Physical activity during pregnancy and the risk of gestational diabetes mellitus: a systematic review and meta-analysis of randomised controlled trials

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ABSTRACT

Objectives We performed a systematic review and meta-analysis to assess the effects of physical activity in preventing gestational diabetes mellitus (GDM).

Search strategy We searched the literature in six electronic databases and bibliographies of relevant articles.

Selection criteria We included randomised controlled trials on pregnant women who did not have GDM and other complications previously and had increased physical activity as the only intervention. The risk of developing GDM was documented separately for the intervention and control groups.

Data collection and analysis Two reviewers extracted data and assessed quality independently. Data from the included trials were combined using a fixed-effects model. The effect size was expressed as relative risk (RR) and 95% CI.

Main results Of the 1110 studies identified, six randomised controlled trials met the inclusion criteria. In three trials, the incidence of GDM was lower in the intervention group than in the control group, whereas two trials showed a higher incidence of GDM in the intervention group and the remaining trial found no GDM in either the intervention or control group. The meta-analysis resulted in a relative risk (RR) of GDM of 0.91 (95% CI 0.57 to 1.44), suggesting no significant difference in the risk of developing GDM between the intervention and the control groups. No indication of publication bias was found.

Conclusions Evidence was insufficient to suggest that physical activity during pregnancy might be effective to lower the risk of developing GDM.

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most common complications of pregnancy[1] and is associated with numerous unfavourable outcomes for both the offspring and the mothers—because of the transient abnormality in carbohydrate metabolism and glycaemic control.[2] The prevalence of gestational diabetes has been reported to be as high as 14%.[3] It is not only increasing worldwide, but varies with diagnostic criteria, ethnicity and the population studied.[4] Women with GDM are at a higher risk of undergoing caesarean section[5] and induction of labour[6] and developing type 2 diabetes mellitus (T2DM)[7] than those who have had a normal glycaemic pregnancy. As for infants born by women with GDM, they are more likely to experience overweight or obesity, develop type 1 or type 2 diabetes mellitus and have impaired intellectual achievement.[8–10] The non-modifiable risk factors for GDM are varied: advanced maternal age, non-white race/ethnicity, history of macrosomia (birthweight at least 4000 g) and history of GDM.[11–13] Fortunately, because GDM is a consequence of glycaemic control, it may be modifiable by dietary or physical activity.[12 14 15] Physical exercise has been proved to successfully improve glucose homeostasis through its direct or indirect impact on insulin sensitivity through several mechanisms in the non-pregnant state.[16 17] It also plays an important role in the prevention and treatment of type 2 diabetes.[18] Nevertheless, exercise must be undertaken regularly to have continued benefits.[19]

In 2002, the American College of Obstetricians and Gynecologists (ACOG) recommended that healthy pregnant women exercise at moderate intensity for at least 30 min most days of the week.[20] Recently, a meta-analysis about observational studies (including five prospective cohorts, two retrospective case–control studies and two cross-sectional study designs) concluded that physical activity before pregnancy or in early pregnancy is associated with lower risk of developing GDM.[21] However, little robust evidence from randomised controlled trials was available to confirm these findings.[12]

The purpose of our study was to collect all the evidence available from randomised controlled trials regarding the association between physical exercise during pregnancy and the incidence of GDM to assess the effects of physical exercise for preventing gestational diabetes.

METHODS

Search strategy and study selection

Literature searches were performed via electronic searches in the databases of PUBMED (1966–2012), ISI Web of Knowledge (1974–2012), Cochrane CENTRAL Library Issue 12, 2012, CBM (1978–2012), CNKI (1979–2012) and VIP (1989–2012). We used different combinations of keywords because of the varying search surfaces between the databases ('pregnancy' OR 'gestation' OR 'gestational' OR 'maternal' OR 'prenatal') AND ('exercise' OR 'locomotion' OR 'physical activity' OR 'motor activity' OR 'training' OR 'sports' OR 'physical exercise') AND ('gestational diabetes' OR 'gestational diabetes mellitus' OR 'insulin sensitivity' OR 'glucose tolerance' OR 'diabetes mellitus' OR 'diabetes'). Besides, bibliographies of relevant articles identified were searched to ensure a complete collection. The systematic literature search was performed between December 2012 and March 2013,

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and was updated in April 2013. Studies were included into the meta-analysis if they met the following inclusion criteria:

1. Randomised controlled trial.
2. Subjects were pregnant women without previous GDM and other complications.
3. Increased physical activity was the only intervention.
4. Incidence of GDM was documented separately for the control and intervention groups, with diagnosis criteria as defined in individual trials.

The articles were screened by title and abstract. Two review authors analysed and selected independently to include all the potential studies identified as a result of the search strategy. Differences between reviewers were resolved by discussion or by consulting a third person.

Data extraction and management

For each included article, we designed a form to extract data. Two review authors extracted the data independently using the agreed form and following the inclusion criteria. We resolved discrepancies through discussion and consulted a third person when necessary.

Quality assessment

The methodological quality of the trials was assessed according to the Cochrane handbook and the CONSORT statement: (1) random sequence generation; (2) allocation concealment; (3) blinding; (4) incomplete outcome data; (5) selection reporting and (6) other potential sources of bias.[22 23]

Statistical analysis

For each trial, we calculated the relative risk (RR) between physical exercise and routine care groups. We performed a meta-analysis to assess a summary estimate of the effects in each article by calculating a fixed-effects model. Higgins' I^2 was used to test heterogeneity, and potential publication bias was assessed in a funnel plot.

Because the interventions in each trial may have differed in their beginning gestation weeks, intensity, types and/or duration of exercise, we calculated metabolic equivalents (METs) for energy expenditure according to the Compendium of Physical Activities Tracking Guide.[24] For example, 1 min of muscle strengthening and toning programme accounts for 5.5 METs, whereas 1 min of water aerobics accounts for 4.0 METs.

We entered data into Review Manager software (RevMan 2012) and checked for accuracy. When details regarding any of the above were unclear or unknown, we contacted the authors for more information.

RESULTS

Included studies

The review process is outlined in figure 1. Of the 1110 articles initially identified from searching the databases and bibliographies, 17 studies were considered relevant after title and abstract screening. The review authors then read the full text if GDM was mentioned in the abstract. Finally, six randomised controlled trials met the inclusion criteria and were eligible for analysis: five trials were performed in developed countries, one in the USA,[25] one in Norway,[26] one in Australia[27] and two in Spain[28 29]; and the only trial performed in developing countries was in India.[30] Of the 11 excluded trials, 9 had deficient or missing data for the incidence of GDM[31–39] and 2 had pregnant women with previous GDM.[40 41]

The pooled RCTs assigned a total of 1278 pregnant women to intervention or control groups, and 1089 of them completed the trials. The outcomes investigated in the trials were the incidence of GDM, with the diagnosis criteria as defined in individual trials.

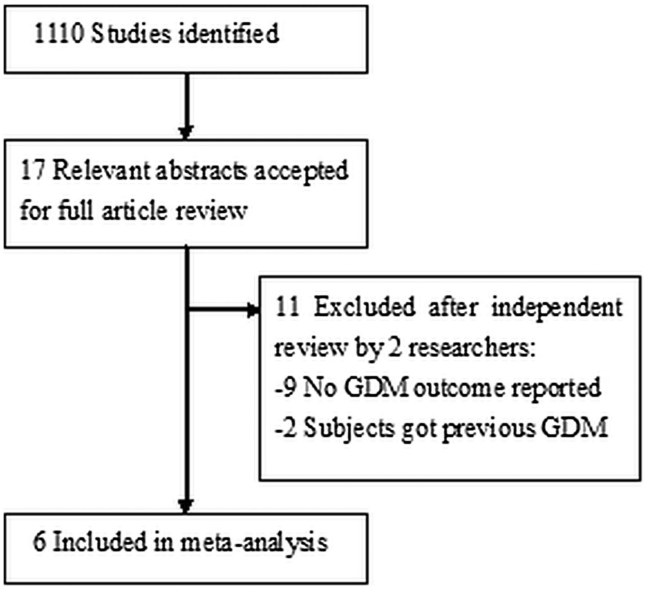

Figure 1 Flow chart of search results.

Interventions

The interventions varied by their beginning gestation weeks (6–18 weeks), intensity, duration (12–32 weeks) and types of activity (table 1). In general, women exercised about three times a week for at least 30 min up to 1 h, performing aerobic training, resistance exercise, brisk walk, water aerobics or muscle strength. All of these RCTs' interventions translated into METs per intervention in the range 9300–27772.5.[25 26] Five trials started in the second trimester,[25–27 29 30] and the remaining one started in the first trimester (6 gestational week)[28]; all interventions persisted to the third trimester[25 26 28–30] or until delivery.[27] The subjects in none of the control groups exercised regularly during pregnancy, except in one trial where the controls were offered a conventional antenatal exercise (walking for half an hour in the morning and/or evening).[30]

With regard to supervision, two trials provided heart-rate monitors[28 29] and one trial used a training diary to ensure moderate intensity during the home exercise programme,[26] whereas the other articles did not provide any information on supervision. No serious adverse events related to physical exercise were reported in the six included articles.

GDM is usually diagnosed by an oral glucose tolerance test (OGTT). Nevertheless, the OGTT procedure and the diagnostic criteria used varied.[42] The GDM diagnosis criteria were described in all trials but one,[29] which did not provide any information on it (table 1).

Methodological quality

Overall, the six included trials had a moderate risk of bias (figure 2).

Methodological quality was assessed in table 2. Two of the six articles did not describe the randomisation and allocation concealment in detail,[25 28] while the other four trials described in detail the generation of randomised sequence.[26 27 29 30] In Callaway 2010,[27] Stafne 2012,[26] Barakat 2009[29] and Rakhshani 2012,[30] randomisation was conducted by a third party at another location outside the hospital. The other two trials had

Table 1 Characteristics of six included studies on the effect of physical exercises on the prevention of gestational diabetes mellitus (GDM)

Author, publication year, country	Characteristics of subjects	Intervention n	Control n	GDM diagnostic criteria	Intervention group treatment	Beginning of intervention (gest. week)	Duration of intervention (weeks)	Assessed METs per week
Barakat, 2009,[29] Spain	Previously sedentary nulliparous women	72	70	Not reported	Light-intensity resistance exercise training, 3 sessions a week, consisting of an 8 min warm-up period, a 20 minute toning and resistance exercise, and a cool-down period of 8 min, 80% of max heart rate	12–13	25–27	600
Barakat, 2011,[28] Spain	Healthy pregnant women	40	43	ADA	A 35–45 min session performed 3 times a week, with two land aerobic sessions and one aquatic activities session. 70% of max heart rate	6–9	27–32	687.5
Callaway, 2010,[27] Australia	Obese pregnant women	22	19	ADIPS	(1) An individualised exercise plan; (2) regular exercise advice; and (3) paper-based diaries for self-monitoring	12	26	900
Price, 2012,[25] America	Sedentary singleton pregnant women	31	31	ADA	Aerobic training of 45–60 min, performed 4 times/week; and a brisk 30–60 min walk once weekly	12–14	22–24	1207.5
Rakhshani, 2012,[30] India	Pregnant women in high risk of pregnancy complications	29	30	Self-report	A 1 yoga session 3 times a week	12	16	720
Stafne, 2012,[26] Norway	18 years or older with a singleton fetus	375	327	WHO	Low-impact aerobics 30–35 min, including strength exercise 20–25 min, light stretching 5–10 min once a week;30 min endurance training and 15 min strength and balance exercise at least twice a week	18–22	12	775

ADIPS, Australasian Diabetes in Pregnancy Society; ADA, American Diabetes Association.

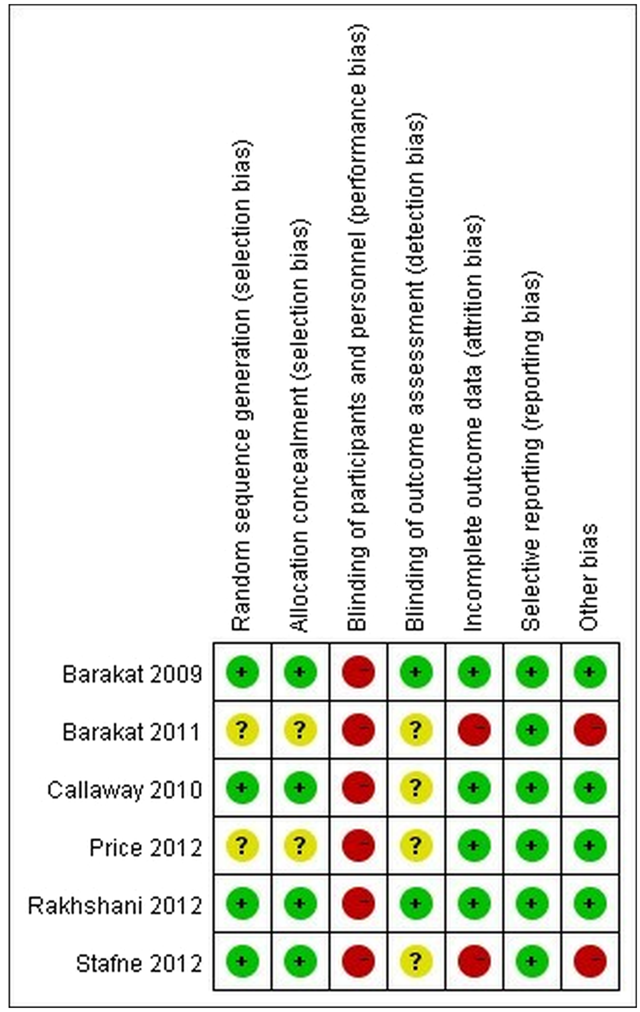

Figure 2 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

no information on allocation concealment.[25 28] Only two of the six articles reported that assessors were blinded to group allocation,[29 30] but none of the participants in all six trials were blinded. In Barakat 2011,[28] 10 women from the exercise group and seven women from the control group did not complete the study and were excluded from the analysis. In Stafne,[26] 153 women were lost to follow-up or excluded at 32–36 weeks assessment. Reasons for exclusion were provided in both cases. The other four trials[25 27 29 30] described the completeness of outcome data for GDM, attrition and exclusion, as well as the reasons for attrition/exclusion. No obvious risk of selective reporting was found in all of the six articles. In Barakat,[28] baseline imbalance was observed in the maternal education level, parity and exercise habits before gestation between the two study groups. In Stafne,[26] baseline imbalance was observed in insulin resistance between women in the exercise group and in the control group. No obvious risk of potential sources of bias in the other four included trials was found.

Summary results

GDM in the intervention and control groups, n/N.

The results of the individual studies were inconsistent (table 3). Three trials showed a lower incidence of GDM in the intervention group thank in the control group,[25 28 30] but one study reported that physical activity had significant (p=0.05) effects on lowering

Table 2 Assessment quality of included trials: randomised controlled trials on the effect of physical exercises on the prevention of GDM

Author (year)	Population representat-iveness	Random sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective reporting	Sample size	Other potential sources of bias
Barakat *et al* (2009)[29]	Yes	Yes	Yes	The assessors blinded, the subjects not	No	No	160	No obvious risk of potential biases
Barakat *et al*, (2011)[28]	Yes	Exact method not described	Exact method not described	The subjects not blinded, the others unclear	Yes	No	100	Baseline imbalance; no other obvious risk of potential biases
Callaway *et al*, (2010)[27]	Yes	Yes	Yes	The subjects not blinded, the others unclear	No	No	50	No obvious risk of potential biases
Price *et al*, (2012)[25]	Yes	Exact method not described	Exact method not described	The subjects not blinded, the others unclear	No	No	91	No obvious risk of potential biases
Rakhshani *et al*, (2012)[30]	Yes	Yes	Yes	The assessors blinded, the subjects not	No	No	68	No obvious risk of potential biases
Stafne *et al*, (2012)[26]	Yes	Yes	Yes	The subjects not blinded, the others unclear	Yes	No	855	Baseline imbalance; no other obvious risk of potential biases

GDM, gestational diabetes mellitus.

the incidence of GDM.[30] The other two trials found that the incidence of GDM was higher in the intervention group,[26 27] whereas the remaining one did not estimate the result.[29]

Meta-analysis on the results of the individual studies suggested no significant difference in the intervention groups (p=0.68) with an RR of 0.91 (95% CI 0.57, 1.44; figure 3). There was low heterogeneity between the individual trials as indicated by Higgins' I^2 (I^2=26%).

The funnel plot indicated no considerable publication bias (figure 4).

Sensitivity analysis

We conducted a sensitivity analysis by removing the two trials with a high risk of bias, because they did not provide the details of random sequence generation and allocation concealment, and the participants were not blinded.[25 28] An RR of 1.02 (95% CI 0.62 to 1.68) was obtained (data not shown).

DISCUSSION

Quality of the evidence

On the basis of the current available evidence from six randomised controlled trials with data available from 1089 women, we found that increasing physical activity during pregnancy had no significant differences in the incidence of developing GDM, and that the overall risk of bias for the six included trials was judged to be moderate. The methods of generating random sequence and allocation concealment were unclear in two trials (Barakat[28]; Price[25]). Risk of performance bias is not easy to avoid since behavioural interventions cannot easily be blinded from participants or investigators. This was seen in Callaway[27] and Stafne,[26] where it was noted that women in the control group voluntarily increased the amount of physical activity they undertook. In Barakat[28] and Stafne,[26] baseline imbalances were noted in maternal education level, parity, exercise habits before gestation and insulin resistance between the two study groups.

Table 3 Results: The incidence of GDM in the six included studies on the effect of physical exercises on the prevention of GDM

Author	Incidence of GDM (%)		P reported
	Exercise	Control	
Stafne *et al*[26]	6.7 (25/375)	5.5 (18/327)	0.52
Callaway *et al*[27]	22.7 (5/22)	15.8 (3/19)	0.57
Barakat *et al*[29]	0 (0/72)	0 (0/70)	Not estimated
Barakat *et al*[28]	0 (0/40)	7.0 (3/43)	>0.05
Rakhshani *et al*[30]	3.4 (1/29)	20.0 (6/30)	0.05
Price *et al*[25]	9.6(3/31)	12.9 (4/31)	0.66

GDM, gestational diabetes mellitus.

Implications

An increasing amount of evidence has been found to support the beneficial effects that improved muscular strength has on the prevention of chronic diseases and on the ability to cope with daily living activities in healthy and diseased people.[43 44] Investigators have reported that physical exercise was effective in preventing and managing T2DM by reducing insulin resistance in men and non-pregnant women.[45–48] Clapp[45] found that the effect of decreasing circulating glucose and insulin concentration was greatest with low-intensity prolonged exercise that utilises a large muscle mass in late pregnancy shortly (less than 2 h) after food intake. The potential benefits of resistance training during pregnancy include decreased risk of insulin dependence in overweight women with GDM,[49] reduction of depression symptoms, prevention of gestational low back pain and strengthening of the pelvic floor.[50 51] These research findings all suggest that physical exercise during normal pregnancy may be effective in preventing GDM. Nevertheless, Oostdam *et al*[52] found that it was not cost-effective to perform a twice weekly exercise programme for pregnant women at risk for GDM compared to standard care, because there were no statistically significant differences in outcome measure, such as maternal fasting blood glucose levels, insulin sensitivity and infant birth weight. These contradictory findings suggest that more evidence should be provided and caution should be taken when considering the effect and cost-effectiveness of physical exercise during pregnancy in future research.

During pregnancy, an increase in insulin resistance occurs secondary to the diabetogenic effect of one or more of the

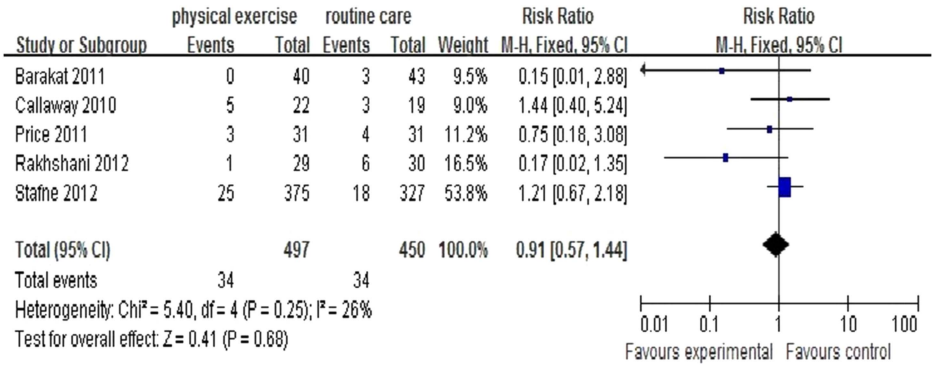

Figure 3 Relative risk in physical exercise between exercise and control groups, calculated by a fixed-effects model. The square represents the point estimate of each study; the horizontal lines depict the respective 95% CI. The diamond represents the overall pooled estimate of the treatment effect.

gestational hormones secreted by the placenta,[53] and an increase in lipid and glucose homeostasis metabolic stress disturbance in the third trimester.[54 55] Oken *et al*[56] showed that vigorous physical activity before pregnancy and continuation of activity into early pregnancy may reduce a woman's risk for development of abnormal glucose tolerance and gestational diabetes. This may be one of the reasons why these trials found no significant difference between the intervention and control groups. In the six included trials in this study, only one trial began interventions in the first trimester[28] while all the other five started in the second trimester.[25–27 29 30] This may mean that the effect of physical exercise to lower the incidence of GDM is possibly better before pregnancy and in early pregnancy than during the second and third trimesters. Because chronic changes in the regulation of skeletal muscle glucose uptake are adapted, women may be better able to handle the metabolic stress of a pregnancy.[26] Another reason could be that the exercise plans in each intervention treatment were too modest to have an effect on the incidence of developing GDM compared to the vigorous physical activity before pregnancy. Therefore, on the premise of ensuring the safety of mothers and infants, the investigators can try to increase the energy expenditure goal properly in future studies.

Another hypothesis is that the effect of physical exercise on glucose metabolism differs in pregnant and non-pregnant women mainly, because adherence to physical exercise varies from person to person in the intervention groups. For instance, Stafne *et al*[26] noted that adherence to protocol (exercising 3 days/week or more at moderate to high intensity) was 55% in the intervention group and only 10% in the control group (exercised 3 days/ or more at moderate to high intensity at follow-up), which showed that women in the control group voluntarily increased the amount of physical activity. Barakat *et al*[28] found that compliance in the intervention group was 85%. Pregnant women were less likely to incorporate exercise into their daily routine usually due to pregnancy symptoms, child care and work commitments.[27] These reasons made it difficult for us to conclude what possible direct effects physical exercise might have had on glucose metabolism. It is therefore even more difficult to implement a physical exercise programme with moderate to high intensity 3 times/week for pregnant women as suggested in the general recommendations.[26] We think that pregnant women should adhere to the physical exercise protocol in future studies.

One strength of the present study is a broad search strategy including three Chinese databases. In addition, unlike previous observational meta-analysis,[21] the articles included in our study were all randomised controlled trials, which could provide more robust evidence to confirm the association between physical exercise and the prevalence of GDM.

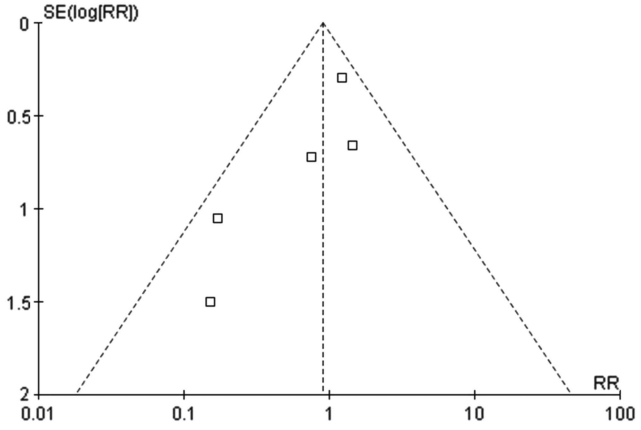

Figure 4 Funnel plot of SE by log (relative risk) for assessment of publication bias. Each dot denotes a study included in the meta-analysis. The vertical line represents the effect of the fixed effects model.

CONCLUSION

In summary, this systematic review on interventional trials suggests that the evidence is not enough to prove the effect of physical exercise on lowering GDM incidence between women receiving an additional exercise intervention and those receiving routine care.

Given the limited number of randomised controlled trials included in the analysis, the findings from our meta-analysis should be confirmed in future research. Larger, well-designed randomised trials with standardised behavioural interventions are needed to assess the effects of physical exercise on lowering the risk of developing GDM.

The new findings

- We found that the evidence was insufficient to suggest that physical activity during pregnancy might be effective to lower the risk of developing gestational diabetes mellitus (GDM).
- We concluded that to lower the incidence of GDM it is better to perform physical exercise before pregnancy or in early pregnancy than during the second and third trimesters.
- We believed that the effect of physical exercise on glucose metabolism is different in pregnant and non-pregnant women.

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Contributors YY-n was involved in the literature review, meta-analysis and was the principal author of the manuscript. LX-l was involved in statistical analysis and contributed to the first draft of the manuscript. TT-j and LS-j were involved in the literature review and contributed to the final draft of the manuscript. LB-r was involved in the conception of the research questionnaire and contributed to the final draft of the manuscript.

Competing interests None.

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