Impact of prenatal exercise on neonatal and childhood outcomes: a systematic review and meta-analysis

Margie H Davenport,[1] Victoria L Meah,[1] Stephanie-May Ruchat,[2] Gregory A Davies,[3] Rachel J Skow,[1] Nick Barrowman,[4] Kristi B Adamo,[5] Veronica J Poitras,[6] Casey E Gray,[7] Alejandra Jaramillo Garcia,[6] Frances Sobierajski,[1] Laurel Riske,[1] Marina James,[1] Amariah J Kathol,[1] Megan Nuspl,[8] Andree-Anne Marchand,[9] Taniya S Nagpal,[10] Linda G Slater,[11] Ashley Weeks,[12] Ruben Barakat,[13] Michelle F Mottola[10]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/bjsports-2018-099836).

For numbered affiliations see end of article.

Correspondence to
Dr Margie H Davenport, Program for Pregnancy and Postpartum Health, Faculty of Kinesiology, Sport, and Recreation, University of Alberta, Edmonton AB T6G 2R3, Canada; mdavenpo@ualberta.ca

Accepted 4 September 2018

To cite: Davenport MH, Meah VL, Ruchat S-M, *et al*. *Br J Sports Med* 2018;**52**:1386–1396.

ABSTRACT

Objective We aimed to identify the relationship between maternal prenatal exercise and birth complications, and neonatal and childhood morphometric, metabolic and developmental outcomes.

Design Systematic review with random-effects meta-analysis and meta-regression.

Data sources Online databases were searched up to 6 January 2017.

Study eligibility criteria Studies of all designs were eligible (except case studies and reviews) if published in English, Spanish or French, and contained information on the relevant population (pregnant women without contraindication to exercise), intervention (subjective/objective measures of frequency, intensity, duration, volume or type of exercise, alone ('exercise-only') or in combination with other intervention components (eg, dietary; 'exercise+cointervention')), comparator (no exercise or different frequency, intensity, duration, volume, type or trimester of exercise) and outcomes (preterm birth, gestational age at delivery, birth weight, low birth weight (<2500 g), high birth weight (>4000 g), small for gestational age, large for gestational age, intrauterine growth restriction, neonatal hypoglycaemia, metabolic acidosis (cord blood pH, base excess), hyperbilirubinaemia, Apgar scores, neonatal intensive care unit admittance, shoulder dystocia, brachial plexus injury, neonatal body composition (per cent body fat, body weight, body mass index (BMI), ponderal index), childhood obesity (per cent body fat, body weight, BMI) and developmental milestones (including cognitive, psychosocial, motor skills)).

Results A total of 135 studies (n=166 094) were included. There was 'high' quality evidence from exercise-only randomised controlled trials (RCTs) showing a 39% reduction in the odds of having a baby >4000 g (macrosomia: 15 RCTs, n=3670; OR 0.61, 95% CI 0.41 to 0.92) in women who exercised compared with women who did not exercise, without affecting the odds of growth-restricted, preterm or low birth weight babies. Prenatal exercise was not associated with the other neonatal or infant outcomes that were examined.

Conclusions Prenatal exercise is safe and beneficial for the fetus. Maternal exercise was associated with reduced odds of macrosomia (abnormally large babies) and was not associated with neonatal complications or adverse childhood outcomes.

INTRODUCTION

Neonatal outcomes, such as premature birth, small-for-gestational age (SGA) or large-for-gestational age (LGA) birth weight, and intrauterine growth restriction (IUGR), are associated with increased risk of infant morbidity and mortality.[1 2] Neonates born prematurely and/or growth-restricted (SGA or IUGR) are more likely to require admission to the neonatal intensive care unit (NICU) after delivery, have greater risk of infection, and suffer from respiratory and metabolic disorders in infancy.[3 4] Babies born LGA are more likely to be delivered by caesarean section, experience shoulder dystocia during delivery, and have hypoglycaemia or jaundice.[5 6] Such neonatal complications are increased in pregnant women who are overweight or obese,[7] have excessive gestational weight gain,[8] and/or develop cardiovascular and metabolic disorders during pregnancy.[9–11] Other reviews in this special issue[12 13] have shown the positive effects of prenatal physical activity on each of these maternal risk factors for neonatal complications.

In addition to the short-term impact of neonatal complications, there is increasing evidence that neonatal complications are associated with negative long-term effects on childhood development (eg, neurodevelopment scores)[14] and health across the lifespan (eg, obesity, diabetes, cardiovascular disease).[15–18] Whether maternal physical activity impacts the incidence of neonatal complications[17–23] is not known.

Since the first guidelines for prenatal exercise were developed by the American College of Obstetricians and Gynecologists in 1985,[24] a growing body of literature has overwhelmingly demonstrated the safety and benefits of exercise for the mother.[12 13 25–32] Despite this, only 9%–15% of pregnant women[33 34] meet the current physical activity recommendations of moderate-intensity activity for 150 min per week,[35 36] with some women concerned that prenatal exercise may harm the fetus.[37] Although such risks of activity have not been substantiated within the literature,[38–42] the associations between maternal physical activity and short-term neonatal outcomes are yet to be fully elucidated.[38–46]

The present systematic review and meta-analysis was conducted as part of a series of reviews that form the evidence base for the development of the *2019 Canadian guideline for physical activity throughout pregnancy* (herein referred to as the *Guideline*).[47] The purpose of this review was to evaluate the effect of prenatal exercise on neonatal and childhood health outcomes, and to establish whether a dose–response relationship existed between frequency, intensity and volume of maternal exercise, and the outcomes of interest, specifically (1) birth complications, and (2) neonatal and childhood morphometric, metabolic and developmental outcomes.

METHODS

In October 2015, the Guidelines Consensus Panel assembled to identify priority outcomes for the *Guideline* development. The Guidelines Consensus Panel included researchers, methodological experts, a fitness professional, and representatives from the Canadian Society for Exercise Physiology (CSEP), the Society of Obstetricians and Gynaecologists of Canada (SOGC), the College of Family Physicians of Canada, the Canadian Association of Midwives, the Canadian Academy of Sport and Exercise Medicine, Exercise is Medicine Canada, and a representative health unit (the Middlesex-London Health Unit). The Guidelines Consensus Panel selected 20 'critical' and 17 'important' outcomes related to prenatal exercise and maternal/fetal health. Six of the 'critical' outcomes and six of the 'important' outcomes were examined in this review. This systematic review and meta-analysis was conducted as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and the checklist was completed.[48]

Protocol and registration

Two systematic reviews examining the impact of prenatal exercise on fetal and maternal health outcomes were registered a priori with PROSPERO, the International Prospective Register of Systematic Reviews (*fetal health*: trial registration number CRD42016029869; *maternal health*: trial registration number CRD42016032376). Since the relationships between prenatal exercise and neonatal outcomes were examined in studies related to both fetal and maternal health, records retrieved from both of these reviews were evaluated for inclusion in the present study.

Eligibility criteria

The PICOS (population, intervention, comparison, outcome and study design) framework[49] was used to guide this review.

Population

The population of interest was pregnant women without absolute or relative contraindication to exercise (according to the SOGC/CSEP and the American College of Obstetricians and Gynecologists guidelines; see online supplementary materials for more details).[35 50] Absolute contraindications to exercise were defined as high-order pregnancy, gestational hypertension, pre-eclampsia, uncontrolled type 1 diabetes, hypertension or thyroid disease, or other serious cardiovascular, respiratory or systemic disorders, persistent second or third trimester bleeding, placenta previa, incompetent cervix, IUGR, ruptured membranes, and premature labour. Relative contraindications were defined as a history of spontaneous abortion or premature labour, mild/moderate cardiovascular or respiratory disease, anaemia, iron deficiency, malnutrition, eating disorder, twin pregnancy after 28 weeks or other significant medical conditions.[35 50]

Intervention (exposure)

The intervention/exposure of interest was subjective or objective measures of frequency, intensity, duration, volume or type of exercise. Although exercise is a subtype of physical activity, for the purpose of this review the terms are used interchangeably. Exercise and physical activity were defined as any bodily movement generated by the skeletal muscles that resulted in energy expenditure above the resting levels.[51] Acute (ie, a single exercise session) or habitual (ie, usual activity) prenatal exercise, as well as interventions including exercise alone (termed 'exercise-only' interventions, which could include standard care) or in combination with other interventions (such as diet; termed 'exercise+cointerventions'), were considered. Studies were not eligible if exercise was performed after the beginning of labour.

Comparison

Eligible comparators were no exercise; different frequency, intensity, duration, volume or type of exercise; different intervention duration; or exercise in a different trimester.

Outcome

Relevant 'critical' outcomes were preterm birth, low birth weight (<2500 g), high birth weight (>4000 g), SGA, LGA, IUGR, neonatal hypoglycaemia and childhood obesity (up to 18 years; per cent body fat, body weight, body mass index (BMI)). Relevant 'important' outcomes included gestational age, birth weight, metabolic acidosis (cord blood pH, base excess), hyperbilirubinaemia, Apgar scores, NICU admittance, shoulder dystocia, brachial plexus injury, neonatal body composition (per cent body fat, fat mass, body weight, BMI, ponderal index) and developmental milestones (ie, cognitive, psychosocial, motor skills).

Study design

Primary studies of any design were eligible, except for case studies (n=1) or reviews. A staged approach was used to determine inclusion of study designs other than randomised controlled trials (RCTs), as follows. For each outcome, evidence from RCTs was initially examined. If fewer than 2000 women were included in the meta-analysis of RCTs for a given outcome, the impact of prenatal exercise on the specific outcome was explored further using evidence from observational studies (non-randomised interventions, cohort, cross-sectional and case–control studies).

Information sources

A comprehensive search was created and run by a research librarian (LGS) in the following databases: MEDLINE, EMBASE, PsycINFO, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Scopus and Web of Science Core Collection, CINAHL Plus with Full Text, Child Development & Adolescent Studies, Education Resources Information Center, SPORTDiscus, ClinicalTrials.gov and the Trip Database up to 6 January 2017 (see online supplementary materials for complete search strategies).

Study selection and data extraction

Two independent reviewers screened the titles and abstracts of all retrieved articles. Abstracts that were judged to have met the initial screening criteria by at least one reviewer were retrieved as full-text articles. Full-text articles were reviewed for relevant PICO information by two independent reviewers. If there was a difference of opinion regarding inclusion, the characteristics of the study were presented to the Guidelines Steering Committee who oversaw the systematic reviews (MHD, MFM, S-MR, CEG, VJP, AJG and NB), and a final decision was made by consensus. All included studies were imported into DistillerSR (Evidence Partners, Ottawa, Ontario, Canada) for data extraction. At this point, studies from the maternal and fetal reviews that were included were de-duplicated against one another in DistillerSR and were considered as one review from this point forward.

Data extraction tables were created in DistillerSR in consultation with methodological experts and the Guidelines Steering Committee. Data were extracted by one person; a content expert (MHD, MFM or S-MR) then independently verified the extracted data. Reviewers were not blinded to study authors. For each single study, the most recent or complete version (publication) was selected as the 'parent' paper; however, relevant data from all publications related to each unique study were extracted. Information on study characteristics (ie, year, study design, country) and population characteristics (eg, number of participants, age, prepregnancy BMI, parity and pregnancy complications), intervention/exposure (measured and/or prescribed exercise frequency, intensity, duration and type, duration of the intervention, measure of physical activity) and outcomes was extracted (online supplementary table 1). If data were not available for extraction, attempts were made to contact the corresponding authors for additional information.

Quality of evidence assessment

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework was used to assess the quality of evidence across studies for each study design and health outcome.

Accordingly, evidence from RCTs was considered 'high' quality and evidence from non-randomised studies was considered 'low' quality unless it was graded down based on concerns with risk of bias, indirectness, inconsistency or imprecision because the presence of these factors reduce the level of confidence in the observed effects. The risk of bias in RCTs and non-randomised intervention studies was assessed following the Cochrane Handbook,[52] and the risk of bias in observational studies was assessed using the characteristics recommended by Guyatt *et al*.[53] All studies were assessed for potential sources of selection bias, reporting bias, performance bias, detection bias, attrition bias and 'other' sources of bias. Risk of bias across studies was rated as 'serious' when studies with the greatest influence on the pooled result (assessed using weight (%) given in forest plots or sample size in studies that were narratively synthesised) presented 'high' risk of bias. The greatest influence on the pooled result was determined as follows: the studies that had the greatest individual % contribution in the meta-analyses, when taken together, contribute to >50% of the weight of the pooled estimate. Additionally, studies were considered to reflect a serious risk of bias when the sample size of narratively synthesised studies was similar to the total sample size of studies contributing to >50% of the weight of the pooled estimate in the meta-analyses. Given the nature of exercise interventions, it is not possible to blind participants to group allocation, and the risk of selection bias was rated as 'low' if this was the only source of bias identified. Performance bias was rated as 'high' when <60% of participants performed 100% of prescribed exercise sessions or attended 100% of counselling sessions (defined as low compliance), or when compliance to the intervention was not reported. Attrition bias was rated as 'high' when >10% of data were missing at the end of the study and intention-to-treat analysis was not used.

Inconsistency across studies was considered serious when heterogeneity was high ($I^2 \geq 50\%$) or when only one study was assessed (I^2 unavailable). Indirectness was considered serious when the effect of exercise+cointervention on an outcome was assessed. Imprecision was considered serious when the 95% CI crossed the line of no effect, and was wide, such that interpretation of the data would be different if the true effect were at one end of the CI or the other. When only one study was assessed, imprecision was not considered serious because inconsistency was already considered serious for this reason. For birth weight the 95% CI was considered wide if it was >500 g (as determined by the Guidelines Consensus Panel). Finally, publication bias was assessed if possible (ie, at least 10 studies were included in the forest plot) via funnel plots (see online supplementary materials). If there were fewer than 10 studies, publication bias was deemed non-estimable and not rated down. If there were no important threats to validity, the quality of the evidence was eligible to be upgraded if there was a large magnitude of effect and there was evidence of a dose–response gradient in the findings.[54]

Due to time constraints and feasibility, one reviewer evaluated the quality of evidence across each health outcome using the protocol, and a second person reviewed the GRADE tables as a quality control measure. Quality of evidence assessment is presented in online supplementary tables 2–17.

Evidence synthesis: statistical analysis and narrative synthesis

Statistical analyses were conducted using Review Manager V.5.3 (Cochrane Collaboration, Copenhagen, Denmark). Statistical significance was set at $p<0.05$. Odds ratios (ORs) were calculated for all dichotomous outcomes. Inverse-variance weighting was applied to obtain ORs using a random-effects model. For continuous outcomes, mean differences (MD) between the exercise and control groups were calculated. Separate meta-analyses were performed according to study design (in cases where multiple study designs were included, as per the staged approach described earlier). For RCTs and non-randomised interventions, sensitivity analyses were performed to evaluate whether the effects were different when examining relationships between exercise-only interventions versus exercise+cointerventions and the outcomes of interest. In studies where there were no observed events in the intervention or control group, data were entered into forest plots, but were considered 'not estimable' and excluded from the pooled analysis as per the recommendation in the Cochrane Handbook.[55]

When possible, the following a priori determined subgroup analyses were conducted for exercise-only interventions and observational studies: (1) women diagnosed with diabetes (gestational, type 1 or type 2) compared with women without diabetes; (2) samples of women with overweight or obesity (mean BMI>25.0 kg/m^2) prior to pregnancy compared with samples of women who were of various BMI (mean BMI<25 kg/m^2 but possibly with some individuals with BMI>25.0 kg/m^2); (3) women >35 years of age compared with women <35 years of age; and (4) women who were previously inactive compared with those who were previously active (as defined by individual study authors). If a study did not provide sufficient detail to allow for inclusion in subanalyses, then a third group called 'unspecified' was created. Tests for subgroup differences were conducted with statistical significance set at $p<0.05$. Effects within subgroups were only interpreted when statistically significant differences between subgroups were found. Subgroup analyses were conducted for exercise-only RCTs reporting on 'critical' outcomes to identify whether a specific type of exercise was associated with greater benefit. I^2 was calculated for subgroup analyses to indicate the per cent of total variability that was attributable to between-study heterogeneity.

Dose–response meta-regression[56–58] was carried out by weighted no-intercept regression of log ORs with a random-effects for study, using the metafor[59] package in R[60] V.3.4.1. Models did not include an intercept term since the log OR is assumed to be zero when the exercise dose is zero. Restricted cubic splines with knots at the 10th, 50th and 90th percentiles of the explanatory variable[61] were used to investigate whether there was evidence for a non-linear relationship. Fitting was performed by maximum likelihood, and non-linearity was assessed using a likelihood ratio test. Although both linear and spline regressions were performed, only the model with the best fit was reported. It was determined that an accepted cut-off point for a clinically meaningful decrease does not exist in the literature. Therefore, a 25% reduction in the odds of the outcomes of interest was selected by expert opinion of the Guidelines Steering Committee.

For outcomes or for subsets of studies where a meta-analysis was not possible, a narrative synthesis of the results was presented, organised around each outcome. Unless otherwise specified, studies were not included in meta-analyses if data were reported incompletely (SD, SE or number of cases/controls not provided), if data were adjusted for confounding factors or if the study did not include a non-exercising control group. In studies where data were included in the meta-analysis but additional information was available, the studies were included in both the meta-analysis and narrative synthesis. Within each outcome, the results were presented by study design.

RESULTS

Study selection

The initial search was not limited by language. However, the Guidelines Steering Committee decided to exclude studies published in languages other than English, Spanish or French for feasibility reasons. A PRISMA diagram of the search results, including reasons for exclusion, is shown in figure 1. A comprehensive list of excluded studies is presented in the online

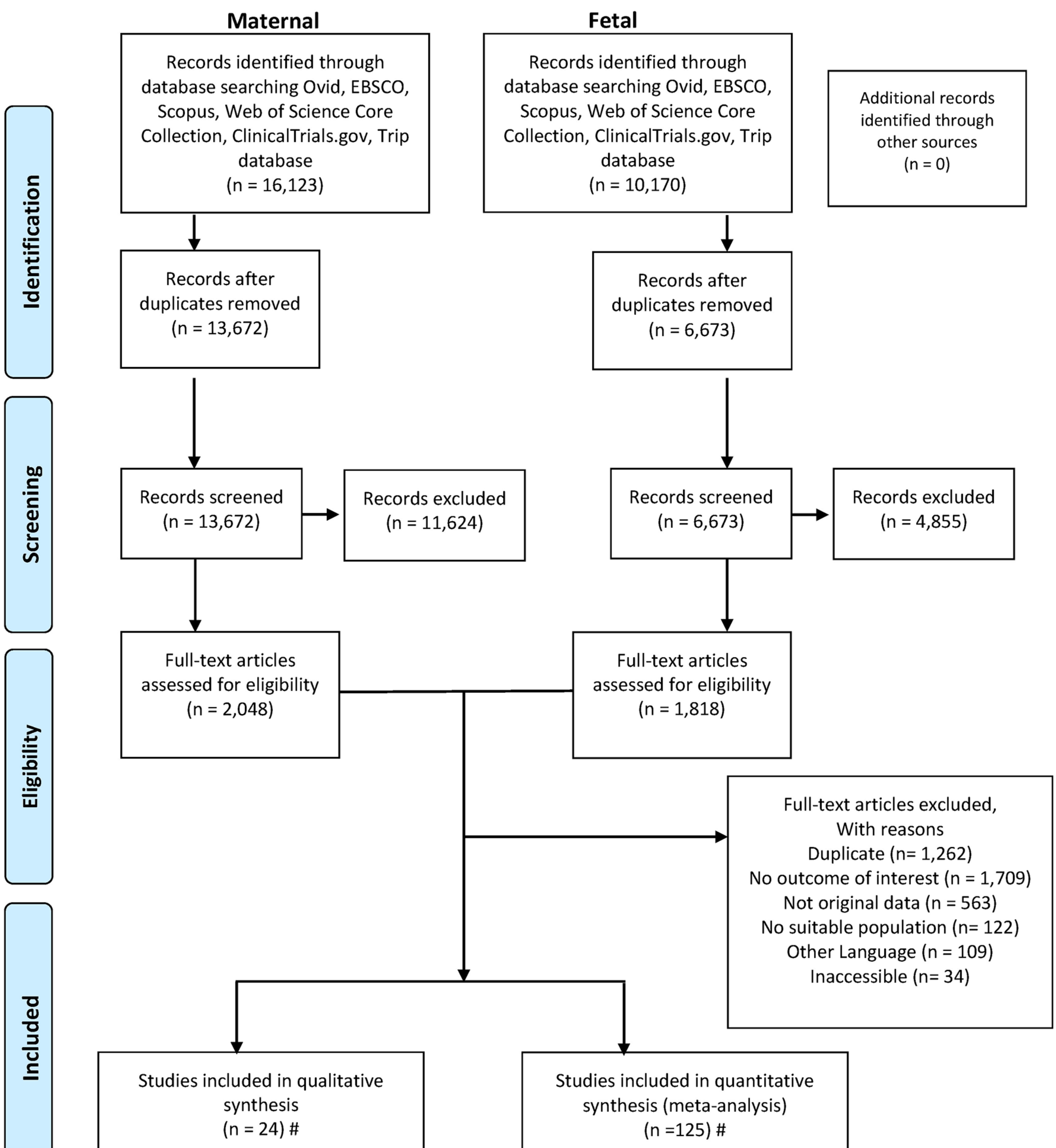

Figure 1 Flow diagram of studies selected for the present study. #14 studies were included in both the qualitative and quantitative analyses.

Davenport MH, *et al*. *Br J Sports Med* 2018;**52**:1386–1396. doi:10.1136/bjsports-2018-099836

supplementary materials. Consistent with the planned staged approach, if fewer than 2000 participants were included in RCTs, data from other study designs were included.

Study characteristics

Overall, 135 unique studies (n=166 094 women) from 32 countries were included in the analysis of both neonatal and childhood outcomes. There were 91 RCTs, 8 non-randomised interventions, 30 cohort, 2 cross-sectional and 4 case–control studies. Among the included exercise interventions, the frequency of exercise ranged from 1 to 7 days per week, the intensity of exercise ranged from low to vigorous, the duration of exercise ranged from 10 to 90 min per session, and the types of exercise were walking, swimming, cycling, water gymnastics, resistance training, stretching, yoga and pelvic floor muscle training. RCTs were initiated in the first (n=23), second (n=52) and third (n=15) trimester, while one RCT was unspecified. Non-randomised interventions were initiated in the second trimester (one was unspecified). Sixty-one RCTs and three non-randomised interventions were exercise-only interventions. The cointerventions included diet, insulin, education about healthy pregnancy and behaviour change, and relaxation techniques. Additional details about the studies can be found in the online supplementary materials (Study characteristics and online supplementary table 1).

Quality of evidence

Overall, the quality of evidence ranged from ‘very low’ to ‘high’ (online supplementary tables 2–17). The most common reasons for downgrading the quality of evidence were (1) serious risk of bias, (2) indirectness of the interventions and (3) imprecision. Common sources of bias included poor or unreported compliance with the intervention and inappropriate treatment of missing data when attrition rate was high. Publication bias was not identified among the analyses where it was possible to systematically assess this using funnel plots.

Meta-regression

The results of the meta-regression analysis are presented in the online supplementary materials (Meta-regressions and online supplementary figures 94–121). For the meta-regression analyses, linear regression was a better fit than spline for all outcomes. However, there was no significant dose–response relationship between prenatal exercise (frequency, intensity, duration or volume) and any outcome.

Birth weight

There was ‘low’ quality evidence from 73 RCTs (n=14 978; downgraded for serious risk of bias and indirectness) regarding the association between prenatal exercise and birth weight. Overall, prenatal exercise was not associated with birth weight (MD −0.02 kg, 95% CI −0.04 to 0.00, I^2=38%; online supplementary figure 1).[62–134] Three RCTs included in the pooled estimates reported additional data showing no association between prenatal exercise and birth weight.[94 112 135]

Sensitivity analysis

The pooled estimate for the exercise-only interventions was not significantly different from the pooled estimate for the exercise+cointerventions (p=0.38). Both exercise-only interventions (‘moderate’ quality evidence; downgraded for serious risk of bias) and exercise+cointerventions (‘low’ quality evidence; downgraded for serious risk of bias and indirectness) did not affect birth weight compared with no exercise (online supplementary figure 1).

Subgroup analyses

The tests for subgroup differences performed for exercise-only interventions were significant subgroups based on previous physical activity levels (p=0.0003) and gestational diabetes status (p=0.01). Specifically, among women who were previously inactive, those who participated in exercise-only interventions had babies with a significantly lower birth weight than those who did not exercise (‘moderate’ quality evidence; downgraded for serious risk of bias; p=0.002).[63 64 66 71 72 76–78 80 81 84 86–88 91 93 100 101 104 110] Among women who were previously active, those who participated in exercise-only interventions had babies with a higher birth weight than those who did not exercise (‘low’ quality evidence; downgraded for serious risk of bias and inconsistency; p=0.003)[92] (online supplementary figure 5). Additionally, among women who exercised during pregnancy, there was ‘moderate’ quality evidence (downgraded for serious risk of bias) that women with gestational diabetes mellitus (GDM) had babies with lower birth weight[80 85 101] compared with babies of women without GDM (p=0.005; online supplementary figure 3). The remaining test for subgroup differences (ie, for women of various BMI vs women with overweight/obesity) was not statistically significant (see online supplementary figure 4). Subgroup analysis by maternal age ≥35 years could not be conducted.

Birth weight <2500 g

There was ‘very low’ quality evidence (downgraded for serious risk of bias, inconsistency, indirectness and imprecision) from 22 RCTs (n=6351) indicating no effect of prenatal exercise on the odds of birth weight <2500 g (pooled estimated based on 20 RCTs, n=6094; OR 0.91, 95% CI 0.73 to 1.14, I^2=0%; figure 2).[64–66 72 83 86–88 93 97 98 100 109 114 130 131 136–141] Two RCTs that could not be included in the analysis reported no association between prenatal exercise and birth weight <2500 g.[65 72] Three RCTs included in the pooled estimates reported additional data showing no association between prenatal exercise and birth weight <2500 g.[65 72]

Sensitivity analysis

The pooled estimate for the exercise-only interventions was not significantly different from the pooled estimate for the exercise+cointervention subgroups (p=0.96). Both exercise-only interventions (‘low’ quality evidence; downgraded for serious risk of bias, inconsistency and imprecision) and exercise+cointerventions (‘very low’ quality evidence; downgraded for serious risk of bias, indirectness and imprecision) did not affect birth weight <2500 g compared with no exercise (figure 2).

Subgroup analysis

The tests for subgroup differences performed for exercise-only interventions were not statistically significant (see online supplementary figures 6–9).

Birth weight <10th percentile

There was ‘very low’ quality evidence (downgraded for serious risk of bias, indirectness and imprecision) from 15 RCTs indicating no effect of prenatal exercise on the odds of birth weight <10th percentile (n=5178; OR 1.20, 95% CI 0.96 to 1.49, I^2=0%; online supplementary figure 10).[72 75 76 78 82 88 97 111 112 128 131–134 142] Two RCTs included in the pooled estimates reported

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
4.4.1 Exercise only						
Barakat, 2009	4	71	4	70	2.4%	0.99 [0.24, 4.10]
Barakat, 2016	16	382	25	383	11.7%	0.63 [0.33, 1.19]
Cavalcante, 2009	3	33	2	37	1.4%	1.75 [0.27, 11.18]
Cordero, 2015	3	101	9	156	2.7%	0.50 [0.13, 1.89]
Haakstad, 2011	1	52	1	53	0.6%	1.02 [0.06, 16.74]
Kasawara, 2013	9	55	11	53	5.1%	0.75 [0.28, 1.98]
Kong, 2014- OB	0	9	0	10		Not estimable
Kong, 2014- OW	0	9	0	9		Not estimable
Murtezani, 2014	3	30	0	33	0.5%	8.53 [0.42, 172.27]
Nobles, 2015	9	124	6	122	4.3%	1.51 [0.52, 4.39]
Prabhu, 2015	1	52	1	53	0.6%	1.02 [0.06, 16.74]
Ruiz, 2013 - NW	19	335	15	352	10.1%	1.35 [0.67, 2.70]
Ruiz, 2013 - OW/OB	5	146	6	129	3.3%	0.73 [0.22, 2.44]
Santos, 2005	2	37	1	35	0.8%	1.94 [0.17, 22.43]
Seneviratne, 2016	1	37	1	37	0.6%	1.00 [0.06, 16.61]
Suputtitada, 2002	0	32	0	35		Not estimable
Ussher, 2015	38	353	44	359	22.8%	0.86 [0.54, 1.37]
Subtotal (95% CI)		**1858**		**1926**	**67.0%**	**0.91 [0.70, 1.20]**
Total events	114		126			
Heterogeneity: Tau² = 0.00; Chi² = 7.54, df = 13 (P = 0.87); I² = 0%						
Test for overall effect: Z = 0.65 (P = 0.51)						
4.4.2 Exercise plus co-intervention						
Ferrara, 2011	4	96	4	101	2.4%	1.05 [0.26, 4.34]
Miquelutti, 2013	4	74	4	68	2.4%	0.91 [0.22, 3.81]
Phelan, 2011 - OW/OB	5	81	4	86	2.7%	1.35 [0.35, 5.21]
Phelan, 2011- NW	4	90	5	92	2.7%	0.81 [0.21, 3.12]
Polley, 2002 - NW	4	30	3	31	1.9%	1.44 [0.29, 7.04]
Polley, 2002 - OW/OB	1	27	2	22	0.8%	0.38 [0.03, 4.55]
Poston, 2015	31	761	36	751	20.1%	0.84 [0.52, 1.38]
Subtotal (95% CI)		**1159**		**1151**	**33.0%**	**0.90 [0.62, 1.33]**
Total events	53		58			
Heterogeneity: Tau² = 0.00; Chi² = 1.27, df = 6 (P = 0.97); I² = 0%						
Test for overall effect: Z = 0.52 (P = 0.60)						
Total (95% CI)		**3017**		**3077**	**100.0%**	**0.91 [0.73, 1.14]**
Total events	167		184			
Heterogeneity: Tau² = 0.00; Chi² = 8.81, df = 20 (P = 0.98); I² = 0%						
Test for overall effect: Z = 0.83 (P = 0.41)						
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.96), I² = 0%						

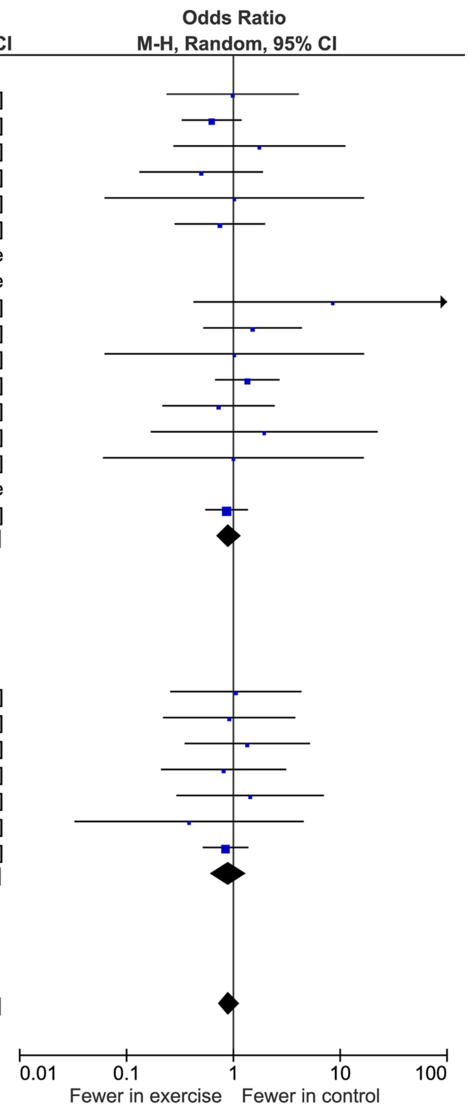

Figure 2 Effects of prenatal exercise compared with control on the odds of birth weight <2500 g (randomised controlled trials). Sensitivity analyses were conducted with studies including exercise-only interventions and those including exercise+cointerventions. Analyses conducted with a random-effects model. *Note: Studies with zero events in both arms are included in the forest plot but are 'not estimable' and not included in the pooled analysis*. M-H, Mantel-Haenszel method; NW, normal weight; OB, obese; OW, overweight.

additional data showing no association between prenatal exercise and birth weight <10th percentile.[112,128]

Sensitivity analysis

The pooled estimate for the exercise-only interventions was not significantly different from the pooled estimate for the exercise+cointervention subgroups (p=0.35). Both exercise-only interventions and exercise+cointerventions did not affect the odds of birth weight <10th percentile compared with no exercise (online supplementary figure 10).

Subgroup analyses

The test for subgroup differences performed for exercise-only interventions were not statistically significant (online supplementary figures 12–14).

Intrauterine growth restriction

Overall, there was 'moderate' quality evidence (downgraded due to inconsistency) from one RCT (n=334) indicating no association between prenatal exercise and IUGR compared with no exercise (OR 1.11, 95% CI 0.48 to 2.60; online supplementary figure 15).[94]

Findings from other study designs (non-randomised interventions, cohort and case–control studies) were not in accordance with findings from RCTs and suggested a reduction in the odds of having IUGR (see online supplementary materials).

Macrosomia (birth weight >4000 g)

There was 'low' quality evidence from 33 RCTs (n=9444 women; downgraded for serious risk of bias and indirectness) indicating no association between prenatal exercise and macrosomia. The pooled estimate was based on 31 RCTs (n=8937; OR 0.85, 95% CI 0.71 to 1.02, I^2=21%; figure 3).[66,71,80,83,86,87,93,94,97,100,101,109,115–118,121,124,126,128,130,131,133,134,136,137,140–143] The two RCTs[72,95] that could not be included in the analysis also found no relationship between prenatal exercise and macrosomia. Five RCTs included in the pooled estimates reported additional data; four of them indicated no association between prenatal exercise

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
6.4.1 Exercise only						
Avery, 1997	3	15	3	14	0.9%	0.92 [0.15, 5.53]
Barakat, 2009	1	71	7	70	0.7%	0.13 [0.02, 1.07]
Barakat, 2011	2	40	3	30	0.9%	0.47 [0.07, 3.03]
Barakat, 2013	2	210	15	218	1.3%	0.13 [0.03, 0.58]
Barakat, 2016	7	382	18	383	3.3%	0.38 [0.16, 0.92]
Cordero, 2015	5	101	7	156	2.0%	1.11 [0.34, 3.59]
Haakstad, 2011a	5	52	9	53	2.1%	0.52 [0.16, 1.67]
Kasawara, 2013	5	55	2	53	1.1%	2.55 [0.47, 13.76]
Kong, 2014- OB	2	9	5	10	0.8%	0.29 [0.04, 2.11]
Kong, 2014- OW	3	9	1	9	0.5%	4.00 [0.33, 48.66]
Murtezani, 2014	2	30	1	33	0.5%	2.29 [0.20, 26.58]
Prabhu, 2015	5	52	9	53	2.1%	0.52 [0.16, 1.67]
Renault, 2014	37	125	17	67	5.0%	1.24 [0.63, 2.42]
Ruiz, 2013 - NW	8	335	14	352	3.3%	0.59 [0.24, 1.43]
Ruiz, 2013 - OW/OB	2	146	12	129	1.3%	0.14 [0.03, 0.62]
Seneviratne, 2016	10	37	7	37	2.3%	1.59 [0.53, 4.75]
Tomic, 2013	10	166	21	168	4.0%	0.45 [0.20, 0.98]
Subtotal (95% CI)		**1835**		**1835**	**31.9%**	**0.61 [0.41, 0.92]**
Total events	109		151			
Heterogeneity: Tau² = 0.26; Chi² = 26.98, df = 16 (P = 0.04); I² = 41%						
Test for overall effect: Z = 2.36 (P = 0.02)						
6.4.2 Exercise plus co-intervention						
Althuizen, 2013	20	103	15	107	4.4%	1.48 [0.71, 3.07]
Bung, 1993	2	17	4	17	0.9%	0.43 [0.07, 2.76]
de Barros, 2010	1	32	3	32	0.6%	0.31 [0.03, 3.17]
Ferrara, 2011	16	96	11	101	3.7%	1.64 [0.72, 3.73]
Guelinckx, 2010	5	42	3	43	1.3%	1.80 [0.40, 8.07]
Hollingsworth, 1987	1	12	0	8	0.3%	2.22 [0.08, 61.40]
Hollingsworth, 1987 - Type 1 Diabetes	1	13	4	21	0.6%	0.35 [0.04, 3.58]
Hui, 2006	2	24	4	21	0.9%	0.39 [0.06, 2.36]
Koivusalo, 2016	6	144	5	125	1.9%	1.04 [0.31, 3.51]
Luoto, 2011	37	216	36	179	7.1%	0.82 [0.49, 1.37]
Phelan, 2011 - OW/OB	14	81	14	86	3.8%	1.07 [0.48, 2.42]
Phelan, 2011- NW	6	90	3	92	1.5%	2.12 [0.51, 8.75]
Polley, 2002 - NW	1	30	0	31	0.3%	3.20 [0.13, 81.78]
Polley, 2002 - OW/OB	0	27	0	22		Not estimable
Poston, 2015	105	761	105	751	11.6%	0.98 [0.74, 1.32]
Renault, 2014 - Exercise + Diet	29	130	17	67	4.8%	0.84 [0.42, 1.68]
Sagedal, 2017	33	296	39	295	7.3%	0.82 [0.50, 1.35]
Stafne, 2012	71	426	78	425	10.1%	0.89 [0.62, 1.27]
Vinter, 2011	40	150	39	154	7.0%	1.07 [0.64, 1.79]
Subtotal (95% CI)		**2690**		**2577**	**68.1%**	**0.97 [0.83, 1.13]**
Total events	390		380			
Heterogeneity: Tau² = 0.00; Chi² = 10.21, df = 17 (P = 0.89); I² = 0%						
Test for overall effect: Z = 0.40 (P = 0.69)						
Total (95% CI)		**4525**		**4412**	**100.0%**	**0.85 [0.71, 1.02]**
Total events	499		531			
Heterogeneity: Tau² = 0.05; Chi² = 43.26, df = 34 (P = 0.13); I² = 21%						
Test for overall effect: Z = 1.73 (P = 0.08)						
Test for subgroup differences: Chi² = 4.24, df = 1 (P = 0.04), I² = 76.4%						

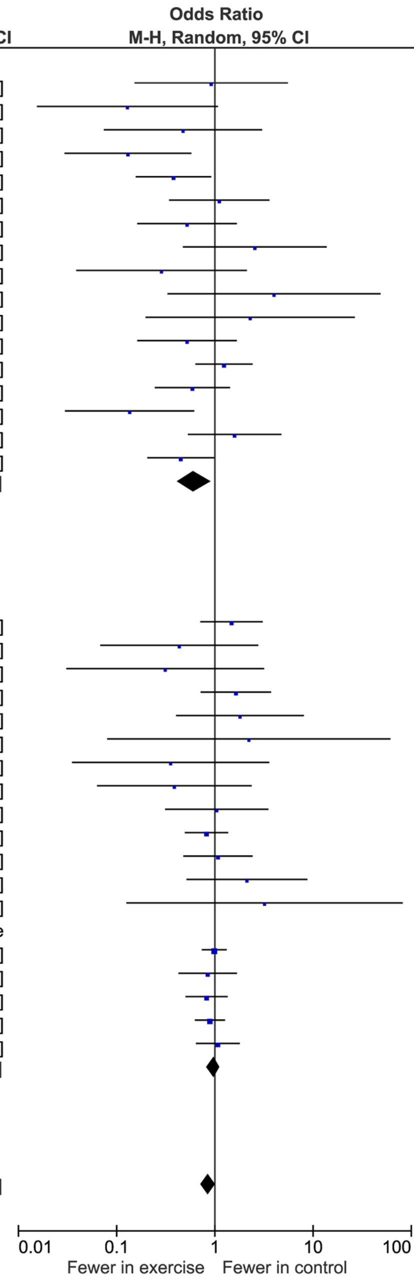

Figure 3 Effects of prenatal exercise compared with control on the odds of birth weight >4000 g (randomised controlled trials). Sensitivity analyses were conducted with studies including exercise-only interventions and those including exercise+cointerventions. Analyses conducted with a random-effects model. *Note: Studies with zero events in both arms are included in the forest plot but are 'not estimable' and not included in the pooled analysis*. M-H, Mantel-Haenszel method; NW, normal weight; OB, obese; OW, overweight; type 1 diabetes, women with type 1 diabetes.

and birth weight >4000 g,[80 94 128 136] while one showed that women who were inactive during pregnancy had an increased odds of having a baby >4000 g.[109]

Sensitivity analysis

The pooled estimate for the exercise-only interventions was significantly different from the pooled estimate for the exercise+cointervention subgroups (p=0.04). There was 'high' quality evidence from 15 exercise-only RCTs showing a 39% decrease in the odds of macrosomia with exercise compared with no exercise (n=3670 women; OR 0.61, 95% CI 0.41 to 0.92, I^2=41%; figure 3).[66 71 80 83 86 87 93 94 97 100 101 109 136 137 142] The two RCTs[72 95] that could not be included in the analysis also found no relationship between prenatal exercise and macrosomia. However, there was no significant effect of exercise+cointerventions on the odds of macrosomia with exercise compared with no exercise (n=5267 women; OR 0.97, 95% CI 0.83 to 1.13, I^2=0%; figure 3).

Subgroup analysis

The tests for subgroup differences performed for exercise-only intervention were not statistically significant for prepregnancy BMI, previous activity level or GDM (see online supplementary figures 19–21). The test for subgroup differences by type of exercise was statistically significant (p=0.04). There was 'high' quality evidence that interventions combining more than one type of exercise reduced the odds of having a baby with a birth weight >4000 g (n=2755 women; OR 0.46, 95% CI 0.29 to

0.73, I^2=18%; online supplementary figure 22).[71 80 83 87 93 100 109 137] Interventions including aerobic exercise and resistance training were not significant.

Birth weight >90th percentile

Overall, there was 'very low' quality evidence (downgraded for serious risk of bias, indirectness and imprecision) from 19 RCTs (n=5268) indicating no association between prenatal exercise and birth weight >90th percentile (OR 0.91, 95% CI 0.74 to 1.11, I^2=8%; online supplementary figure 23).[72 76 78 82 88 95 97 111 112 122 123 128 131–133 136 142–144] Two RCTs included in the pooled estimates reported additional data; one RCT[112] did not identify a relationship between exercise and birth weight >90th percentile; however, a cluster RCT[128] identified a reduction in the odds of having an LGA baby in women who were active during pregnancy (OR 0.55, 95% CI 0.30 to 0.98; Online Supplementary Table 6).

Sensitivity analysis

The pooled estimate for the exercise-only interventions was not significantly different from the exercise+cointervention subgroups (p=0.49). Both exercise-only interventions and exercise+cointerventions did not affect birth weight >90th percentile (online supplementary figure 23).

Subgroup analysis

The tests for subgroup differences (previous level of physical activity, women with overweight/obesity and women with GDM) among exercise-only interventions were not statistically significant (see online supplementary figures 25–27). Subgroup analysis by maternal age or women with GDM could not be conducted.

Gestational age at delivery

Overall, there was 'low' quality evidence (downgraded for serious risk of bias and indirectness) from 61 RCTs (n=13 989 women) regarding the association between prenatal exercise and gestational age at delivery[63 65 66 68–71 73–77 79–83 85–89 92–97 99–103 106 108–114 116–124 126 128–131 133 134 136 142 145 146] (online supplementary figure 28). The pooled estimate based on 61 studies (n=13 989) indicated no significant effect of exercise on gestational age compared with no exercise (p=0.58, MD 0.02, 95% CI −0.06 to 0.10, I^2=40%; online supplementary figure 28). Additional data from one RCT[94] that could not be included in the meta-analysis did not identify a significant relationship between prenatal exercise and gestational age.

Sensitivity analysis

The pooled estimate for the comparison of exercise versus control groups was not significantly different from the pooled estimate for the comparison of exercise+cointerventions versus control groups (p=0.62). Both exercise-only interventions and exercise+cointerventions did not affect gestational age at delivery compared with no exercise (online supplementary figure 28).

Subgroup analysis

The tests for subgroup differences (previous level of physical activity, women with overweight/obesity and women with GDM) among exercise-only interventions were not statistically significant (see online supplementary figures 30–32).

Preterm birth

Overall, there was 'very low' quality evidence (downgraded for serious risk of bias, inconsistency, indirectness and imprecision) from 41 RCTs (n=10 232) indicating no association between prenatal exercise and preterm birth. The pooled estimate was based on 40 RCTs[46 63–66 68 73 78 80 81 84–86 88 93 94 97 98 100 101 109 110 114 115 117 121 129–134 136 137 139 142 –144 147 148] (n=10 303; OR 1.00, 95% CI 0.85 to 1.18, I^2=0%; figure 4). The one study that could not be included in the pooled estimated indicated no association between prenatal exercise and preterm birth.[138]

Sensitivity analysis

The pooled estimate for the comparison of exercise versus control groups was not significantly different from the pooled estimate for the comparison of exercise+cointerventions versus control groups (p=0.20). Both exercise-only interventions and exercise+cointerventions did not affect birth weight compared with control (figure 4).

Subgroup analysis

The tests for subgroup differences (previous level of physical activity, women with overweight/obesity, women with GDM and type of exercise) among exercise-only interventions were not statistically significant (see online supplementary figures 33–36).

Additional outcomes

There were no significant associations between prenatal exercise and any remaining outcomes (ie, IUGR, Apgar scores, neonatal per cent body fat, neonatal fat mass, ponderal index, neonatal BMI, cord blood pH, hyperbilirubinaemia, neonatal hypoglycaemia, childhood developmental outcomes (ie, cognitive, psychosocial, motor skills), childhood per cent body fat, childhood body weight and childhood BMI) compared with no exercise, for either the complete sample or examined subgroups (see the online supplementary materials for detailed results). Data for the relationships between prenatal exercise and NICU admittance, shoulder dystocia, brachial plexus injury and base excess were not identified.

DISCUSSION

In this comprehensive systematic review and meta-analysis of 135 studies, there was 'very low' to 'high' quality evidence from exercise-only RCTs indicating that prenatal exercise was associated with a 39% decreased odds of macrosomia (birth weight >4000 g) without any increase in the odds of preterm birth, low birth weight (<2500 g), SGA (<10th percentile) or IUGR. Moreover, there was 'very low' to 'high' quality evidence from exercise-only RCTs indicating that prenatal exercise did not affect gestational age, birth weight, LGA, neonatal hypoglycaemia, metabolic acidosis (cord blood pH), hyperbilirubinaemia, Apgar scores, neonatal body composition (per cent body fat, body weight, BMI), childhood obesity (per cent body fat, body weight, fat mass) and developmental milestones (ie, cognitive, psychosocial, motor skills). No information was found regarding the associations between prenatal exercise and NICU admittance, shoulder dystocia, brachial plexus injury and base excess. Findings from the meta-regressions identified no dose–response relationship between maternal exercise and neonatal or childhood outcomes. Overall, these results confirm that prenatal exercise in women without contraindication does not adversely affect neonatal or childhood outcomes, and is beneficial in reducing the odds of macrosomia.

The incidence of adverse neonatal outcomes is rising,[1] possibly as a result of increased rates of maternal obesity,[149] excessive

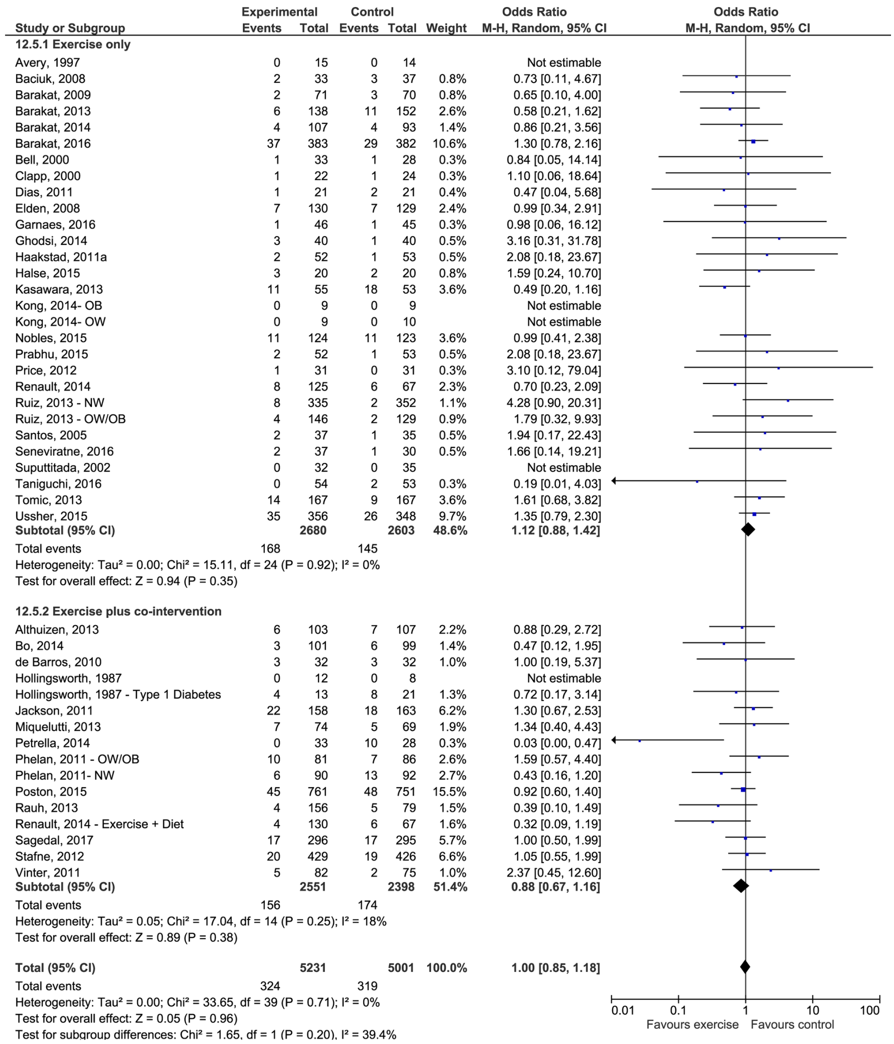

Figure 4 Effects of prenatal compared with control on the odds of preterm birth (randomised controlled trials). Analyses conducted with a random-effects model. *Note: Studies with zero events in both arms are included in the forest plot but are 'not estimable' and not included in the pooled analysis*. M-H, Mantel-Haenszel method; NW, normal weight; OB, obese; OW, overweight; type 1 diabetes, women with type 1 diabetes.

gestational weight gain,[150] complications such as GDM[23] and pregnancy-related hypertensive disorders.[151 152] Women who develop GDM are more likely to give birth to LGA babies, with increased risks of complicated deliveries, whereas women who develop pregnancy-related hypertensive disorders are more likely to deliver SGA or IUGR babies prematurely.[9–11 152] In other papers in the current issue of the *British Journal of Sports Medicine*, it was identified that prenatal exercise reduced the odds of maternal metabolic and hypertensive disorders[12] and also played a role in managing gestational weight gain.[13] These positive maternal benefits likely also transfer to reducing the risks of unfavourable neonatal outcomes.

The current findings demonstrated lower odds of delivering a macrosomic baby with exercise-only interventions. In another systematic review in this issue, we showed that prenatal exercise was beneficial in the control of maternal blood glucose,[30] a key determinant of fetal growth.[153] Pregnancy is associated with mild insulin resistance, an adaptation that ensures adequate fetal nutrition; however, instances of greater maternal insulin resistance lead to increased fetal size.[153–155] Acute and regular exercise in pregnant women improves glycaemic control.[156–161] In combination with reduced excessive gestational weight gain associated with prenatal exercise, physical activity during pregnancy may prevent excessive fetal weight gain and therefore macrosomia. Additionally, prenatal exercise promotes placental growth and vascular development,[162 163] which may also enable appropriate growth for gestational age. Macrosomia has been associated with significant short-term neonatal complications,[5 6] and as such reducing the odds would improve clinical infant outcomes.[164]

The present analyses did not show any significant association between prenatal exercise and LGA (>90th percentile). This discrepancy between two seemingly similar neonatal outcome parameters (birth weight >4000 g and >90th percentile) may be due to differences in the number of women included in exercise-only RCTs, as well as the quality of evidence. The analysis of macrosomia included a greater number of women, had higher quality evidence and likely had more power than the analysis of birth weight >90th percentile to detect a difference between the intervention and control group (n=3670, 'high' quality vs n=1407, 'low' quality, respectively). Additionally, our subgroup analyses showed that exercise-only interventions were more beneficial in reducing the odds of macrosomia than exercise+cointerventions. The majority of studies included in the analysis of birth weight >90th percentile were exercise+cointerventions, where there were other factors that confounded potential relationships. Importantly, the majority of these studies included unsupervised exercise or counselling-based interventions that are typically associated with lower intervention adherence[165] and tended to have lower compliance (defined as <60% of participants performing 100% of prescribed exercise).

For decades, women have avoided prenatal exercise for fear of raising the risk of adverse pregnancy outcomes, including growth restriction and preterm birth.[166] Early research in this area raised concerns of growth restriction or preterm birth as a result of exercise-induced redirection of blood flow and nutrients away from the growing baby and towards the working maternal muscle.[43–46] However, the present analyses did not show any increased odds of SGA, IUGR or preterm birth with prenatal exercise, in agreement with other findings.[38–42] We also showed no association of prenatal exercise with gestational age at delivery or birth weight. Our analyses did not identify a dose–response relationship between increasing frequency, intensity, duration or volume of prenatal exercise with these neonatal outcomes. Furthermore, there were no associations between prenatal exercise and neonatal morphometric outcomes, metabolic birth outcomes or Apgar scores. These data strongly support the safety of prenatal exercise.

The 'Developmental Origins of Health and Disease' hypothesis states that the in utero environment and the neonatal period have critical implications for long-term health.[167] This hypothesis has been largely supported by examining neonatal outcomes and their association with long-term effects on health.[167] As such, all factors that reduce these potential complications should be encouraged to promote lifelong health.[168] For example, it has been shown that infants born LGA are at an increased risk of overweight and obesity later in life.[169] Although the present findings demonstrate reduced odds of macrosomia in neonates of mothers who exercised compared with those who did not, no long-term impacts of maternal exercise on childhood morphometrics (ie, infant BMI, fat mass, body weight) or developmental outcomes (ie, cognitive, psychosocial, motor skills) were found. Only nine observational studies assessed the impact of maternal exercise on morphometric and developmental outcomes in children (details in the online supplementary materials). More RCTs examining the effect of prenatal exercise on long-term child health are needed to fill this critical gap in the literature.

This systematic review and meta-analysis was conducted using rigorous methodological standards (GRADE) to guide the systematic review process. A variety of study designs and articles in different languages (English, French and Spanish) were included. The analyses of birth outcomes such as LGA, SGA and preterm birth demonstrated the safety of exercise. However, analyses of IUGR, metabolic birth outcomes (cord blood pH), childhood developmental and both neonatal and childhood morphometric outcomes included small sample sizes (the majority of outcomes were <100 women) and were likely not adequately powered to detect an effect of prenatal exercise. More studies are needed to establish the effect of prenatal exercise on these parameters. In the majority of analyses, the level of quality evidence from RCTs was downgraded due to serious risk of bias, including high risk of performance and attrition bias. Authors of future studies should therefore monitor compliance to the exercise intervention more rigorously and consider factors that may influence compliance and retention of study participants. Additionally, researchers should consider confounding variables, such as maternal nutritional intake[170] and socioeconomic status, which also influence fetal growth.[171] Finally, quality evidence from the majority of observational studies was rated down due to risk of bias related to performance bias, specifically due to potentially flawed measurement of the physical activity.

In conclusion, the current systematic review and meta-analysis identified that prenatal exercise-only interventions were associated with a 39% reduction in the odds of macrosomia (birth weight >4000 g), and were not significantly associated with preterm birth, gestational age at delivery, birth weight, low birth weight (<2500 g), SGA (<10th percentile), LGA (>90th percentile), IUGR, neonatal hypoglycaemia, metabolic acidosis (cord blood pH), hyperbilirubinaemia, Apgar scores, neonatal body composition (per cent body fat, body weight, BMI), childhood obesity (per cent body fat, body weight, fat mass) and developmental milestones (including cognitive, psychosocial, motor skills). These results reinforce the positive effects of prenatal exercise for newborns in addition to the more established benefits for mothers.

What is already known

- Fetal and neonatal complications, such as intrauterine growth restriction, preterm birth, and low birth weight or high birth weight, are associated with long-term health issues.
- Such neonatal complications can increase the risk of childhood obesity and the development of cardiovascular and metabolic diseases in later life.
- Despite having many known benefits for the mother, prenatal exercise has previously been suggested to potentially increase the odds of neonatal complications such as preterm birth and intrauterine growth restriction.

What are the new findings

- Interventions that comprised exercise alone reduced the odds of high birth weight babies (>4000 g) by 39%.
- There were no associations between prenatal exercise and birth weight, gestational age at delivery, preterm birth or low birth weight.

Author affiliations
[1]Program for Pregnancy and Postpartum Health, Physical Activity and Diabetes Laboratory, Faculty of Kinesiology, Sport and Recreation, Women and Children's Health Research Institute, Alberta Diabetes Institute, University of Alberta, Edmonton, Alberta, Canada
[2]Department of Human Kinetics, Université du Québec à Trois-Rivières, Trois-Rivières, Quebec, Canada
[3]Department of Obstetrics and Gynecology, Queen's University, Kingston, Ontario, Canada
[4]Clinical Research Unit, Children's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada
[5]School of Human Kinetics, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
[6]Independent Researcher, Ottawa, Ontario, Canada
[7]Healthy Active Living and Obesity Research Group, Children's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada
[8]Alberta Research Centre for Health Evidence, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada
[9]Department of Anatomy, Université du Québec à Trois-Rivières, Trois-Rivières, Quebec, Canada
[10]R Samuel McLaughlin Foundation - Exercise and Pregnancy Laboratory, School of Kinesiology, Faculty of Health Sciences, Department of Anatomy and Cell Biology, Schulich School of Medicine & Dentistry, Children's Health Research Institute, The University of Western Ontario, London, Ontario, Canada
[11]John W Scott Health Sciences Library, University of Alberta, Edmonton, Alberta, Canada
[12]School of Interdisciplinary Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
[13]Facultad de Ciencias de la Actividad Física y del Deporte-INEF, Universidad Politécnica de Madrid, Madrid, Spain

Acknowledgements The authors would like to thank Bailey Shandro (UAlberta), Anne Courbalay (UQTR) and Meghan Sebastianski (Alberta SPOR SUPPORT Unit

Knowledge Translation Platform), University of Alberta, for their assistance with the meta-analysis. The authors wish to acknowledge Mary Duggan from the Canadian Society for Exercise Physiology, who is one of the primary knowledge users.

Contributors MHD, S-MR, MFM, GAD, KBA contributed to the conception of the study. MHD, S-MR, MFM, GAD, KBA, AJG, NB, VJP, CEG, LGS, RB contributed to the design of the study and development of the search strategy. LGS conducted the systematic search. VLM, RS, FS, LR, MJ, AJK, A-AM, TSN, AW completed the acquisition of data. MHD, NB, MN performed the data analysis. All authors assisted with the interpretation. MHD, VLM were the principal writers of the manuscript. All authors contributed to the drafting and revision of the final article. All authors approved the final submitted version of the manuscript.

Funding This was funded by a Canadian Institutes of Health Research Knowledge Synthesis Grant (140995). MHD is funded by an Advancing Women's Heart Health Initiative New Investigator Award supported by Health Canada and the Heart and Stroke Foundation of Canada (0033140). RS is funded by a Canadian Institutes of Health Research Doctoral Research Award (146252). A-AM is funded by a Fonds de Recherche en Santé du Québec Doctoral Research Award (34399).

Competing interests None declared.

Patient consent Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Liu L, Oza S, Hogan D, *et al*. Global, regional, and national causes of under-5 mortality in 2000-15: an updated systematic analysis with implications for the Sustainable Development Goals. *Lancet* 2016;388:3027–35.
2 Moss W, Darmstadt GL, Marsh DR, *et al*. Research priorities for the reduction of perinatal and neonatal morbidity and mortality in developing country communities. *J Perinatol* 2002;22:484–95.
3 Harrison W, Goodman D. Epidemiologic Trends in Neonatal Intensive Care, 2007-2012. *JAMA Pediatr* 2015;169:855–62.
4 Blencowe H, Cousens S, Chou D, *et al*. Born too soon: the global epidemiology of 15 million preterm births. *Reprod Health* 2013;10(Suppl 1):S2.
5 Barber EL, Lundsberg LS, Belanger K, *et al*. Indications contributing to the increasing cesarean delivery rate. *Obstet Gynecol* 2011;118:29–38.
6 Rosen H, Shmueli A, Ashwal E, *et al*. Delivery outcomes of large-for-gestational-age newborns stratified by the presence or absence of gestational diabetes mellitus. *Int J Gynaecol Obstet* 2018;141.
7 Marchi J, Berg M, Dencker A, *et al*. Risks associated with obesity in pregnancy, for the mother and baby: a systematic review of reviews. *Obes Rev* 2015;16:621–38.
8 Faucher MA, Hastings-Tolsma M, Song JJ, *et al*. Gestational weight gain and preterm birth in obese women: a systematic review and meta-analysis. *BJOG* 2016;123:199–206.
9 Hollegaard B, Lykke JA, Boomsma JJ. Time from pre-eclampsia diagnosis to delivery affects future health prospects of children. *Evol Med Public Health* 2017;2017:53–66.
10 Metzger BE. Long-term outcomes in mothers diagnosed with gestational diabetes mellitus and their offspring. *Clin Obstet Gynecol* 2007;50:972–9.
11 Sibai BM, Ross MG. Hypertension in gestational diabetes mellitus: pathophysiology and long-term consequences. *J Matern Fetal Neonatal Med* 2010;23:229–33.
12 Davenport MH, Ruchat S-M, Poitras VJ, *et al*. Prenatal exercise for the prevention of gestational diabetes mellitus and hypertensive disorders of pregnancy: a systematic review and meta-analysis. *Br J Sports Med* 2018:1367–76.
13 Ruchat SM, Mottola MF, Skow RJ, *et al*. Effectiveness of exercise interventions in the prevention of excessive gestational weight gain and postpartum weight retention: a systematic review and meta-analysis. *Br J Sports Med* 2018:1347–56.
14 Arcangeli T, Thilaganathan B, Hooper R, *et al*. Neurodevelopmental delay in small babies at term: a systematic review. *Ultrasound Obstet Gynecol* 2012;40:267–75.
15 Swamy GK, Ostbye T, Skjaerven R. Association of preterm birth with long-term survival, reproduction, and next-generation preterm birth. *JAMA* 2008;299:1429–36.
16 Lewandowski AJ, Augustine D, Lamata P, *et al*. Preterm heart in adult life: cardiovascular magnetic resonance reveals distinct differences in left ventricular mass, geometry, and function. *Circulation* 2013;127:197–206.
17 Longo S, Bollani L, Decembrino L, *et al*. Short-term and long-term sequelae in intrauterine growth retardation (IUGR). *J Matern Fetal Neonatal Med* 2013;26:222–5.
18 Bjarnegård N, Morsing E, Cinthio M, *et al*. Cardiovascular function in adulthood following intrauterine growth restriction with abnormal fetal blood flow. *Ultrasound Obstet Gynecol* 2013;41:177–84.
19 Theodore RF, Broadbent J, Nagin D, *et al*. Childhood to early-midlife systolic blood pressure trajectories: early-life predictors, effect modifiers, and adult cardiovascular outcomes. *Hypertension* 2015;66:1108–15.
20 Vasylyeva TL, Barche A, Chennasamudram SP, *et al*. Obesity in prematurely born children and adolescents: follow up in pediatric clinic. *Nutr J* 2013;12:150.
21 Gaskins RB, LaGasse LL, Liu J, *et al*. Small for gestational age and higher birth weight predict childhood obesity in preterm infants. *Am J Perinatol* 2010;27:721–30.
22 Gillman MW, Rifas-Shiman S, Berkey CS, *et al*. Maternal gestational diabetes, birth weight, and adolescent obesity. *Pediatrics* 2003;111:e221–6.
23 Chiavaroli V, Derraik JG, Hofman PL, *et al*. Born large for gestational age: bigger is not always better. *J Pediatr* 2016;170:307–11.
24 ACOG. Technical Bulletin. In: *Exercise during pregnancy and the postnatal period*. Washington, DC, 1985.
25 Davenport MH, Kathol A, Mottola MF, *et al*. Prenatal exercise is not associated with fetal mortality: a systematic review and meta-analysis. *Br J Sports Med* 2018. [Epub ahead of print].
26 Davenport MH, Marchand A-A, Mottola MF, *et al*. Exercise for the prevention and treatment of low back, pelvic girdle and lumbopelvic pain during pregnancy: a systematic review and meta-analysis. *Br J Sports Med* 2018. [Epub ahead of print].
27 Davenport MH, McCurdy AP, Mottola MF, *et al*. Impact of pre-natal exercise on both pre-natal and post-natal anxiety and depressive symptoms: a systematic review and meta-analysis. *Br J Sports Med* 2018. [Epub ahead of print].
28 Davenport MH, Nagpal TS, Mottola MF, *et al*. Prenatal exercise (including but not limited to pelvic floor muscle training) on and urinary incontinence during and following pregnancy: a systematic review and meta-analysis. *Br J Sports Med* 2018. [Epub ahead of print].
29 Davenport MH, Ruchat S-M, Sobierajski F, *et al*. Impact of prenatal exercise on maternal harms, labour and delivery outcomes: a systematic review and meta-analysis. *Br J Sports Med* 2018. [Epub ahead of print].
30 Davenport MH, Sobierajski F, Mottola MF, *et al*. Glucose responses to acute and chronic exercise during pregnancy: a systematic review and meta-analysis. *Br J Sports Med* 2018;52:1357–67.
31 Mottola MF, Nagpal TS, Bgeginski R, *et al*. Is supine exercise associated with adverse maternal and fetal outcomes? A systematic review. *Br J Sports Med* 2018. [Epub ahead of print].
32 Skow RJ, Davenport MH, Mottola MF, *et al*. Effects of prenatal exercise on fetal heart rate, umbilical and uterine blood flow: a systematic review and meta-analysis. *Br J Sports Med* 2018. [Epub ahead of print].
33 Evenson KR, Wen F. Prevalence and correlates of objectively measured physical activity and sedentary behavior among US pregnant women. *Prev Med* 2011;53(1-2):39–43.
34 Santo EC, Forbes PW, Oken E, *et al*. Determinants of physical activity frequency and provider advice during pregnancy. *BMC Pregnancy Childbirth* 2017;17:286.
35 Davies GA, Wolfe LA, Mottola MF, *et al*. Joint SOGC/CSEP clinical practice guideline: exercise in pregnancy and the postpartum period. *Can J Appl Physiol* 2003;28:329–41.
36 Evenson KR, Barakat R, Brown WJ, *et al*. Guidelines for physical activity during pregnancy: comparisons from around the world. *Am J Lifestyle Med* 2014;8:102–21.
37 Evenson KR, Moos MK, Carrier K, *et al*. Perceived barriers to physical activity among pregnant women. *Matern Child Health J* 2009;13:364–75.
38 Sanabria-Martínez G, García-Hermoso A, Poyatos-León R, *et al*. Effects of Exercise-Based Interventions on Neonatal Outcomes: A Meta-Analysis of Randomized Controlled Trials. *Am J Health Promot* 2016;30:214–23.
39 Wiebe HW, Boulé NG, Chari R, *et al*. The effect of supervised prenatal exercise on fetal growth: a meta-analysis. *Obstet Gynecol* 2015;125:1185–94.
40 Kramer MS, McDonald SW. Aerobic exercise for women during pregnancy. *Cochrane Database Syst Rev* 2006;3:CD000180.
41 Aune D, Schlesinger S, Henriksen T, *et al*. Physical activity and the risk of preterm birth: a systematic review and meta-analysis of epidemiological studies. *BJOG* 2017;124:1816–26.
42 Di Mascio D, Magro-Malosso ER, Saccone G, *et al*. Exercise during pregnancy in normal-weight women and risk of preterm birth: a systematic review and meta-analysis of randomized controlled trials. *Am J Obstet Gynecol* 2016;215:561–71.
43 Clapp JF, Dickstein S. Endurance exercise and pregnancy outcome. *Med Sci Sports Exerc* 1984;16:556–62.
44 Berkowitz GS, Kelsey JL, Holford TR, *et al*. Physical activity and the risk of spontaneous preterm delivery. *J Reprod Med* 1983;28:581–8.
45 Clapp JF, Capeless EL. Neonatal morphometrics after endurance exercise during pregnancy. *Am J Obstet Gynecol* 1990;163:1805–11.
46 Bell RJ, Palma SM, Lumley JM. The effect of vigorous exercise during pregnancy on birth-weight. *Aust N Z J Obstet Gynaecol* 1995;35:46–51.
47 Mottola MF, Davenport MH, Ruchat S-M, *et al*. 2019 Canadian guideline for physical activity throughout pregnancy. *Br J Sports Med* 2018;52:1339–46.
48 Liberati A, Altman DG, Tetzlaff J, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009;339:b2700.
49 Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1.
50 Artal R. Exercise in Pregnancy: Guidelines. *Clin Obstet Gynecol* 2016;59:639–44.
51 Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep* 1985;100:126–31.

52 The Cochrane Collaboration. *Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0*, 2011.
53 Guyatt GH, Oxman AD, Vist G, *et al*. GRADE guidelines: 4. Rating the quality of evidence–study limitations (risk of bias). *J Clin Epidemiol* 2011;64:407–15.
54 Balshem H, Helfand M, Schünemann HJ, *et al*. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 2011;64:401–6.
55 Higgins JPT, Green S. *Cochrane handbook for systematic reviews of interventions*. 2011: The Cochrane Collaboration.
56 Greenland S, Longnecker MP. Methods for trend estimation from summarized dose-response data, with applications to meta-analysis. *Am J Epidemiol* 1992;135:1301–9.
57 Orsini N, Li R, Wolk A, *et al*. Meta-analysis for linear and nonlinear dose-response relations: examples, an evaluation of approximations, and software. *Am J Epidemiol* 2012;175:66–73.
58 Aune D, Sen A, Henriksen T, *et al*. Physical activity and the risk of gestational diabetes mellitus: a systematic review and dose-response meta-analysis of epidemiological studies. *Eur J Epidemiol* 2016;31:967–97.
59 Viechtbauer W. Conducting Meta-Analyses in *R* with the metafor package. *J Stat Softw* 2010;36:1–48.
60 R Core Team. *R: A language and environment for statistical computing. R Foundation for statistical computing*. Vienna, Austria, 2017.
61 Frank E, Harrell J. *Regression modeling strategies with applications to linear models, logistic and ordinal regression and survival analysis*. 2nd edn. Cham: Springer-Verlag, 2015.
62 Bell R, Palma S. Antenatal exercise and birthweight. *Aust N Z J Obstet Gynaecol* 2000;40:70–3.
63 Clapp JF, Kim H, Burciu B, *et al*. Beginning regular exercise in early pregnancy: effect on fetoplacental growth. *Am J Obstet Gynecol* 2000;183:1484–8.
64 Suputtitada A, Wacharapreechanont T, Chaisayan P. Effect of the sitting pelvic tilt exercise during the third trimester in primigravidas on back pain. *J Med Assoc Thai* 2002;85(Suppl 1):S170–9.
65 Baciuk EP, Pereira RI, Cecatti JG, *et al*. Water aerobics in pregnancy: cardiovascular response, labor and neonatal outcomes. *Reprod Health* 2008;5:10.
66 Barakat R, Ruiz JR, Stirling JR, *et al*. Type of delivery is not affected by light resistance and toning exercise training during pregnancy: a randomized controlled trial. *Am J Obstet Gynecol* 2009;201:590.e1–6.
67 Chuntharapat S, Petpichetchian W, Hatthakit U. Yoga during pregnancy: effects on maternal comfort, labor pain and birth outcomes. *Complement Ther Clin Pract* 2008;14:105–15.
68 Elden H, Ostgaard HC, Fagevik-Olsen M, *et al*. Treatments of pelvic girdle pain in pregnant women: adverse effects of standard treatment, acupuncture and stabilising exercises on the pregnancy, mother, delivery and the fetus/neonate. *BMC Complement Altern Med* 2008;8:34.
69 Garshasbi A, Faghih Zadeh S. The effect of exercise on the intensity of low back pain in pregnant women. *Int J Gynaecol Obstet* 2005;88:271–5.
70 Barakat R, Cordero Y, Coteron J, *et al*. Exercise during pregnancy improves maternal glucose screen at 24-28 weeks: a randomised controlled trial. *Br J Sports Med* 2012;46:656–61.
71 Barakat R, Pelaez M, Montejo R, *et al*. Exercise during pregnancy improves maternal health perception: a randomized controlled trial. *Am J Obstet Gynecol* 2011;204:402.e1–7.
72 de Oliveria Melo AS, Silva JL, Tavares JS, *et al*. Effect of a physical exercise program during pregnancy on uteroplacental and fetal blood flow and fetal growth: a randomized controlled trial. *Obstet Gynecol* 2012;120:302–10.
73 Dias LA, Driusso P, Aita DL, *et al*. Effect of pelvic floor muscle training on labour and newborn outcomes: a randomized controlled trial. *Rev Bras Fisioter* 2011;15:487–93.
74 Field T, Diego M, Hernandez-Reif M, *et al*. Yoga and massage therapy reduce prenatal depression and prematurity. *J Bodyw Mov Ther* 2012;16:204–9.
75 Hopkins SA, Baldi JC, Cutfield WS, *et al*. Exercise training in pregnancy reduces offspring size without changes in maternal insulin sensitivity. *J Clin Endocrinol Metab* 2010;95:2080–8.
76 Nascimento SL, Surita FG, Parpinelli MÂ, *et al*. The effect of an antenatal physical exercise programme on maternal/perinatal outcomes and quality of life in overweight and obese pregnant women: a randomised clinical trial. *BJOG* 2011;118:1455–63.
77 Pinzón DC, Zamora K, Martínez JH, *et al*. Type of delivery and gestational age is not affected by pregnant Latin-American women engaging in vigorous exercise: a secondary analysis of data from a controlled randomized trial. *Rev Salud Publica* 2012;14:731–43.
78 Price BB, Amini SB, Kappeler K. Exercise in pregnancy: effect on fitness and obstetric outcomes-a randomized trial. *Med Sci Sports Exerc* 2012;44:2263–9.
79 Rodríguez YC, Puente MP, de Miguel M, *et al*. ¿Puede el ejercicio físico moderado durante el embarazo actuar como un factor de prevención de la Diabetes Gestacional?/Can moderate physical exercise during pregnancy act as a factor in preventing Gestational Diabetes? *Revista Internacional de Ciencias del Deporte* 2012;VIII;27:3–19.
80 Barakat R, Pelaez M, Lopez C, *et al*. Exercise during pregnancy and gestational diabetes-related adverse effects: a randomised controlled trial. *Br J Sports Med* 2013;47:630–6.
81 Barakat R, Perales M, Bacchi M, *et al*. A program of exercise throughout pregnancy. Is it safe to mother and newborn? *Am J Health Promot* 2014;29:2–8.
82 Bisson M, Alméras N, Dufresne SS, *et al*. A 12-Week Exercise Program for Pregnant Women with Obesity to Improve Physical Activity Levels: An Open Randomised Preliminary Study. *PLoS One* 2015;10:e0137742.
83 Cordero Y, Mottola MF, Vargas J, *et al*. Exercise is associated with a reduction in gestational diabetes mellitus. *Med Sci Sports Exerc* 2015;47:1328–33.
84 Ghodsi Z, Asltoghiri M. Effects of aerobic exercise training on maternal and neonatal outcome: a randomized controlled trial on pregnant women in Iran. *J Pak Med Assoc* 2014;64:1053–6.
85 Halse RE, Wallman KE, Dimmock JA, *et al*. Home-Based exercise improves fitness and exercise attitude and intention in women with GDM. *Med Sci Sports Exerc* 2015;47:1698–704.
86 Kong KL, Campbell CG, Foster RC, *et al*. A pilot walking program promotes moderate-intensity physical activity during pregnancy. *Med Sci Sports Exerc* 2014;46:462–71.
87 Murtezani A, Paçarada M, Ibraimi Z, *et al*. The impact of exercise during pregnancy on neonatal outcomes: a randomized controlled trial. *J Sports Med Phys Fitness* 2014;54:802–8.
88 Nobles C, Marcus BH, Stanek EJ, *et al*. Effect of an exercise intervention on gestational diabetes mellitus: a randomized controlled trial. *Obstet Gynecol* 2015;125:1195–204.
89 Okido MM, Valeri FL, Martins WP, *et al*. Assessment of foetal wellbeing in pregnant women subjected to pelvic floor muscle training: a controlled randomised study. *Int Urogynecol J* 2015;26:1475–81.
90 Lekskulchai O, Wanichsetakul P. Effect of pelvic floor muscle training (PFMT) during pregnancy on bladder neck descend and delivery. *J Med Assoc Thai* 2014;97(Suppl 8):S156–63.
91 Perales M, Mateos S, Vargas M, *et al*. Fetal and maternal heart rate responses to exercise in pregnant women. A randomized Controlled Trial. *Archivos de medicina del deporte* 2015;32:361–7.
92 Petrov Fieril K, Glantz A, Fagevik Olsen M. The efficacy of moderate-to-vigorous resistance exercise during pregnancy: a randomized controlled trial. *Acta Obstet Gynecol Scand* 2015;94:35–42.
93 Ruiz JR, Perales M, Pelaez M, *et al*. Supervised exercise-based intervention to prevent excessive gestational weight gain: a randomized controlled trial. *Mayo Clin Proc* 2013;88:1388–97.
94 Tomić V, Sporiš G, Tomić J, *et al*. The effect of maternal exercise during pregnancy on abnormal fetal growth. *Croat Med J* 2013;54:362–8.
95 Oostdam N, van Poppel MN, Wouters MG, *et al*. No effect of the FitFor2 exercise programme on blood glucose, insulin sensitivity, and birthweight in pregnant women who were overweight and at risk for gestational diabetes: results of a randomised controlled trial. *BJOG* 2012;119:1098–107.
96 Perales M, Cordero Y, Vargas M, *et al*. Exercise and depression in overweight and obese pregnant women: a randomized controlled trial. *Archivos de medicina del deporte* 2015;32:70–7.
97 Seneviratne SN, Jiang Y, Derraik J, *et al*. Effects of antenatal exercise in overweight and obese pregnant women on maternal and perinatal outcomes: a randomised controlled trial. *BJOG* 2016;123:588–97.
98 Santos IA, Stein R, Fuchs SC, *et al*. Aerobic exercise and submaximal functional capacity in overweight pregnant women: a randomized trial. *Obstet Gynecol* 2005;106:243–9.
99 Gorbea Chávez V, Velázquez Sánchez MP, Kunhardt Rasch JR. Effect of pelvic floor exercise during pregnancy and puerperium on prevention of urinary stress incontinence. *Ginecol Obstet Mex* 2004;72:628–36.
100 Haakstad LA, Bo K. Effect of regular exercise on prevention of excessive weight gain in pregnancy: a randomised controlled trial. *Eur J Contracept Reprod Health Care* 2011;16:116–25.
101 Avery MD, Leon AS, Kopher RA. Effects of a partially home-based exercise program for women with gestational diabetes. *Obstet Gynecol* 1997;89:10–15.
102 Morkved S, Bo K, Schei B, *et al*. Pelvic floor muscle training during pregnancy to prevent urinary incontinence: a single-blind randomized controlled trial. *Obstet Gynecol* 2003;101:313–9.
103 Ko CW, Napolitano PG, Lee SP, *et al*. Physical activity, maternal metabolic measures, and the incidence of gallbladder sludge or stones during pregnancy: a randomized trial. *Am J Perinatol* 2014;31:39–48.
104 Marquez-Sterling S, Perry AC, Kaplan TA, *et al*. Physical and psychological changes with vigorous exercise in sedentary primigravidae. *Med Sci Sports Exerc* 2000;32:58–62.
105 Fritel X, de Tayrac R, Bader G, *et al*. Preventing Urinary Incontinence With Supervised Prenatal Pelvic Floor Exercises: A Randomized Controlled Trial. *Obstet Gynecol* 2015;126:370–7.
106 Callaway LK, Colditz PB, Byrne NM, *et al*. Prevention of gestational diabetes: feasibility issues for an exercise intervention in obese pregnant women. *Diabetes Care* 2010;33:1457–9.

107 Ko PC, Liang CC, Chang SD, *et al*. A randomized controlled trial of antenatal pelvic floor exercises to prevent and treat urinary incontinence. *Int Urogynecol J* 2011;22:17–22.
108 Kihlstrand M, Stenman B, Nilsson S, *et al*. Water-gymnastics reduced the intensity of back/low back pain in pregnant women. *Acta Obstet Gynecol Scand* 1999;78:180–5.
109 Barakat R, Pelaez M, Cordero Y, *et al*. Exercise during pregnancy protects against hypertension and macrosomia: randomized clinical trial. *Am J Obstet Gynecol* 2016;214:649.e1–8.
110 Taniguchi C, Sato C. Home-based walking during pregnancy affects mood and birth outcomes among sedentary women: A randomized controlled trial. *Int J Nurs Pract* 2016;22:420–6.
111 Guelfi KJ, Ong MJ, Crisp NA, *et al*. Regular exercise to prevent the recurrence of gestational diabetes mellitus: a randomized controlled trial. *Obstet Gynecol* 2016;128:819–27.
112 Simmons D, Devlieger R, van Assche A, *et al*. Effect of Physical Activity and/or Healthy Eating on GDM Risk: The DALI Lifestyle Study. *J Clin Endocrinol Metab* 2017;102:903–13.
113 Labonte-Lemoyne E, Curnier D, Ellemberg D. Exercise during pregnancy enhances cerebral maturation in the newborn: A randomized controlled trial. *J Clin Exp Neuropsychol* 2017;39:347–54.
114 Ussher M, Lewis S, Aveyard P, *et al*. Physical activity for smoking cessation in pregnancy: randomised controlled trial. *BMJ* 2015;350:h2145.
115 Althuizen E, van der Wijden CL, van Mechelen W, *et al*. The effect of a counselling intervention on weight changes during and after pregnancy: a randomised trial. *BJOG* 2013;120:92–9.
116 Bung P, Bung C, Artal R, *et al*. Therapeutic exercise for insulin-requiring gestational diabetics: effects on the fetus–results of a randomized prospective longitudinal study. *J Perinat Med* 1993;21:125–37.
117 de Barros MC, Lopes MA, Francisco RP, *et al*. Resistance exercise and glycemic control in women with gestational diabetes mellitus. *Am J Obstet Gynecol* 2010;203:556.e1–6.
118 Guelinckx I, Devlieger R, Mullie P, *et al*. Effect of lifestyle intervention on dietary habits, physical activity, and gestational weight gain in obese pregnant women: a randomized controlled trial. *Am J Clin Nutr* 2010;91:373–80.
119 Harrison CL, Lombard CB, Teede HJ. Limiting postpartum weight retention through early antenatal intervention: the HeLP-her randomised controlled trial. *Int J Behav Nutr Phys Act* 2014;11:134.
120 Hawkins M, Hosker M, Marcus BH, *et al*. A pregnancy lifestyle intervention to prevent gestational diabetes risk factors in overweight Hispanic women: a feasibility randomized controlled trial. *Diabet Med* 2015;32:108–15.
121 Hollingsworth DR, Moore TR. Postprandial walking exercise in pregnant insulin-dependent (type I) diabetic women: reduction of plasma lipid levels but absence of a significant effect on glycemic control. *Am J Obstet Gynecol* 1987;157:1359–63.
122 Hui A, Back L, Ludwig S, *et al*. Lifestyle intervention on diet and exercise reduced excessive gestational weight gain in pregnant women under a randomised controlled trial. *BJOG* 2012;119:70–7.
123 Hui AL, Back L, Ludwig S, *et al*. Effects of lifestyle intervention on dietary intake, physical activity level, and gestational weight gain in pregnant women with different pre-pregnancy Body Mass Index in a randomized control trial. *BMC Pregnancy Childbirth* 2014;14:331.
124 Hui AL, Ludwig S, Gardiner P, *et al*. Community-based exercise and dietary intervention during pregnancy:a pilot study. *Can J Diabetes* 2006;30:1–7.
125 Jovanovic-Peterson L, Durak EP, Peterson CM. Randomized trial of diet versus diet plus cardiovascular conditioning on glucose levels in gestational diabetes. *Am J Obstet Gynecol* 1989;161:415–9.
126 Koivusalo SB, Rönö K, Klemetti MM, *et al*. Gestational diabetes mellitus can be prevented by lifestyle intervention: the Finnish Gestational Diabetes Prevention Study (RADIEL): a randomized controlled trial. *Diabetes Care* 2016;39:24–30.
127 Korpi-Hyövälti E, Heinonen S, Schwab U, *et al*. Effect of intensive counselling on physical activity in pregnant women at high risk for gestational diabetes mellitus. A clinical study in primary care. *Prim Care Diabetes* 2012;6:261–8.
128 Luoto R, Kinnunen TI, Aittasalo M, *et al*. Primary prevention of gestational diabetes mellitus and large-for-gestational-age newborns by lifestyle counseling: a cluster-randomized controlled trial. *PLoS Med* 2011;8:e1001036.
129 Petrella E, Malavolti M, Bertarini V, *et al*. Gestational weight gain in overweight and obese women enrolled in a healthy lifestyle and eating habits program. *J Matern Fetal Neonatal Med* 2014;27:1348–52.
130 Phelan S, Phipps MG, Abrams B, *et al*. Randomized trial of a behavioral intervention to prevent excessive gestational weight gain: the Fit for Delivery Study. *Am J Clin Nutr* 2011;93:772–9.
131 Poston L, Bell R, Croker H, *et al*. Effect of a behavioural intervention in obese pregnant women (the UPBEAT study): a multicentre, randomised controlled trial. *Lancet Diabetes Endocrinol* 2015;3:767–77.
132 Rauh K, Gabriel E, Kerschbaum E, *et al*. Safety and efficacy of a lifestyle intervention for pregnant women to prevent excessive maternal weight gain: a cluster-randomized controlled trial. *BMC Pregnancy Childbirth* 2013;13:151.
133 Sagedal LR, Øverby NC, Bere E, *et al*. Lifestyle intervention to limit gestational weight gain: the Norwegian Fit for Delivery randomised controlled trial. *BJOG* 2017;124:97–109.
134 Stafne SN, Salvesen KÅ, Romundstad PR, *et al*. Regular exercise during pregnancy to prevent gestational diabetes: a randomized controlled trial. *Obstet Gynecol* 2012;119:29–36.
135 Ussher M, Lewis S, Aveyard P, *et al*. The London Exercise And Pregnant smokers (LEAP) trial: a randomised controlled trial of physical activity for smoking cessation in pregnancy with an economic evaluation. *Health Technol Assess* 2015;19:1–136.
136 Kasawara KT, Burgos CS, do Nascimento SL, *et al*. Maternal and perinatal outcomes of exercise in pregnant women with chronic hypertension and/or previous preeclampsia: a randomized controlled trial. *ISRN Obstet Gynecol* 2013;2013:1–8.
137 Prabhu N. Effect of a exercise by pregnant women and birth weight: a randomized controlled trial. *J Evo Med Den Sci* 2015;04:1509–16.
138 Cavalcante SR, Cecatti JG, Pereira RI, *et al*. Water aerobics II: maternal body composition and perinatal outcomes after a program for low risk pregnant women. *Reprod Health* 2009;6:1.
139 Miquelutti MA, Cecatti JG, Makuch MY. Evaluation of a birth preparation program on lumbopelvic pain, urinary incontinence, anxiety and exercise: a randomized controlled trial. *BMC Pregnancy Childbirth* 2013;13:154.
140 Polley BA, Wing RR, Sims CJ. Randomized controlled trial to prevent excessive weight gain in pregnant women. *Int J Obes Relat Metab Disord* 2002;26:1494–502.
141 Ferrara A, Hedderson MM, Albright CL, *et al*. A pregnancy and postpartum lifestyle intervention in women with gestational diabetes mellitus reduces diabetes risk factors: a feasibility randomized control trial. *Diabetes Care* 2011;34:1519–25.
142 Renault KM, Nørgaard K, Nilas L, *et al*. The Treatment of Obese Pregnant Women (TOP) study: a randomized controlled trial of the effect of physical activity intervention assessed by pedometer with or without dietary intervention in obese pregnant women. *Am J Obstet Gynecol* 2014;210:134.e1–9.
143 Vinter CA, Jensen DM, Ovesen P, *et al*. The LiP (Lifestyle in Pregnancy) study: a randomized controlled trial of lifestyle intervention in 360 obese pregnant women. *Diabetes Care* 2011;34:2502–7.
144 Bo S, Rosato R, Ciccone G, *et al*. Simple lifestyle recommendations and the outcomes of gestational diabetes. A 2 × 2 factorial randomized trial. *Diabetes Obes Metab* 2014;16:1032–5.
145 Sedaghati P, Ziaee V, Ardjmand A. The effect of an ergometric training program on pregnants weight gain and low back pain. *Gazzetta Medica Italiana Archivo per le Scienze Mediche* 2007;166:209–13.
146 Ronnberg AK, Ostlund I, Fadl H, *et al*. Intervention during pregnancy to reduce excessive gestational weight gain—a randomised controlled trial. *BJOG* 2015;122:537–44.
147 Garnæs KK, Mørkved S, Salvesen Ø, *et al*. Exercise Training and Weight Gain in Obese Pregnant Women: A Randomized Controlled Trial (ETIP Trial). *PLoS Med* 2016;13:e1002079.
148 Jackson RA, Stotland NE, Caughey AB, *et al*. Improving diet and exercise in pregnancy with Video Doctor counseling: a randomized trial. *Patient Educ Couns* 2011;83:203–9.
149 Radulescu L, Munteanu O, Popa F, *et al*. The implications and consequences of maternal obesity on fetal intrauterine growth restriction. *J Med Life* 2013;6:292–8.
150 Stotland NE, Cheng YW, Hopkins LM, *et al*. Gestational weight gain and adverse neonatal outcome among term infants. *Obstet Gynecol* 2006;108:635–43.
151 McCowan L, Horgan RP. Risk factors for small for gestational age infants. *Best Pract Res Clin Obstet Gynaecol* 2009;23:779–93.
152 American College of Obstetricians and Gynecologists. ACOG Practice bulletin no. 134: fetal growth restriction. *Obstet Gynecol* 2013;121:1122–33.
153 Catalano PM, Drago NM, Amini SB. Maternal carbohydrate metabolism and its relationship to fetal growth and body composition. *Am J Obstet Gynecol* 1995;172:1464–70.
154 Catalano PM, Ehrenberg HM. The short- and long-term implications of maternal obesity on the mother and her offspring. *BJOG* 2006;113:1126–33.
155 Catalano PM, Tyzbir ED, Roman NM, *et al*. Longitudinal changes in insulin release and insulin resistance in nonobese pregnant women. *Am J Obstet Gynecol* 1991;165(6 Pt 1):1667–72.
156 Hedderson MM, Gunderson EP, Ferrara A. Gestational weight gain and risk of gestational diabetes mellitus. *Obstet Gynecol* 2010;115:597–604.
157 Ruchat SM, Davenport MH, Giroux I, *et al*. Effect of exercise intensity and duration on capillary glucose responses in pregnant women at low and high risk for gestational diabetes. *Diabetes Metab Res Rev* 2012;28:669–78.
158 Clapp JF. Effects of Diet and Exercise on Insulin Resistance during Pregnancy. *Metab Syndr Relat Disord* 2006;4:84–90.
159 Clapp JF. Effect of dietary carbohydrate on the glucose and insulin response to mixed caloric intake and exercise in both nonpregnant and pregnant women. *Diabetes Care* 1998;21(Suppl 2):B107–12.
160 Clapp JF, Capeless EL. The changing glycemic response to exercise during pregnancy. *Am J Obstet Gynecol* 1991;165(6 Pt 1):1678–83.
161 Sobierajski FM, Purdy GM, Usselman CW, *et al*. Maternal physical activity is associated with improved blood pressure regulation during late pregnancy. *Can J Cardiol* 2018;34:485–91.

162 Genest DS, Falcao S, Gutkowska J, *et al*. Impact of exercise training on preeclampsia: potential preventive mechanisms. *Hypertension* 2012;60:1104–9.
163 Brett KE, Ferraro ZM, Holcik M, *et al*. Prenatal physical activity and diet composition affect the expression of nutrient transporters and mTOR signaling molecules in the human placenta. *Placenta* 2015;36:204–12.
164 Rossi AC, Mullin P, Prefumo F. Prevention, management, and outcomes of macrosomia: a systematic review of literature and meta-analysis. *Obstet Gynecol Surv* 2013;68:702–9.
165 Nagpal TS, Prapavessis H, Campbell C, *et al*. Measuring adherence to a nutrition and exercise lifestyle intervention: is program adherence related to excessive gestational weight gain? *Behav Anal Pract* 2017;10:347–54.
166 Haakstad LAH, Vistad I, Sagedal LR, *et al*. How does a lifestyle intervention during pregnancy influence perceived barriers to leisure-time physical activity? The Norwegian fit for delivery study, a randomized controlled trial. *BMC Pregnancy Childbirth* 2018;18:127.
167 Barker DJ. The fetal and infant origins of adult disease. *BMJ* 1990;301:1111.
168 Sattar N, Greer IA. Pregnancy complications and maternal cardiovascular risk: opportunities for intervention and screening? *BMJ* 2002;325:157–60.
169 Schellong K, Schulz S, Harder T, *et al*. Birth weight and long-term overweight risk: systematic review and a meta-analysis including 643,902 persons from 66 studies and 26 countries globally. *PLoS One* 2012;7:e47776.
170 Clapp JF. Maternal carbohydrate intake and pregnancy outcome. *Proc Nutr Soc* 2002;61:45–50.
171 Hopkins SA, Cutfield WS. Exercise in pregnancy: weighing up the long-term impact on the next generation. *Exerc Sport Sci Rev* 2011;39:120–7.