Exercise during pregnancy in normal-weight women and risk of preterm birth: a systematic review and meta-analysis of randomized controlled trials

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BACKGROUND: Preterm birth is the major cause of perinatal mortality in the United States. In the past, pregnant women have been recommended to not exercise because of presumed risks of preterm birth. Physical activity has been theoretically related to preterm birth because it increases the release of catecholamines, especially norepinephrine, which might stimulate myometrial activity. Conversely, exercise may reduce the risk of preterm birth by other mechanisms such as decreased oxidative stress or improved placenta vascularization. Therefore, the safety of exercise regarding preterm birth and its effects on gestational age at delivery remain controversial.
OBJECTIVE: The objective of the study was to evaluate the effects of exercise during pregnancy on the risk of preterm birth.
DATA SOURCES: MEDLINE, EMBASE, Web of Sciences, Scopus, ClinicalTrial.gov, OVID, and Cochrane Library were searched from the inception of each database to April 2016.
STUDY DESIGN: Selection criteria included only randomized clinical trials of pregnant women randomized before 23 weeks to an aerobic exercise regimen or not. Types of participants included women of normal weight with uncomplicated, singleton pregnancies without any obstetric contraindication to physical activity. The summary measures were reported as relative risk or as mean difference with 95% confidence intervals. The primary outcome was the incidence of preterm birth <37 weeks.
TABULATION, INTEGRATION, AND RESULTS: Of the 2059 women included in the meta-analysis, 1022 (49.6%) were randomized to the exercise group and 1037 (50.4%) to the control group. Aerobic exercise lasted about 35—90 minutes 3—4 times per week. Women who were randomized to aerobic exercise had a similar incidence of preterm birth of <37 weeks (4.5% vs 4.4%; relative risk, 1.01, 95% confidence interval, 0.68—1.50) and a similar mean gestational age at delivery (mean difference, 0.05 week, 95% confidence interval, —0.07 to 0.17) compared with controls. Women in the exercise group had a significantly higher incidence of vaginal delivery (73.6% vs 67.5%; relative risk, 1.09, 95% confidence interval, 1.04—1.15) and a significantly lower incidence of cesarean delivery (17.9% vs 22%; relative risk, 0.82, 95% confidence interval, 0.69—0.97) compared with controls. The incidence of operative vaginal delivery (12.9% vs 16.5%; relative risk, 0.78, 95% confidence interval, 0.61—1.01) was similar in both groups. Women in the exercise group had a significantly lower incidence of gestational diabetes mellitus (2.9% vs 5.6%; relative risk, 0.51, 95% confidence interval, 0.31-0.82) and a significantly lower incidence of hypertensive disorders (1.0% vs 5.6%; relative risk, 0.21, 95% confidence interval, 0.09-0.45) compared with controls. No differences in low birthweight (5.2% vs 4.7%; relative risk, 1.11, 95% confidence interval, 0.72—1.73) and mean birthweight (mean difference, —10.46 g, 95% confidence interval, —47.10 to 26.21) between the exercise group and controls were found.
CONCLUSION: Aerobic exercise for 35—90 minutes 3—4 times per week during pregnancy can be safely performed by normal-weight women with singleton, uncomplicated gestations because this is not associated with an increased risk of preterm birth or with a reduction in mean gestational age at delivery. Exercise was associated with a significantly higher incidence of vaginal delivery and a significantly lower incidence of cesarean delivery, with a significantly lower incidence of gestational diabetes mellitus and hypertensive disorders and therefore should be encouraged.

Key words: exercise during pregnancy, obstetric outcomes, physical activity, pregnancy outcomes, preterm birth, preterm delivery

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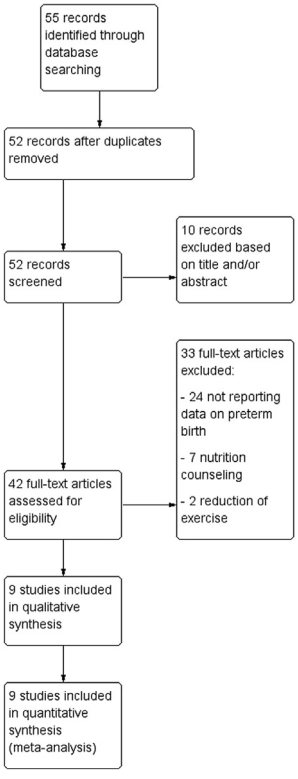
Preterm birth is the major cause of perinatal mortality in the United States.[1] In the past, pregnant women have been advised against exercise because of presumed risks of pregnancy loss and preterm birth, possibly because of reduced placental circulation.[2] Physical activity has been theoretically related to preterm birth because it increases the release of catecholamines, especially norepinephrine, which might stimulate myometrial activity.[3]

Conversely, exercise may reduce the risk of preterm birth by other mechanisms such as decreased oxidative stress or improved placenta vascularization,[4] an adaptive response to intermittent reduction in uterine blood flow, as well as increased blood volume found in pregnant women during exercise.[5] Physical activity during pregnancy may be decreased because of a lack of time, lack of energy, discomfort or pain, and concern about the baby's health.[6] In fact, bed rest is commonly recommended in pregnancy.[7] Therefore, the safety of exercise regarding preterm birth, and its effects on gestational age at delivery, remain controversial.

The aim of this systematic review and meta-analysis was to evaluate the effects of exercise during pregnancy on the risk of preterm birth.

FIGURE 1
Flow diagram of studies identified in the systematic review



Data are from the Prisma template (Preferred Reporting Item for Systematic Reviews and Meta-analyses).

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Materials and Methods

Search strategy

This meta-analysis was performed according to a protocol recommended for systematic review.[8] The review protocol was designed a priori defining methods for collecting, extracting, and analyzing data. The research was conducted using MEDLINE, EMBASE, Web of Sciences, Scopus, ClinicalTrial.gov, OVID, and Cochrane Library as electronic databases. The trials were identified with the use of a combination of the following text words: exercise or physical activity and pregnancy and preterm birth or preterm delivery and randomized trial as publication type, from the inception of each database to April 2016. Review of articles also included the abstracts of all references retrieved from the search.

Study selection

Selection criteria included only randomized clinical trials of pregnant women randomized to an exercise regimen or not. We included only randomized clinical trials reporting preterm birth as an outcome. Types of participants included women with uncomplicated, singleton pregnancies without any obstetric contraindication to physical activity.

In all the trials, the intervention group participated in planned aerobic exercise. In the control group, women did not participate in exercise sessions and only attended regular scheduled obstetric visits. When possible, data only on women with normal body mass index ($18.5-24.9$ kg/m^2) were selected. Randomized clinical trials including only underweight (body mass index ≤ 18.5 kg/m^2) or only overweight or obese (body mass index ≥ 25 kg/m^2) women, those including diet, counseling, and/or weight monitoring, and those assessing reduction in exercise, were excluded. Quasirandomized trials (ie, trials in which allocation was done on the basis of a pseudorandom sequence (eg, odd/even hospital number or date of birth, alternation) were also excluded.

Data extraction and risk of bias assessment

The risk of bias in each included study was assessed by using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*.[8] Seven domains related to risk of bias were assessed in each included trial because there is evidence that these issues are associated with biased estimates of treatment effect including the following: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting; and (7) other bias. Review authors' judgments were categorized as low risk, high risk, or unclear risk of bias.[8]

All analyses were done using an intention-to-treat approach, evaluating women according to the treatment group to which they were randomly allocated in the original trials. The primary outcome was the incidence of preterm birth at <37 weeks. Secondary outcomes were gestational age at delivery, spontaneous vaginal delivery, operative vaginal delivery, cesarean delivery, gestational diabetes, hypertensive disorders (defined as gestational hypertension or preeclampsia), and neonatal outcomes including birthweight and low birthweight (ie, birthweight <2500 g).

We assessed the primary outcome (ie, incidence of preterm birth <37 weeks) in a sensitivity analysis according to the risk of bias of the included trials[8] and in subgroup analysis according to the type and length of exercise.

Data analysis

Data analysis was completed using Review Manager 5.3 (The Nordic Cochrane Center, Cochrane Collaboration, 2014; Copenhagen, Denmark).[8] Statistical heterogeneity between studies was assessed using the Higgins I^2 statistics. In case of statistical significant heterogeneity ($I^2 \geq 0$), the random effects model of DerSimonian and Laird was used to obtain the pooled risk ratio estimate; otherwise, in case of no inconsistency in risk estimates ($I^2 = 0$), a fixed-effect model was used.[8]

The summary measures were reported as relative risk or as mean difference with 95% confidence intervals. Potential publication biases were assessed graphically by using the funnel plot and statistically by using Begg's and Egger's tests. A value of $P < .05$ was considered statistically significant.

The meta-analysis was reported following the Preferred Reporting Item for Systematic Reviews and Meta-Analyses statement.[9] Before data extraction, the review was registered with the International Prospective Register of Systematic Reviews (PROSPERO, registration number CRD42016037841).

Three authors (D.D.M., E.R.M.-M., G.S.) independently assessed inclusion criteria, risk of bias, data extraction, and data analysis. Disagreements were resolved by discussion with a fourth reviewer (V.B.). Data from each eligible study were extracted without modification of original data onto custom-made data collection forms. Differences were reviewed and further resolved by common review of the entire process. Data not presented in the original publications were requested from the principal investigators.

Results

Study selection and study characteristics

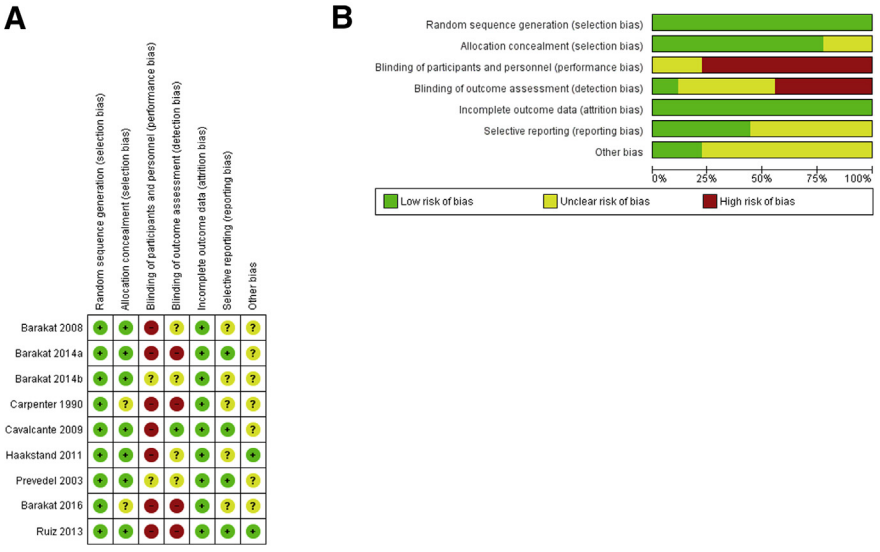
Figure 1 shows the flow diagram (Preferred Reporting Item for Systematic Reviews and Meta-Analyses template) of information derived from a review of potentially relevant articles. Nine randomized clinical trials, including 2059 sedentary women with an uncomplicated, singleton pregnancy, were included in the meta-analysis.[10-18] One study was published in abstract form only.[10]

The quality of randomized clinical trials included in our meta-analysis was assessed by the Cochrane Collaboration's tool.[8] All the included studies, except one,[10] used a computer-generated table of random numbers and had a low risk of bias in incomplete outcome data. No method of blinding as to the group allocation was reported (Figure 2). Figure 3 shows the funnel plot for the primary outcome for assessing publication bias; the symmetric plot suggests no publication bias. Publication bias, assessed using Begg's and Egger's tests, was not significant ($P = .48$ and $P = .51$, respectively). Unpublished data were kindly provided by an author.[10]

Table 1 shows the characteristics of the included trials. In 5 trials,[12,15-18] women were randomized during the first trimester; in 4 studies,[10,11,13,14] women were randomized during the early second trimester (≤22 weeks). Table 2 shows inclusion and exclusion criteria of these trials. Characteristics of the women included are reported in Table 3.

All studies randomized only sedentary, pregnant women with uncomplicated, singleton gestations. Women were excluded if any obstetric contraindications, mostly as recommended by the American College of Obstetricians and

FIGURE 2
Assessment of risk of bias



A, Summary of the risk of bias for each trial. *Plus sign* indicates a low risk of bias; *minus sign* indicates a high risk of bias; *question mark* indicates an unclear risk of bias. **B,** Graph of risk of bias about each risk of bias item presented as percentages across all included studies.

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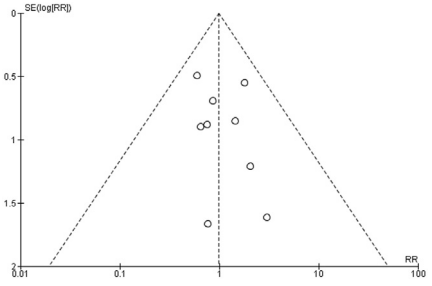
FIGURE 3
Funnel plot for assessing publication bias



Funnel plot for assessing the publication bias in the primary outcome (ie, incidence of preterm birth).

RR, relative risk.

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TABLE 1
Characteristics of the included trials

Study	Carpenter et al, 1990[10]	Prevedel et al, 2003[11]	Barakat et al, 2008[12]	Calvalcante et al, 2009[13]	Haakstad et al, 2011[14]	Ruiz et al, 2013[15]	Barakat et al, 2014[16]	Barakat et al, 2014[17]	Barakat et al, 2016[18]
Study location	United States	Brazil	Spain	Brazil	Norway	Spain	Spain	Spain	Spain
Sample size[a]	14 (7 vs 7)	41 (22 vs 19)	142 (72 vs 70)	71 (34 vs 37)	105 (52 vs 53)	687 (335 vs 352)	200 (107 vs 93)	290 (138 vs 152)	513 (257 vs 256)
GA (wks) at randomization Mean ± SD or WR	20–22	16–20	12–13	16–20	17.3 ± 4.1 vs 18.0 ± 4.3	5–6	6–7[b]	8–10	9–11
Type of exercise	30 min of physical training preceded and followed by 30 min of cycle ergometry at 60% maximum VO_2	Hydrotherapy exercises: stretching; resistance, targeted, respiratory exercises in an indoor swimming pool with water at 28–32°C	Stretching; toning and joint mobilization exercises; resistance exercises	Water aerobics in an indoor swimming pool with water at 28–30°C	Aerobic dance followed by abdominal, pelvic floor and back muscle training, stretching, relaxation, and body awareness exercises	Aerobic, resistance, and stretching exercises	Walking and stretching followed by toning and joint mobilization exercises, aerobic dance, and specific exercises for leg, buttocks, and abdomen	Toning, joint mobilization, and resistance exercises preceded and followed by walking and light stretching	Aerobic exercise, aerobic dance, muscular strength, and flexibility exercises preceded by walking and light stretching and followed by relaxation and pelvic floor exercise
Duration of a single session, min	90	60	35	50	60	50–55	55–60	55–60	50–55
Times per week, number of days	4	3	3	3	3	3	3	3	3
Intensity of exercise (HR)	NR	NR	<80% of their age-predicted maximum HR	<70% of their age-predicted maximum HR	NR	<60% of their age-predicted maximum HR	<60% of their age-predicted maximum HR	<60-75% of their age-predicted maximum HR	<70% of their age-predicted maximum HR
Self-reported intensity of exercise, Borg scale[c]	NR	NR	NR	NR	12–14	10–12	12–13	NR	12–14

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(continued)

TABLE 1
Characteristics of the included trials *(continued)*

Study	Carpenter et al, 1990[10]	Prevedel et al, 2003[11]	Barakat et al, 2008[12]	Calvalcante et al, 2009[13]	Haakstad et al, 2011[14]	Ruiz et al, 2013[15]	Barakat et al, 2014[16]	Barakat et al, 2014[17]	Barakat et al, 2016[18]
Control group	10 wks of nonexercise	No hydrotherapy program	No exercise, except those activities necessary for daily living	No regular physical activity during the entire pregnancy	Women were neither encouraged nor discouraged from exercising	Regular scheduled visits, every 4—5 wks until the 35th wk of GA, then weekly until delivery. Women received general nutrition and physical activity counseling and were not discouraged from exercising.	No exercise during pregnancy	NR	General advice from their health care provider about positive effects of physical activity; regular scheduled visits; women not discouraged from exercising on their own and asked by telephone about their exercise once each trimester
Primary outcome	Change in resting heart rate; exercise stroke volume; exercise VO_2; O_2 pulse	Maternal outcomes: body composition and cardiovascular capacity; perinatal outcomes: weight and prematurity	Healthy gravidae and GA at delivery	Evolution of pregnancy (GA at delivery, preterm birth), maternal body composition (weight gain, BMI, proportion of fat mass), and perinatal outcomes (Apgar score, weight at birth, and birthweight adequate for GA)	Infant birthweight	Maternal weight gain	Maternal (GA, preterm birth, blood pressure, weight gain, type of delivery, GDM) and fetal (birthweight, head circumference, birth size, Apgar score, pH of umbilical cord, sex) outcomes	GA at delivery	Gestational hypertension
Other comments	Physical training only 10 wks in midpregnancy	—	—	—	In addition to joining the scheduled exercise sessions, all women in the exercise group were asked to include 30 min of moderate self-imposed physical activity on the remaining weekdays	Sample size refers to only normal-weight women included in the original trial	—	—	Sample size refers to only normal-weight women included in the original trial

BMI, body mass Index; *GA*, gestational age; *GDM*, gestational diabetes mellitus; *HR*, heart rate; *NR*, not reported; *VO_2*, O_2 consumption; *WR*, week range.

[a] Data are presented as total number (number in the intervention group vs number in the control group); [b] Pregnant women who underwent their first ultrasound examination at 10—12 weeks were offered the opportunity to participate, following a randomization process; [c] Borg scale is a 15 category scale (from 6 to 20) to measure the level of perceived exertion. Light exercise is about 6—11; 13 somewhat hard; 15 hard; 19 extremely hard.

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TABLE 2
Inclusion and exclusion criteria of the women included in the trials

Study	Inclusion criteria	Exclusion criteria
Carpenter et al, 1990[10]	Sedentary, pregnant women	Not reported
Prevedel et al, 2003[11]	Nulliparous with singleton, uncomplicated gestations	Any medical or obstetrical contraindication
Barakat et al, 2008[12]	Women with singleton, uncomplicated gestations, not at high risk of preterm delivery	Any obstetric contraindication to exercise suggested by ACOG; not planning to give birth in the same obstetrics hospital department; not to be under medical follow-up throughout the entire pregnancy; any serious medical condition
Calvalcante et al, 2009[13]	Low-risk, sedentary pregnant women with uncomplicated, singleton gestations	History of 2 or more cesarean deliveries; medical conditions contraindicating the practice of physical exercise and/or practical impediments
Haakstad et al, 2011[14]	Nulliparous women with uncomplicated, singleton gestations whose prepregnancy exercise levels did not include participation in a structured exercise program; ability to read, understand, and speak Norwegian; to be within the first 24 wks of pregnancy	History of more than 2 miscarriages, severe heart disease, and persistent bleeding after 12 wks of gestation; multiple pregnancy; poorly controlled thyroid disease; gestational hypertension or preeclampsia; diabetes or gestational diabetes
Ruiz et al, 2013[15]	Sedentary women with singleton, uncomplicated gestations, not at high risk of preterm delivery, and not participating in any other trial	Any obstetric contraindication to exercise suggested by ACOG
Barakat et al, 2014[16]	Women with uncomplicated, singleton gestations	Any obstetric contraindication to exercise suggested by ACOG; not planning to give birth in the obstetrics department of the study; not receiving medical follow-up throughout pregnancy; participating in another physical program or having a high level of pregestational physical exercise
Barakat et al, 2014[17]	Women with uncomplicated, singleton gestations	Any obstetric contraindication to exercise suggested by ACOG; not planning to give birth in the obstetrics department of the study; not receiving medical follow-up throughout pregnancy; participating in another physical program or having a high level of pregestational physical exercise
Barakat et al, 2016[18]	Women with uncomplicated, singleton gestations	Any obstetric contraindication to exercise suggested by ACOG; not planning to give birth in the obstetrics department of the study; not receiving medical follow-up throughout pregnancy; history of risk of preterm birth

ACOG, American Congress of Obstetricians and Gynecologists; *BMI*, body mass index.

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Gynecologists (Table 2).[19] In all 9 trials, the intervention group participated in aerobic exercise. Seven trials[10,12,14-18] studied toning, resistance, and flexibility exercise together with joint mobilization activities, mostly according to American College of Obstetricians and Gynecologists recommendations.[19] Two trials[11,13] studied water aerobics. The mean time of every session was 57 minutes, 3 times a week in 8 trials,[11-18] and 4 times a week in 1 trial.[10] In the control group, women did not participate in any structured exercise sessions and attended only regularly scheduled obstetric visits.

Synthesis of results

Of the 2059 women included in the meta-analysis, 1022 (49.6%) were randomized to the exercise group and 1037 (50.4%) to the control group. The statistical heterogeneity within the studies was low with no inconsistency ($I^2 = 0$) for the risk estimates. Table 4 shows the pooled data of primary and secondary outcomes of the meta-analysis.

Pregnant women who were randomized before 23 weeks to 35−90 minutes of aerobic exercise 3−4 times per week for 10 weeks or up to delivery had a similar incidence of preterm birth <37 weeks (4.5% vs 4.4%; relative risk, 1.01, 95% confidence interval, 0.68−1.50) (Figure 4) and a similar mean gestational age at delivery (mean difference, 0.05 week, 95% confidence interval, −0.07 to 0.17) compared with controls. Women in the exercise group had a significantly higher incidence of vaginal delivery (73.6% vs 67.5%; relative risk, 1.09, 95% confidence interval, 1.04−1.15) and a significantly lower incidence of cesarean delivery (17.9% vs 22%; relative risk, 0.82, 95% confidence interval, 0.69−0.97) compared with controls.

TABLE 3
Characteristics of the women included in the trials

Characteristics	Carpenter et al, 1990[10]	Prevedel et al, 2003[11]	Barakat et al, 2008[12]	Calvalcante et al, 2009[13]	Haakstad et al, 2011[14]	Ruiz et al, 2013[15]	Barakat et al, 2014[16]	Barakat et al, 2014[17]	Barakat et al, 2016[18]
Maternal age, y, mean ± SD	NR	20	30.4 ± 2.9 vs 29.5 ± 3.7	25.8 ± 4.6 vs 24.4 ± 5.8	31.2 ± 3.7 vs 30.3 ± 4.4	31.6 ± 4 vs 31.9 ± 4	31.57 ± 3.87 vs 31.51 ± 3.92	31.4 ± 3.2 vs 31.7 ± 4.5	31.6 ± 4.2 vs 31.8 ± 4.5
Parity									
0	NR	NR	72.2% vs 57.1%	47.1%[a] vs 62.2%[a]	NR	NR	60.7% vs 53.9%	60.9% vs 54.6%	67.8% vs 59.8%
1	NR	NR	22.2% vs 35.7%	NR	NR	NR	34.6% vs 40.4%	33.3% vs 39.5%	26.2% vs 33.2%
>1	NR	NR	5.6% vs 7.1%	NR	NR	NR	4.7% vs 5.6%	2.9% vs 5.9%	6% vs 7.1%
Occupation									
Sedentary	NR	NR	26/72 (36.1%) vs 21/70 (30%)	NR	37/52 (71.2%) vs 36/53 (67.9%)	195/476 (41%) vs 184/477 (38.6%)	NR	58/138 (42%) vs 68/152 (44.7%)	171/382 (44.8%) vs 148/383 (38.6%)
Housewife	NR	NR	31/72 (43.1%) vs 30/70 (42.9%)	NR	NR	126/476 (26.5%) vs 118/477 (24.7%)	NR	25/138 (18.1%) vs 33/152 (21.7%)	72/382 (18.9%) vs 93/383 (24.3%)
Active	NR	NR	15/72 (20.8%) vs 19/70 (27.1%)	NR	NR	155/476 (32.5%) vs 175/477 (36.7%)	NR	55/138 (39.9%) vs 51/152 (33.6%)	139/382 (36.4%) vs 142/383 (37.1%)
Daily smokers, %	NR	10% (overall smoking index)	16/72 (22.2%) vs 20/70 (28.6%)	NR	2/52 (3.8%) vs 1/53 (1.9%)	NR	11/107 (10.3%) vs 12/89 (13.5%)	18/138 (13%) vs 29/152 (19.1%)	40/382 (10.5%) vs 54/383 (14.1%)
Prepregnancy BMI, mean ± SD	NR	NR	24.3 ± 0.5 vs 23.4 ± 0.5	24.1 ± 4.5 vs 23.4 ± 3.8	23.8 ± 3.8 vs 23.9 ± 4.7	23.7 ± 3.9 vs 23.5 ± 4.2	23.8 ± 4.4 vs 24.1 ± 4.3	24.0 ± 4.3 vs 23.6 ± 4	23.6 ± 3.8 vs 23.4 ± 4.2
Prepregnancy BMI, %	NR	NR	NR	NR	NR	<18.5[b] 11/480 (2.3%) vs 24/482 (5%) ≥18.5-24.9[b] 323/480 (67.3%) vs 329/482 (68.2%) ≥25-29.9[b] 111/480 (23.1%) vs 92/482 (19.1%) ≥30[b] 35/480 (7.3%) vs 37/482 (7.7%)	<18[b] 1/106 (0.9%) vs 2/90 (2.2%) ≥18-24.9[b] 73/106 (68.9%) vs 58/90 (64.5%) ≥25-29.9[b] 25/106 (23.6%) vs 21/90 (23.3%) ≥30[b] 7/106 (6.6%) vs 9/90 (10%)	NR	<18.5[b] 10/382 (2.6%) vs 20/383 (5.2%) ≥18.5-24.9[b] 258/382 (67.5%) vs 259/383 (67.6%) ≥25-29.9[b] 89/382 (23.3%) vs 75/383 (19.6%) ≥30[b] 25/382 (6.5%) vs 29/383 (7.6%)
Prior PTB	NR	NR	2.8% vs 4.3%	NR	NR	0% vs 0%	NR	5.8% VS 3.9%	0% vs 0%

Data are presented always in the same order: intervention group vs control group.

BMI, body mass index; *NR*, not reported; *PTB*, preterm birth.

[a] These data are taken from elsewhere[26] by the same authors on the very same pregnant women population; [b] Significant results.

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TABLE 4
Primary and secondary outcomes

Outcome	Carpenter et al, 1990[10]	Prevedel et al, 2003[11]	Barakat et al, 2008[12]	Calvalcante et al, 2009[13]	Haakstad, 2011[14]	Ruiz et al, 2013[15]	Barakat et al, 2014[16]	Barakat et al, 2014[17]	Barakat et al, 2016[18]	Total	RR or MD (95% CI)
PTB <37 wks	0/7 (0%) vs 0/7 (0%)	3/22 (13.6%) vs 1/19 (5.3%)	2/72 (2.8%) vs 3/70 (4.3%)	2/33[a] (6.1%) vs 3/37 (8.1%)	2/52 (3.8%) vs 1/53 (1.9%)	8/335 (2.3%) vs 2/352 (0.6%)	4/106 (3.8%) vs 4/91 (4.4%)	6/138 (4.3%) vs 11/152 (7.2%)	19/257 (7.4%)[b] vs 21/256 (8.2%)[b]	46/1022 (4.5%) vs 46/1037 (4.4%)	1.01 [0.68, 1.50]
GA at delivery, wks, mean ± SD	NR	NR	39.57 ± 1.1 vs 39.71 ± 1.4	39.2 ± 2.2[c] vs 39.1 ± 1.6[c]	39.9 ± 1.2 vs 39.6 ± 1.2	39.6 ± 1.5 vs 39.6 ± 1.3	39.46 ± 1.9 vs 39.2 ± 2.2	39.6 ± 1.1 vs 39.7 ± 1.3	39.6 ± 1.74 vs 39.4 ± 1.86	—	0.05 [−0.07, 0.17]
Spontaneous vaginal delivery	NR	NR	51/72 (70.8%)[d] vs 50/70 (71.4%)[d]	21/33 (63.6%) vs 20/37 (54.1%)	NR	280/335 (83.6%) vs 286/352 (81.3%)	72/105 (68.6%) vs 52/91 (57.1%)	100/138 (72.5%)[b] vs 88/152 (57.9%)[b]	260/382 (68.1%) vs 236/383 (61.6%)	784/1065 (73.6%) vs 732/1085 (67.5%)	1.09 [1.04, 1.15][f]
Operative vaginal delivery	NR	NR	10/72 (13.9%)[d] vs 9/70 (12.9%)[d]	NR	NR	NR	15/105 (14.3%) vs 13/91 (14.3%)	16/138 (11.6%)[e] vs 29/152 (19.1%)[e]	49/382 (12.8%) vs 64/383 (16.7%)	90/697 (12.9%) vs 115/696 (16.5%)	0.78 [0.61, 1.01]
Cesarean delivery	NR	NR	11/72 (15.3%)[d] vs 11/70 (15.7%)[d]	12/33 (36.4%) vs 17/37 (45.9%)	NR	55/335 (16.4%) vs 66/352 (18.7%)	18/105 (17.1%) vs 26/91 (28.6%)	22/138 (15.9%)[e] vs 35/152 (23%)[e]	73/382 (19.1%) vs 83/383 (21.7%)	191/1065 (17.9%) vs 238/1085 (22%)	0.82 [0.69, 0.97][f]
GDM	NR	NR	NR	NR	NR	7/335 (2.1%) vs 18/352 (5.1%)	5/106 (4.7%) vs 5/90 (5.6%)	6/138 (4.3%) vs 12/152 (7.9%)	6/257 (2.3%) vs 13/256 (5.1%)	24/836 (2.9%) vs 48/850 (5.6%)	0.51 [0.31, 0.82][f]
Hypertensive disorders	NR	NR	NR	NR	1/52 (1.9%) vs 1/53 (1.9%)	5/335 (1.5%) vs 20/352 (5.7%)	NR	NR	2/257 (0.8%) vs 15/256 (5.9%)	7/644 (1.0%) vs 37/661 (5.6%)	0.21 [0.09, 0.45][f]
Birthweight, g, mean ± SD	NR	3110 vs 3175	3165 ± 411 vs 3307 ± 477	3222.2 ± 562.7 vs 3312.7 ± 656.1	3477 ± 424 vs 3542 ± 464	3219 ± 433 vs 3215 ± 419	3186.6 ± 440.76 vs 3261.18 ± 466.59	3203 ± 461 vs 3232 ± 448	3252 ± 438 vs 3218 ± 453	—	−10.46 [−47.1 to 26,21]
LBW	NR	NR	4/72 (5.6%) vs 4/70 (5.7%)	3/33 (9.1%) vs 2/37 (5.4%)	1/52 (1.9%) vs 1/53 (1.9%)	19/335 (5.7%) vs 15/352 (4.3%)	NR	NR	12/257 (4.7%)[b] vs 14/256 (5.5%)[b]	39/749 (5.2%) vs 36/768 (4.7%)	1.11 [0.72, 1.73]

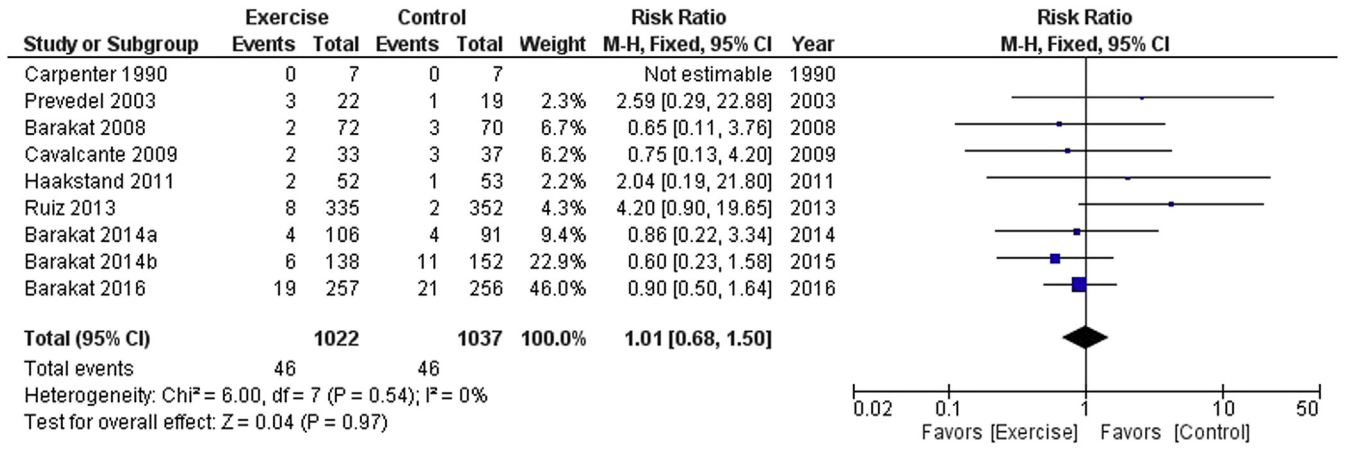
Hypertensive disorders include gestational hypertension and preeclampsia. Data are presented as the number in the intervention group vs the number in the control group with percentage.

CI, confidence interval; *GA*, gestational age; *GDM*, gestational diabetes mellitus; *LBW*, low birthweight; *MD*, mean difference; *PTB*, preterm birth; *RR*, risk ratio.

[a] Authors report that a woman in the exercise group was lost to follow-up: data on her delivery and on the newborn infant are not available; [b] Data from only normal body mass index women subgroup; [c] These data are taken from elsewhere[26] by the same authors on the very same pregnant women population; [d] These data are taken from elsewhere [27] by the same authors on the very same pregnant women population; [e] These data are taken from elsewhere [28] by the same authors on the very same pregnant women population; [f] SIgnificant results.

Di Mascio. Exercise during pregnancy in normal-weight women and risk of preterm birth. Am J Obstet Gynecol 2016.

FIGURE 4
Forest plot for the risk of the primary outcome



Forest plot for the risk of the primary outcome (ie, incidence of preterm birth).

CI, confidence interval; *df*, degrees of freedom; *M-H*, Mantel-Haenszel.

Di Mascio. Exercise during pregnancy in normal-weight women and risk of preterm birth. Am J Obstet Gynecol 2016.

The incidence of operative vaginal delivery (12.9% vs 16.5%; relative risk, 0.78, 95% confidence interval, 0.61−1.01) was similar in both groups. Women in the exercise group had a significantly lower incidence of gestational diabetes mellitus (2.9% vs 5.6%; relative risk, 0.51, 95% confidence interval, 0.31-0.82) and a significantly lower incidence of hypertensive disorders (1.0% vs 5.6%; relative risk, 0.21, 95% confidence interval, 0.09-0.45) compared with controls.

No differences in low birthweight (5.2% vs 4.7%; relative risk, 1.11, 95% confidence interval, 0.72−1.73) and mean birthweight (mean difference, −10.46 g, 95% confidence interval, −47.10 to 26.21) between exercise group and controls were found. A sensitivity analysis, excluding studies judged at high risk of bias,[10,15,16,18] concur with the overall analysis (relative risk, 0.82, 95% confidence interval, 0.42−1.60).

Pooled data from subgroup analyses according to the type of exercise, including trials on water aerobic exercise (relative risk, 1.25, 95% confidence interval, 0.34−4.58),[11,13] and according to the length of exercise, including trials had a length of ≥60 minutes (relative risk, 0.88, 95% confidence interval, 0.44−1.74),[10,11,14,16,17] showed no difference in the primary outcome.

Comment

Main findings

This pooled meta-analysis of 9 randomized clinical trials including 2059 women with uncomplicated, singleton pregnancies showed that exercise during pregnancy in mostly normal-weight women is not associated with an increased risk of preterm birth. Exercise during pregnancy is associated with a significantly increased incidence of vaginal delivery and significantly decreased incidence of cesarean delivery, whereas there is no difference with operative vaginal delivery. Exercise during pregnancy is also associated with a significantly lower incidence of gestational diabetes mellitus and hypertensive disorders.

Comparison with existing literature

A 2006 Cochrane review showed that increasing exercise in sedentary pregnant women was associated with a statistically nonsignificant increase in the risk of preterm birth and with a clinically irrelevant shortening of gestational age at delivery.[20] No significant effects on mean birthweight and on the risk of cesarean delivery were found.[20] However, only 3 trials were included.

In 2012 another meta-analysis of 44 randomized clinical trials including 7278 pregnant women evaluated diet, exercise, and a mixed approach of these 2 interventions.[21] They found an overall trend toward reduction in preterm birth with diet, exercise, and/or mixed approach compared with controls.[21] The subgroup analysis on exercise included only 5 randomized clinical trials with preterm birth outcome, and no effect was found.[21]

A 2015 Cochrane review, evaluating diet or exercise or both during pregnancy showed no difference in preterm birth between the intervention and standard care groups.[22] The subgroup analysis on exercise included only 3 randomized clinical trials with preterm birth outcome and also no effect was found.[22] A 2015 systematic review of randomized clinical trials demonstrated that structured prenatal exercise did not adversely affect birthweight compared with standard prenatal care alone.[23]

Strengths and limitations

Our study has several strengths. This meta-analysis included all randomized clinical trials, 9, published so far on the

topic. These studies in general are of high quality and with a low risk of bias according to the Cochrane risk of bias tools. To our knowledge, no prior meta-analysis with preterm birth as a primary outcome on the issue of exercise during pregnancy is as large, up to date, or comprehensive. The statistical heterogeneity within the studies was low. The number of the included women, 2059, was high. In addition, publication bias was not apparent by statistical analysis. These are key elements that are needed to evaluate the reliability of a meta-analysis.[8]

Limitations of our study include that the trimester in which exercise was performed, the adherence to exercise sessions, and the variation in maternal nutritional intake could all have influenced outcomes. In only 1 study,[15] outcomes are stratified by prepregnancy body mass index categories, whereas in 1 study,[18] only preterm birth and low birthweight are stratified by prepregnancy body mass index categories. Therefore, although mean body mass indices for included women in all randomized studies were always in the normal range (Table 3), some studies included a minority of underweight, overweight, and obese women, which could not be excluded because their outcomes were not reported separately. In 4 studies,[12,16-18] 27 women already randomized to exercise or not (11 in the exercise group and 16 in the control group) were excluded from further analyses because they had preterm labor.

Another limitation of this study is that the individual trials differ somewhat in how they define aerobic exercise, intensity of exercise, and time of exercise. Spontaneous preterm birth was not reported separately in the trials, except in 1 trial,[17] in which iatrogenic preterm birth was excluded as an outcome.

Conclusions and implications

Aerobic exercise for 35−90 minutes 3−4 times per week during pregnancy can be safely performed by normal-weight women with singleton, uncomplicated gestations because this is not associated with an increased risk of preterm birth or with a reduction in mean gestational age at delivery. As supported by recent literature,[24] exercise was associated with a significantly higher incidence of vaginal delivery and significantly lower incidences of cesarean delivery, gestational diabetes, and hypertensive disorders and therefore should be encouraged.

Our findings support the American College of Obstetricians and Gynecologists recommendations about exercise during uncomplicated pregnancies[19] and the US Department of Health and Human Services guidelines for healthy pregnant and postpartum women that recommend at least 150 minutes of moderate-intensity activity per week.[25] ■

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