

## RESEARCH ARTICLE

## Epidemiology

# Exercise during pregnancy for preventing gestational diabetes mellitus and hypertensive disorders: An umbrella review of randomised controlled trials and an updated meta-analysis

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## Abstract

**Objective:** This study aimed to provide, through an umbrella review, an overview of the effect of single exercise interventions during pregnancy on gestational diabetes mellitus (GDM) and hypertensive disorders of pregnancy (HDP). Also, to update the current evidence through an updated meta-analysis.

**Design:** Umbrella review.

**Setting:** PubMed, EMBASE, Web of Science, Cochrane database of systematic reviews, Epistemonikos, SPORTDiscus, [Clinicaltrials.gov](https://www.clinicaltrials.gov), and PROSPERO register were searched from the database inception until August 2021.

**Population:** Peer-reviewed systematic reviews and meta-analyses of randomised controlled trials (RCTs) and RCTs samples.

**Methods:** Random-effects model was used to calculate relative risk with 95% confidence interval in the updated meta-analysis. The reference category was the groups that received usual prenatal care. AMSTAR 2 and the Cochrane Collaboration tool were used to assess the quality and GRADE approach was used to assess the overall certainty of evidence.

**Main outcome measures:** GDM and HDP relative risk.

**Results:** Twenty-three systematic reviews and meta-analyses; and 63 RCTs were included. Single exercise interventions reduced the incidence of GDM and HDP in most systematic reviews and meta-analyses. Moreover, exercise interventions during pregnancy decrease the incidence of developing GDM and GH, particularly when they are supervised, have a low to moderate intensity level, and are initiated during the first trimester of pregnancy.

**Abbreviations:** CG, control group; ES, effect size; GDM, gestational diabetes mellitus; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HDP, hypertensive disorders of pregnancy; IG, intervention group; OR, odds ratio; PA, physical activity; RCT, randomised controlled trials.

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**Conclusion:** Based on the findings, obstetric and physical exercise professionals could recommend exercise interventions during pregnancy as an effective strategy to improve maternal outcomes.

**KEY WORDS**

aerobic, diabetes, gestation, glucose, hypertension, maternal, motor activity, physical activity, pre-eclampsia, pregnancy

## 1 | INTRODUCTION

Gestational diabetes mellitus (GDM), defined as ‘glucose intolerance and insulin resistance first detected during pregnancy’,<sup>1</sup> affects approximately 7% of pregnant women. In more than 50% of cases, GDM may progress to type 2 diabetes mellitus, hypertension and cardiovascular diseases within 5–15 years after pregnancy.<sup>2–6</sup> Additionally, GDM is associated with several maternal and perinatal complications,<sup>7</sup> such as hypertensive disorders of pregnancy (HDP), which include gestational hypertension (GH), pre-eclampsia and eclampsia,<sup>8</sup> affecting 10% of pregnancies.<sup>9</sup> Likewise, HDP are associated with higher life-long cardiovascular risk.<sup>10</sup> Otherwise, fetal overgrowth or macrosomia is one of the fetal complications that occur in up to 45% of GDM pregnancies. These babies have an increased risk of overweight, obesity and type 2 diabetes later in life.<sup>11</sup>

Several studies have suggested that exercise is an effective strategy for preventing and treating diabetes and hypertension in the general population by reducing some of the mechanisms involved in inflammation, oxidative stress and endothelial dysfunction, all of which are pathophysiological mechanisms involved in the genesis of HDP and GDM.<sup>9,12,13</sup> That, in turn, is associated with obesity and physical inactivity.<sup>14</sup> However, the evidence about the effectiveness of exercise in avoiding the development of both disorders during pregnancy is still not consistent. Some reviews reported that physical activity (PA) programmes produced reductions in the prevalence of GDM.<sup>15,16</sup> Regarding the effect of exercise on pre-eclampsia or HDP incidence, some studies did not find protective effect of exercise in the incidence of pre-eclampsia or HDP.<sup>17–20</sup>

Comprehensive evidence synthesis is needed to explore further reasons for these conflicting findings.<sup>21–26</sup> Hence, this umbrella review and updated meta-analysis aimed to provide a comprehensive overview of the effect of exercise interventions during pregnancy on GDM and HDP.

## 2 | METHODS

This umbrella review of systematic reviews and meta-analyses was registered in PROSPERO (Registration number: CRD42019123410) and was developed according to PRISMA and the Cochrane Collaboration Handbook.<sup>27,28</sup> The review protocol has been published elsewhere.<sup>29</sup>

## 2.1 | Search methodology

The PubMed, EMBASE, Web of Science, Cochrane database of systematic reviews, Epistemonikos, SPORTDiscus, [ClinicalTrials.gov](http://ClinicalTrials.gov) and PROSPERO databases were systematically searched from inception to August 2021 for systematic reviews, meta-analyses and randomised controlled trials (RCTs) aimed at assessing the effect of exercise interventions during pregnancy on GDM and HDP.

The search strategy combined the following relevant terms: (1) patients (pregnant OR pregnancy OR gravid OR gestation\* OR maternal); (2) intervention (aerobic OR sport OR exercise OR fitness OR “physical exercise” OR “physical activity” OR “motor activity”); (3) outcome (diabetes OR “diabetes mellitus” OR DM OR “gestational diabetes” OR “glucose intolerance” OR glucose OR insulin OR hyperglycemia OR toxemia OR preeclampsia OR pre-eclampsia OR eclampsia OR “hypertensive disorders” OR “blood pressure” OR hypertension) (in more detail in [Table S1](#)). Additional reviews and RCTs were also identified by screening the references of the included reviews and meta-analyses ([Table S2](#)).

The search strategy was conducted independently by two researchers (GSM and JAMH) to avoid any selection bias. Disagreements were solved by consensus, but if discrepancies persisted, a third researcher was consulted (VMV).

## 2.2 | Study inclusion and exclusion criteria

Systematic reviews and meta-analyses of RCTs written in any language evaluating the effect of exercise interventions during pregnancy on GDM and HDP were selected. Reviews had to contain a quantitative assessment of the exercise effect on GDM and HDP. Diagnostic criteria for GDM varied among studies and were established in each individual trial. The health conditions under HDP were defined by the American College of Obstetricians and Gynecologists (ACOG):<sup>30</sup> pre-eclampsia–eclampsia, chronic hypertension, chronic hypertension with superimposed pre-eclampsia and GH. Participants should be pregnant women with no absolute or relative contraindications to be included in exercise programmes according to the 2020 ACOG recommendations on PA and exercise during pregnancy and postpartum.<sup>31</sup> Moreover, we excluded articles that only included women with a specific disease or with a high incidence of GDM or HDP. Finally, exercise programmes of all exercise

types at any level of intensity were included, but when the meta-analysis included studies with an additional intervention with a nutritional or behavioural component, only information from RCTs with exclusive exercise intervention was extracted. Reviews were excluded if women in the control groups (CGs) were not receiving usual prenatal care.

Two researchers (GSM and JAMH) independently assessed for eligibility in duplicate all abstracts and full texts, as recommended by the Cochrane Handbook.<sup>28</sup> Disagreements on study eligibility were discussed with the study team and resolved by consensus.

## 2.3 | Data extraction

Two researchers (GSM and JAMH) independently extracted data in ad hoc designed forms included in the umbrella review protocol.<sup>29</sup> Potential conflicts were discussed until consensus and a third researcher (VMV) was consulted when agreement was not reached. We collected first author, publication year, years for inclusion, number of RCTs included, intervention group (IG) and CG sample size, sample characteristics, outcomes of interest (GDM, GH, pre-eclampsia), number of cases in each group, pooled risk measure (relative risk or odds ratio [OR]), effect size and its 95% CI of the largest study and overall effect size, the heterogeneity ( $I^2$ ) and any reported measures of publication bias. For each study, we extracted the first author, publication year, country, recruitment years, IG and CG sample size, intervention characteristics (type of exercise, when exercise intervention started and ended, length, session duration, frequency, intensity and supervision), setting, the outcome of interest, and IG and CG cases.

## 2.4 | Assessment of risk of bias

The methodological quality of the included reviews and meta-analyses was independently rated using the AMSTAR 2 tool by two researchers (GSM and JAMH). The AMSTAR2 is an instrument to critically assess the risk of bias of systematic reviews that consists of 16 different domains referring to relevant methodological aspects, which are answered with 'yes', 'no', 'cannot answer' and 'partial yes'. The overall quality of the studies was categorised as follows: high, moderate, low or critically low.<sup>32</sup>

Moreover, we assessed the risk of bias (quality) of the RCTs included in the updated meta-analysis using the Cochrane Collaboration risk of bias tool (Table S13), which assesses eight potential sources of bias: random sequence generation, allocation concealment, blinding of participants, evaluator and outcome assessments, incomplete outcome data, missing data, and other.<sup>33</sup>

The certainty of evidence and strength of recommendations from meta-analyses were assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method.<sup>34</sup> This tool provides a system rate with four categories: 'high', when the systematic review or meta-analysis includes at least two high-quality primary studies; 'moderate',

when it includes at least one high-quality or two moderate-quality primary studies; 'low' when it includes only moderate-quality and/or inconsistent results studies; and 'very low', when no medium- to high-quality studies were identified on this topic. Our starting point was 'high', and this grading decreased when we detected risk of bias, inconsistency of results (i.e.  $I^2$  statistics >50%), indirectness of evidence (i.e. differences in intervention), imprecision (i.e. 95% CI includes 1.0) or publication bias (asymmetry in funnel plot). Additionally, the rating was increased if there was a large intervention effect, in case of a dose-response relation or if all plausible biases would decrease the magnitude of the intervention effect.<sup>34</sup> The GRADE assessment was performed independently by two researchers (GSM and JAMH) with discussion and agreement for any discrepancies.

## 2.5 | Statistical analysis

### 2.5.1 | Primary analysis

The primary analysis in the umbrella review was focused on one measure per individual study and each outcome. Forest plots were designed to synthesise all pooled estimates regarding the effect of exercise on the outcomes (GDM and HDP).

### 2.5.2 | Assessment of summary effects and heterogeneity

The summary meta-analytic odds ratio estimates and their corresponding 95% CI for each meta-analysis were displayed graphically using a random-effects model that was calculated by the original studies.<sup>35,36</sup> Additionally, a pooled analysis was performed with the RCTs included in the systematic reviews and meta-analyses. The RCTs identified in the update with the estimates and corresponding 95% CI using the fixed-effects or random-effects model.<sup>35</sup> In our study, the significance level of the  $p$  values for Egger's test was set at 0.10. For continuous data, we calculated the mean difference, the incidence difference or the Glass  $\Delta$ .<sup>37,38</sup> Trial sequence analysis (TSA) was conducted (Tables S20–S22).<sup>39</sup> The heterogeneity between study associations was assessed using the  $I^2$  statistic.<sup>40</sup>

Sensitivity analyses were conducted to assess the robustness of summary estimates and to detect whether any individual study accounted for a large proportion of heterogeneity.

### 2.5.3 | Subgroup analyses and meta-regression

Subgroup and meta-regression analyses were performed with original study data to examine the influence of some potential mediators on outcomes. For this purpose, the following subgroups were established: (1) body mass index (BMI) categories (>25 kg/m<sup>2</sup> or <25 kg/m<sup>2</sup>); (2) pregnancy trimester in which the intervention was initiated (first or second); (3) session duration (>45 min or <45 min) and (4) supervision during the exercise intervention or not.

## 2.5.4 | Small studies effect assessment and excess significance biases

Egger's regression asymmetry test was used to calculate the evidence of small-study effects.<sup>41</sup> Therefore, a *p* value less than 0.10 was considered to show evidence of small-study effects.<sup>41</sup> Also, we assessed 'p-hacking'<sup>42</sup> and publication bias with PET-PEESE<sup>43,44</sup> and Rucker's analysis.<sup>45</sup>

All statistical analyses and power calculations were performed using STATA V.15.1 software (StataCorp, College Station, TX, USA).

## 3 | RESULTS

### 3.1 | Study selection and study characteristics

We retrieved 696 systematic reviews and meta-analyses after removing duplicates. The reasons to exclude studies are provided in Tables S18–S19. Finally, 23 systematic reviews and meta-analyses were included after full-text assessment (Tables 1 and 2), including 63 RCTs (10 485 and 11 192 women in IG and CG, respectively) (Figure S2). Among them, three RCTs published between 2016 and 2019 were not included in any systematic reviews and meta-analyses, which were selected for the meta-analysis update (Figure S3).<sup>46–48</sup> A characteristics summary of the included

meta-analyses and RCTs can be found in Tables 1 and 2, and Tables S3 and S4.

### 3.2 | Risk of bias of included studies

The methodological quality scores of the 23 systematic reviews and meta-analyses assessed by AMSTAR 2 are shown in Table S5. Seven studies scored moderate quality (33%),<sup>18,21,22,49–52</sup> five scored low quality (21%),<sup>26,53–56</sup> and 11 scored critically low methodological quality (53%).<sup>15,17,24,25,57–63</sup> Only six studies provided an a priori protocol register,<sup>18,21,22,26,49,54</sup> and seven reported a list of excluded studies.<sup>18,21,22,24,49,53,64</sup>

According to the GRADE assessment, reviews included were considered low certainty. For the risk of bias, the scores were very serious because of the lack of blinding of participants (Table S6).

### 3.3 | Synthesis of results

#### 3.3.1 | Gestational diabetes mellitus

Thirteen systematic reviews and meta-analyses found a reduction of GDM incidence in the exercise group<sup>15,21,24,26,27,49–51,53,55,56,59,62,65</sup> and seven did not find

TABLE 1 Meta-analysis of randomised control trials of gestational diabetes mellitus

Reference	Number of RCT	Sample IG/CG	Number of cases IG/CG	Type of measure (RR or OR)	RR/OR and 95% CI of the largest study	RR/OR and 95% CI	<i>I</i> <sup>2</sup> (%)
Aune et al. <sup>24</sup>	12	2015/2030	129/191	RR	0.78 (0.47–1.28)	0.69 (0.50–0.96)	30.2
Bennett et al. <sup>49</sup>	9	1736/1260	111/135	RR	0.70 (0.49–0.99)	0.65 (0.50–0.78)	0
Da Silva et al. <sup>93</sup>	11	1673/1689	NR	RR	0.70 (0.49–0.99)	0.67 (0.49–0.92)	33
Davenport et al. <sup>21</sup>	27	3505/3429	271/380	OR	0.62 (0.40–0.98)	0.62 (0.52–0.75)	0
Di Mascio et al. <sup>56</sup>	4	836/850	20/50	RR	NR	0.41 (0.24–0.68)	NR
Díaz-Burrueco et al. <sup>50</sup>	10	1159/1516	123/204	OR	NR	0.65 (0.43–0.98)	48
Guo et al. <sup>51</sup>	19	Total:5883	NR	RR	0.54 (0.37–0.79)	0.70 (0.59–0.84)	14.9
Han et al. <sup>18</sup>	3	437/389	30/24	RR	1.21 (0.67–2.18)	1.10 (0.66–1.84)	0
Magro-Malosso et al. <sup>57</sup>	7	748/602	40/53	RR	NR	0.61 (0.41–0.90)	NR
Ming et al. <sup>53</sup>	8	1472/1509	88/144	RR	0.70 (0.49–0.99)	0.58 (0.37–0.90)	46
Muhammad et al. <sup>54</sup>	6	314/318	73/101	RR	0.54 (0.37–0.79)	0.78 (0.51–1.19)	49
Nasiri-Amiri et al. <sup>58</sup>	8	727/714	143/196	RR	0.67 (0.47–0.96)	0.76 (0.56–1.03)	50
Rogozinska et al. <sup>26</sup>	27	3153/3015	240/347	OR	NR	0.66 (0.53–0.83)	0
Russo et al. <sup>59</sup>	10	1715/1686	116/159	RR	0.70 (0.49–0.99)	0.74 (0.57–0.97)	12
Sanabria et al. <sup>15</sup>	8	1434/1439	NR	RR	NR	0.69 (0.52–0.91)	0
Doi et al. <sup>55</sup>	11	722/745	100/148	RR	0.54 (0.37–0.79)	0.69 (0.51–0.94)	23.2
Song et al. <sup>60</sup>	10	Total: 4161	NR	RR	0.94 (0.59–1.50)	0.77 (0.54–1.09)	38
Xing et al. <sup>61</sup>	10	794/786	NR	RR	1.30 (0.93–1.82)	0.71 (0.48–1.04)	63.1
Yin et al. <sup>17</sup>	5	497/450	34/34	RR	1.21 (0.67–2.18)	0.91 (0.57–1.44)	26
Yu et al. <sup>62</sup>	6	651/719	117/181	OR	0.62 (0.40–0.98)	0.59 (0.39–0.88)	46
Zheng et al. <sup>63</sup>	5	550/583	116/168	OR	0.62 (0.40–0.98)	0.62 (0.43–0.89)	37

Abbreviations: CG, control group; IG, intervention group; OR, odds ratio; RCT, randomised controlled trial; RR, relative risk.



TABLE 2 Meta-analysis of randomised control trials of hypertensive disorders of pregnancy

Reference	Number of RCT	Sample IG/CG	Main outcome	Number of cases IG/CG	Type of measure (RR or OR)	RR/OR and 95% CI of the largest study	RR/OR and 95% CI	$I^2$ (%)
Davenport et al. <sup>21</sup>	23	2627/2689	GH	61/105	OR	1 (0.46–2.19)	0.61 (0.43–0.85)	0
Magro-Malosso et al. <sup>57</sup>	16	2452/2189	GH	61/100	RR	NR	0.54 (0.40–0.74)	10
Xing et al. <sup>61</sup>	5	428/424	GH	NR	RR	0.74 (0.35–1.55)	0.53 (0.32–0.88)	3.7
Davenport et al. <sup>21</sup>	16	1719/1603	PE	34/49	OR	0.80 (0.27–2.40)	0.59 (0.37–0.94)	0
Da Silva et al. <sup>93</sup>	4	709/708	PE	NR	RR	0.99 (0.50, 1.96)	0.93 (0.55–1.57)	0
Kramer et al. <sup>64</sup>	1	43/39	PE	7/6	RR	1.17 (0.44–3.08)	1.17 (0.44–3.08)	NR
Magro-Malosso et al., <sup>57</sup>	6	1164/1066	PE	26/30	RR	NR	0.79 (0.45–1.38)	0
Xing et al. <sup>61</sup>	5	499/505	PE	NR	RR	NR	1.00 (0.66–1.52)	0
Muhammad et al. <sup>54</sup>	5	324/326	GH and PE	23/30	RR	0.75 (0.36–1.55)	0.77 (0.46–1.30)	0
Rogozinska et al. <sup>26</sup>	20	2513/2359	HDP	106/147	OR	Not reported	0.68 (0.49–0.93)	0

Abbreviations: CG, control group; GH, gestational hypertension; HDP, hypertensive disorders of pregnancy; IG, intervention group; OR, odds ratio; PH, pre-eclampsia; RCT, randomised controlled trial; RR, relative risk.

effect of exercise on the incidence of GDM<sup>18,54,58,60</sup> (Figure 1 and Table S3). Among systematic review and meta-analyses that included women with overweight or obesity,<sup>21,26,49,54,58,61</sup> only one found that exercise reduced GDM incidence (Figure S3 and Table S7).<sup>63</sup>

Regarding the updated meta-analysis, 35 RCTs assessed the effect of exercise on GDM incidence,<sup>46,66–99</sup> whose pooled OR showed a decreased GDM incidence (OR 0.61; 95% CI 0.51–0.74;  $I^2 = 17.79$ ; IG:  $n = 4935$ , CG:  $n = 5354$ ) (Figure S4). The subgroup analyses (Table S8) showed that GDM incidence was reduced when the exercise intervention was: (1) initiated in the first trimester (OR 0.55; 95% CI 0.44–0.68;  $I^2 = 23.40$ ; IG:  $n = 2775$ , CG:  $n = 2899$ ); (2) supervised (OR 0.60; 95% CI 0.50–0.72;  $I^2 = 6.4\%$ ; IG:  $n = 3679$ , CG:  $n = 4670$ ) and (3) light to moderate or moderate intensity (OR 0.58; 95% CI 0.39–0.87;  $I^2 = 0.00\%$ ; IG:  $n = 838$ , CG:  $n = 839$ ; and OR 0.56; 95% CI 0.46–0.68;  $I^2 = 22.56\%$ ; IG:  $n = 2722$ , CG:  $n = 2887$ ) (Table S8). Finally, longer exercise intervention did not reduce the GDM incidence more (OR –0.02, 95% CI –0.05 to 0.00;  $p = 0.06$ ; IG:  $n = 4539$ , CG:  $n = 4936$ ).

### 3.3.2 | Hypertensive disorders of pregnancy

Eight systematic reviews and meta-analyses assessed the effect of exercise on HDP incidence.<sup>21,22,25,26,50,54,60,64</sup> Three systematic reviews and meta-analyses assessed the effect of exercise interventions on GH incidence,<sup>21,22,61</sup> five on pre-eclampsia incidence,<sup>21,22,25,61,64</sup> three on HDP<sup>22,26,50</sup> and one on GH and pre-eclampsia incidence together (Table S4).<sup>54</sup>

All systematic reviews and meta-analyses reported a GH<sup>21,22,61</sup> and HDP<sup>22,26,50</sup> incidence reduction in the exercise group compared with the CG. The studies that reported the effect of exercise on pre-eclampsia incidence had mixed results: one found a decrease on the pre-eclampsia incidence in the exercise group<sup>21</sup> and four did not find effect.<sup>22,25,61,64</sup> Finally, the only study that reported GH and pre-eclampsia incidence together<sup>54</sup> did not find a decrease in the exercise group (Figure 2).

Among the systematic review and meta-analyses that included women with overweight or obesity,<sup>21,26,54,61</sup> one found a reduction in GH incidence,<sup>61</sup> while the others did not find an effect on GH<sup>21</sup> and HDP<sup>21,26,54,61</sup> (Figure S5 and Table S9).

Regarding the updated meta-analysis of RCTs, 28 of them assessed the effect of exercise on HDP incidence.<sup>47,48,68,70,71,74,77,80,82,83,85–87,89–92,94,97,99–107</sup> Among them, 22 studies assessed the effect of exercise on GH incidence,<sup>67,69,70,72,74,76,87,88,89,90,93,94,96,97,100–104,108–110</sup> 20 on pre-eclampsia incidence,<sup>47,72,74,77,79,82,87,90,92–95,100,101,105–107,111–113</sup> one on HDP incidence<sup>114</sup> and the other RCT reported data on eclampsia (Table S3).<sup>98</sup>

The pooled estimates show that exercise reduced the GH incidence (OR 0.53; 95% CI 0.40–0.71;  $I^2 = 0.00$ ; IG:  $n = 2977$ , CG:  $n = 3067$ ) (Figure S6). However, exercise did not reduce the incidence of preeclampsia (OR 0.81; 95% CI 0.61–1.07;  $I^2 = 0.00$ ; IG:  $n = 2573$ , CG:  $n = 2771$ ) (Figure S7). Subgroup

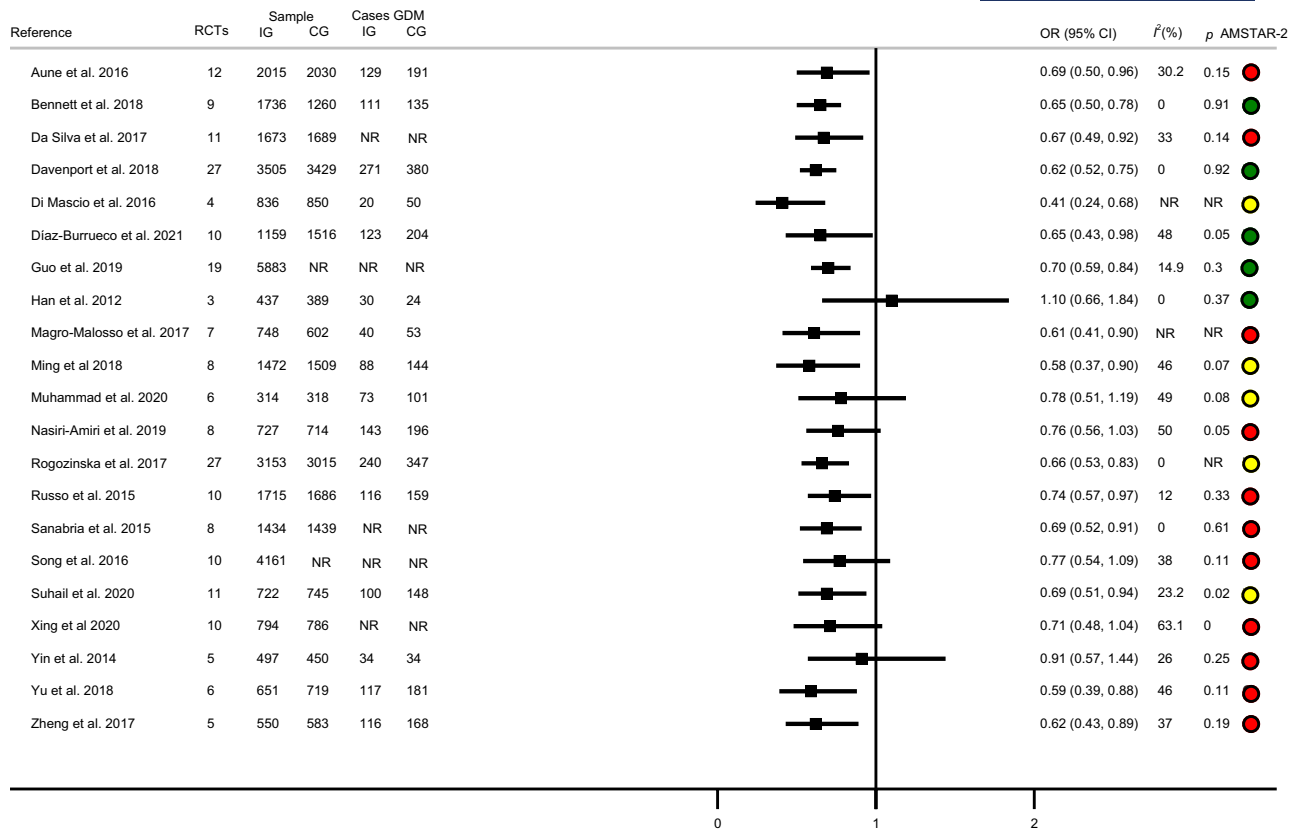


FIGURE 1 Exercise and gestational diabetes mellitus. Systematic review and meta-analyses.

analysis (Table S10) showed lower GH incidence in relation to their counterparts in the CGs in those studies that: (1) included women with all BMI categories (OR 0.50; 95% CI 0.37–0.68;  $I^2 = 0.00$ ; IG:  $n = 2145$ , CG:  $n = 2332$ ); (2) each session was longer than 45 minutes (OR 0.44; 95% CI 0.31–0.64;  $I^2 = 0.00$ ; IG:  $n = 2166$ , CG:  $n = 2241$ ); (3) started exercise interventions in the first and second trimester of pregnancy (OR 0.46; 95% CI 0.30–0.69;  $I^2 = 2.49$ ; IG:  $n = 1451$ , CG:  $n = 1452$  versus OR 0.40; 95% CI 0.20–0.79;  $I^2 = 0.00$ ; IG:  $n = 1242$ , CG:  $n = 1255$ ); (4) exercise was supervised (OR 0.55; 95% CI 0.41–0.73  $I^2 = 0.00$ ; IG:  $n = 2856$ , CG:  $n = 2957$ ); and (5) the intensity of the exercise intervention was light to moderate or moderate, (OR 0.44; 95% CI 0.24–0.80;  $I^2 = 0.00\%$ ; IG:  $n = 657$ , CG:  $n = 658$  and OR 0.58; 95% CI 0.41–0.81;  $I^2 = 22.56\%$ ; IG:  $n = 1874$ , CG:  $n = 1965$ ). The pre-eclampsia incidence was only reduced when initiated in the first trimester (OR 0.34; 95% CI 0.14–0.87;  $I^2 = 0.00\%$ ; IG:  $n = 1451$ , CG:  $n = 1452$ ) (Table S11). Finally, longer exercise intervention did not reduce more HDP incidence (OR –0.02; 95% CI –0.05 to 0.00;  $p = 0.17$ ; IG:  $n = 3266$ , CG:  $n = 3544$ ).

#### Trial sequence analysis

The results of trial sequence analysis are presented in Tables S20–S22 and Figures S8–S10. The required sample size was reached in the main analysis, except for the analysis that assessed the effect of PA intervention on pre-eclampsia.

Additionally, the meta-analysis of blood pressure value showed a reduction in the mean systolic blood pressure

among women in the IG (–9.61 mmHg; 95% CI = –11.34 to –7.87 mmHg;  $I^2 = 93.83\%$ ; IG:  $n = 322$ , CG:  $n = 323$ ) (Table S12).

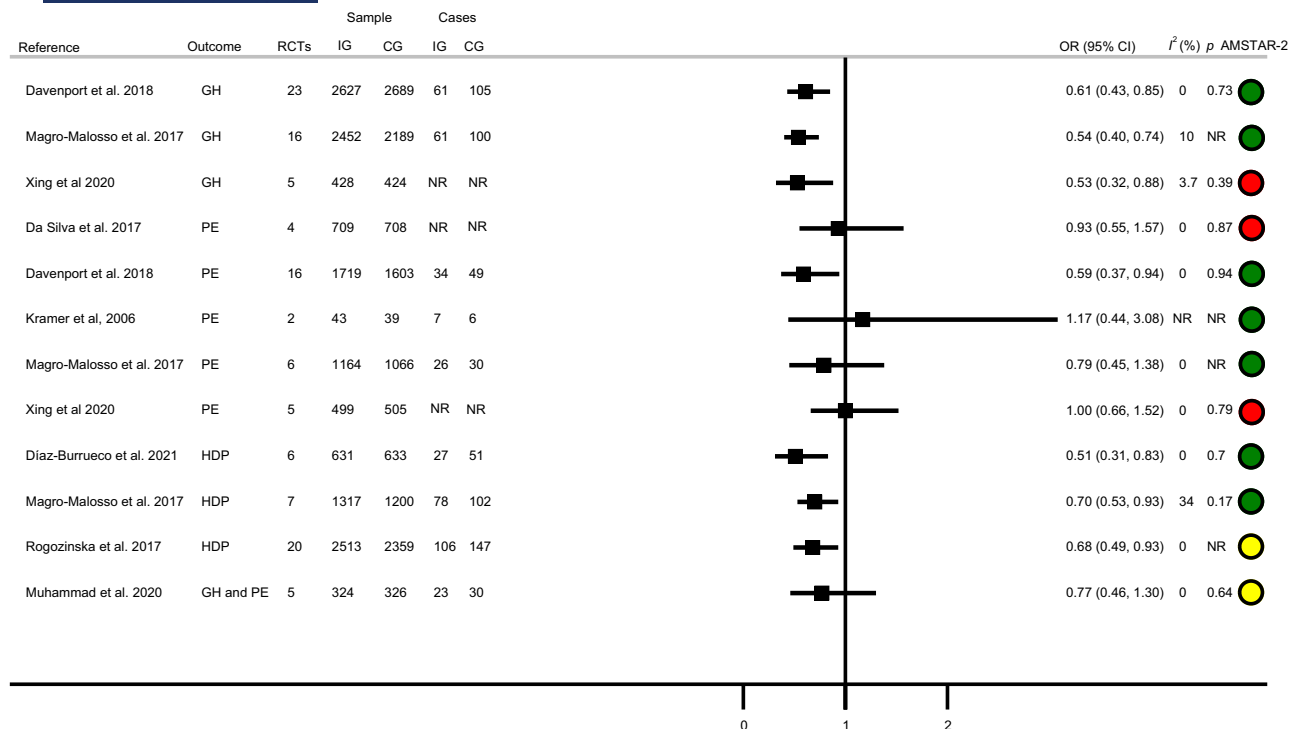
Finally, there was no evidence of ‘p-hacking’ (Tables S30 and S35, Figures S23–S25) or publication bias according to the analyses that assessed the effect of PA intervention on GDM, or of GH on GDM, GH and pre-eclampsia (Figures S11–S22 and Tables S22–S28).

Sensitivity analyses showed that removing studies one-by-one did not modify the pooled odds ratio estimations or heterogeneity.

## 4 | DISCUSSION

### 4.1 | Main findings

Our umbrella review is the first that includes a meta-analysis update to summarise the evidence of the effect of single exercise interventions during pregnancy on GDM and HDP incidence. Based on 21 systematic reviews and meta-analyses, and 54 RCTs, we found that exercise interventions were more effective than standard prenatal care in reducing the incidence of GDM and GH by 39% and 47%, respectively. In contrast, our subgroup analyses showed no effect of exercise on the incidence of HDP in overweight and obese pregnant women or when sessions lasted less than 45 minutes. Meanwhile, our data suggest that exercise is more effective in reducing the GDM and HDP incidence when initiated in the first trimester



**FIGURE 2** Exercise and hypertensive disorders of pregnancy. Systematic reviews and meta-analyses.

of pregnancy, under supervision and with light to moderate intensity, whereas exercise only reduced the incidence of pre-eclampsia when pregnant women started exercise in the first trimester of pregnancy. Trial sequence analysis indicates that additional studies are needed to elucidate the effect of PA interventions on pre-eclampsia incidence.

## 4.2 | Strengths and limitation

Among the strengths and what the study adds, we provide concrete recommendations about duration, intensity and the best moment to start PA intervention to reduce the incidence of GDM, GH and pre-eclampsia, as well as the need for evidence about the effect of PA on pre-eclampsia incidence.

Although this umbrella provides important insights, some limitations should be noted. First, most RCTs and meta-analyses have methodological shortcomings mainly because blinding is not possible in this type of intervention. Second, many of the reviews included in our umbrella review included the same primary studies, revealing a large overlap between published systematic reviews and meta-analyses (Tables S14–S17). We have conducted the pooled meta-analysis with original studies where each study counted once to avoid multiple contributions of the same studies. Third, we excluded studies that only included women with specific diseases, GDM or HDP. Fourth, an important limitation is that most primary studies did not provide data on the pre-pregnancy PA of participants; consequently, this important confounder was not controlled. Fifth, the included meta-analyses had a broad variety in their primary studies, mainly because of their

different included and excluded criteria or the dates for developing, between others. Finally, as a result of the large amount of data, we decided to include only outcomes regarding GDM and HDP of the protocol published.

## 4.3 | Interpretation

Our estimates of a 39% reduction in the incidence of developing GDM agree with those reported by most systematic reviews and meta-analyses<sup>15,21,24,26,49,53,55,58,61,62,65</sup> and reveal that the reduction in GDM incidence still tends to be significant in most subgroup analyses (Table S8). However, six systematic reviews and meta-analyses included in our umbrella review did not find a reduction in GDM.<sup>17,18,54,57,59,60</sup> Most of these were conducted in pregnant women with obesity and overweight. It is known that exercise interventions are generally less effective in women with a high pre-pregnancy BMI.<sup>49</sup> This could be because the largest RCTs included initiated the intervention at 20 weeks of gestation, when insulin resistance is likely to have already developed.<sup>75</sup>

The updated meta-analysis shows that the incidence of GDM in the IGs is 39% lower than in the CGs. Furthermore, according to a previous systematic reviews and meta-analyses,<sup>21</sup> the incidence of GDM was lower when the intervention started during the first trimester of pregnancy, was supervised, or had a light to moderate level of intensity. In addition, supervision during exercise performance has been highlighted as an important determinant in adherence to exercise interventions, and so it would increase the effectiveness in preventing GDM.<sup>115</sup>

ACOG hypothesised that exercise could stimulate placental angiogenesis and improve maternal endothelial function.<sup>116</sup> Subsequent evidence supports that mild and moderate intensity exercise increases angiogenesis without increasing placental oxidative or endoplasmic stress.<sup>117</sup> However, the evidence about the effect of exercise on HDP incidence remains inconsistent.<sup>21,54</sup> Our analyses support, according to previous reports,<sup>22,26</sup> that exercise decreases GH but does not reduce the pre-eclampsia incidence.<sup>22</sup> This could be attributed to differences in the sample characteristics,<sup>54</sup> heterogeneity in the exercise intervention design, or that the number of studies included in the meta-analyses, or their statistical powers, was not sufficient<sup>22</sup> because pre-eclampsia is not a common disorder, occurring in 1.4–4% of all pregnancies.<sup>118</sup>

## 5 | CONCLUSIONS

In summary, the current evidence supports that exercise has a beneficial effect on the incidence of GDM and GH in non-overweight or obese pregnant women. Furthermore, these benefits are greater when exercise interventions are supervised, have a low to moderate intensity level, and are initiated during the first trimester of pregnancy. Nevertheless, more high-quality intervention studies are needed to accurately evaluate the safety and benefits of exercise programmes for specific pregnant populations, such as women with overweight and obesity, and whether higher intensity exercise interventions result in greater benefits in these groups. In addition, according to our data, to achieve greater benefits, the core of our recommendation for clinicians is that exercise should be supervised, initiated in the first trimester of pregnancy, and lasting more than 45 minutes per session. However, few studies have reported a reduction in HDP among women with overweight and obesity. More studies are needed to test the effectiveness of exercise interventions to reduce the incidence of pre-eclampsia in pregnant women with excess weight.

### AUTHOR CONTRIBUTIONS

All authors conceived and designed the study. GSM, JAMH and VMV acquired and collected the data. GSM, JAMH, RFR, CPM, CAB, ICR and VMV analysed the data. All authors drafted and critically revised the manuscript for important intellectual content and gave final approval of the version to be published.

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### CONFLICT OF INTEREST

None declared. Completed disclosure of interests form available to view online as supporting information.

### DATA AVAILABILITY STATEMENT

The protocol can be accessed on PROSPERO (Registration number: CRD42019123410). The review protocol has also been published.<sup>29</sup> In addition, data can be accessed upon request by e-mailing the corresponding author ([gema.sanabria@uclm.es](mailto:gema.sanabria@uclm.es)). Reuse only with permission and with citation. The data that support the findings of this study are available in the Supplementary material of this article.

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