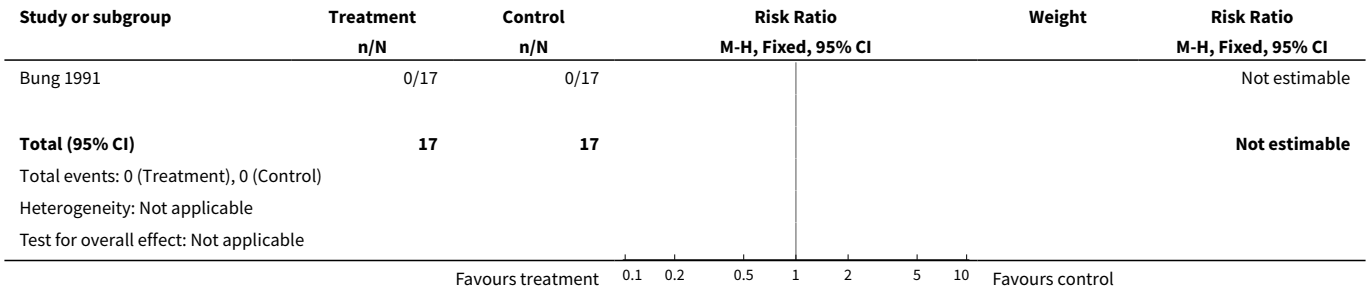


Analysis 2.11. Comparison 2 Diet + exercise versus diet + insulin (not prespecified), Outcome 11 Apgar < 7 at 5 minutes.

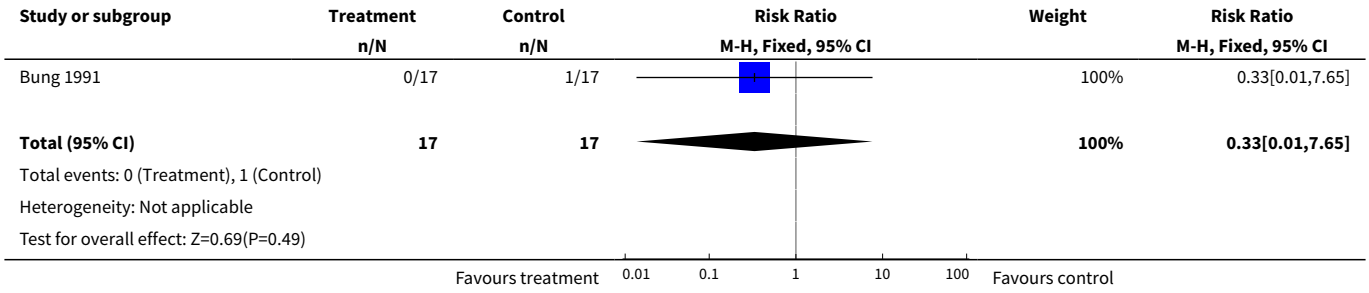




Analysis 2.12. Comparison 2 Diet + exercise versus diet + insulin (not prespecified), Outcome 12 Stillbirth.



Analysis 2.13. Comparison 2 Diet + exercise versus diet + insulin (not prespecified), Outcome 13 Congenital malformation.



WHAT'S NEW

Date	Event	Description
1 October 2009	Amended	Search updated. Six reports added to Studies awaiting classification (Callaway 2007; Ferrara 2008; Hofman 2005; Laitinen 2009; Oostdam 2009; Shaw 2008).

HISTORY

Protocol first published: Issue 1, 2001
Review first published: Issue 3, 2006

Date	Event	Description
13 February 2009	Amended	Contact details updated.
2 September 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

All three review authors wrote the protocol. Gilles Ceysens and Michel Boulvain searched for the trials, assessed the trials to be included, and extracted the data. All three authors analyzed the results and wrote the review.

DECLARATIONS OF INTEREST

None known.

INDEX TERMS

Medical Subject Headings (MeSH)

*Exercise; Diabetes, Gestational [*therapy]; Hypoglycemic Agents [therapeutic use]; Insulin [therapeutic use]; Pregnancy Outcome; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Pregnancy