Effect of diet and physical activity based interventions in pregnancy on gestational weight gain and pregnancy outcomes: meta-analysis of individual participant data from randomised trials

The International Weight Management in Pregnancy (i-WIP) Collaborative Group

Abstract

Objective To synthesise the evidence on the overall and differential effects of interventions based on diet and physical activity during pregnancy, primarily on gestational weight gain and maternal and offspring composite outcomes, according to women’s body mass index, age, parity, ethnicity, and pre-existing medical condition; and secondarily on individual complications.

Design Systematic review and meta-analysis of individual participant data (IPD).

Data sources Major electronic databases from inception to February 2017 without language restrictions.

Eligibility criteria for selecting studies Randomised trials on diet and physical activity based interventions in pregnancy.

Data synthesis Statistical models accounted for clustering of participants within trials and heterogeneity across trials leading to summary mean differences or odds ratios with 95% confidence intervals for the effects overall, and in subgroups (interactions).

Results IPD were obtained from 36 randomised trials (12526 women). Less weight gain occurred in the intervention group than control group (mean difference −0.70 kg, 95% confidence interval −0.92 to −0.48 kg, I²=14.1%; 33 studies, 9320 women). Although summary effect estimates favoured the intervention, the reductions in maternal (odds ratio 0.90, 95% confidence interval 0.79 to 1.03, I²=26.7%; 24 studies, 8852 women) and offspring (0.94, 0.83 to 1.08, I²=0%; 18 studies, 7981 women) composite outcomes were not statistically significant. No evidence was found of differential intervention effects across subgroups, for either gestational weight gain or composite outcomes. There was strong evidence that interventions reduced the odds of caesarean section (0.91, 0.83 to 0.99, I²=0%; 32 studies, 11 410 women), but not for other individual complications in IPD meta-analysis. When IPD were supplemented with study level data from studies that did not provide IPD, the overall effect was similar, with stronger evidence of benefit for gestational diabetes (0.76, 0.65 to 0.89, I²=36.8%; 59 studies, 16 885 women).

Conclusion Diet and physical activity based interventions during pregnancy reduce gestational weight gain and lower the odds of caesarean section. There is no evidence that effects differ across subgroups of women.

Introduction

Half of all women of childbearing age worldwide are overweight or obese.1 2 3 Obesity and excessive gestational weight gain put mother and offspring at risk, both in pregnancy and in later life.4 5 6 The resultant costs to the health service and society are considerable.7 8 9 Increasingly, healthcare organisations and research funding bodies prioritise research on interventions and strategies to reduce maternal weight related adverse outcomes in pregnancy.9 10 11 12

Syntheses of study level data on effects of diet and physical activity based interventions in pregnancy13 have shown an overall benefit on limiting gestational weight gain, but the findings varied for their protective effect on maternal and offspring outcomes.13 14 Importantly, the subgroups of women who may benefit the most from such interventions are not known.15 For this, primary studies do not have sufficient power,16 17 and meta-analyses of study level data are limited by the absence of published details of subgroup effects,18 and by potential ecological bias.19 These problems can be addressed by evidence synthesis using raw individual level data from relevant studies.20 21

We undertook an individual participant data (IPD) meta-analysis to assess the effects of diet and physical activity based interventions, primarily on gestational weight gain and on maternal and offspring composite outcomes, in subgroups defined by body mass index (BMI), age, parity, ethnicity, and pre-existing medical condition. Furthermore, we assessed the overall effects, and those of individual interventions (diet, physical activity, mixed), on critically important maternal and offspring complications. In addition to using IPD, we also...
assessed the impact of incorporating study level data from other studies not providing IPD.

**Methods**

The IPD meta-analysis was performed using a prespecified protocol (PROSPERO CRD42013038042) and was reported in line with recommendations of the Preferred Reporting Items for Systematic reviews and Meta-Analysis of Individual Participant Data (PRISMA-IPD).23

**Literature search and study identification**

We searched the major electronic databases Medline, Embase, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, and Health Technology Assessment Database from October 2013 to March 2015 to update our previous search in this topic for randomised trials on diet and physical activity based interventions in pregnancy.13 The search was further updated in January 2016 and February 2017 to identify new studies. We searched the internet by using general search engines, and contacted researchers in the specialty to identify relevant trials. There were no language restrictions. Web appendix 1 provides details of the search strategy.

Two independent researchers (ER and NM, AAM, or EM) selected studies in a two stage process. In the first stage, potential citations were identified. Next, we did a detailed evaluation of the full manuscripts of potential papers and selected articles that fulfilled the eligibility criteria. We included randomised trials that assessed the effects of interventions based on diet, physical activity, and mixed interventions in pregnancy, on maternal and offspring outcomes. We classified complex interventions on diet and physical activity, including those with behavioural change components, as mixed interventions. We excluded studies that only included women with gestational diabetes at baseline, involved animals, reported only non-clinical outcomes, and were published before 1990. The primary outcomes were gestational weight gain, a composite of maternal outcomes, and a composite of offspring outcomes. The secondary outcomes were individual maternal and offspring complications. The components of the composite outcomes were determined by a two round Delphi survey of researchers in this specialty, and were considered to be critically important to clinical practice.24 The maternal composite outcome included gestational diabetes mellitus, hypertensive disorders of pregnancy, preterm delivery, and caesarean section. The offspring composite outcome included stillbirth, small for gestational age fetus, large for gestational age fetus, and admission of the newborn to a neonatal intensive care unit.

We defined gestational weight gain as the difference between maternal weight at antenatal booking and the last weight measured before delivery. We accepted the primary authors’ definition and reporting of gestational diabetes mellitus, pregnancy induced hypertension, pre-eclampsia, caesarean section, stillbirth, and admission to a neonatal intensive care unit. We defined preterm delivery as birth before 37 weeks of gestation, and small for gestational age and large for gestational age as babies with a birth weight below the 10th and at or over the 90th centiles, respectively, adjusted for mother’s BMI, parity, and gestational age at delivery.25

*Establishment of IPD collaborative network and database—* We established the International Weight Management in Pregnancy IPD Collaborative Group by contacting researchers of eligible studies.20 A bespoke database was developed, and we requested collaborators for relevant data in any format. We sent three reminders when there was no response.

**Quality assessment of the included studies**

Two independent reviewers assessed the quality of the randomised trials using a risk of bias tool for sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other potential sources of bias.26 We considered a study to have a high risk of bias if it scored as such in at least one of the following domains: randomisation, allocation concealment, blinding of outcome assessment, or incomplete outcome data; all items should be scored as low risk for a study to be classified as low risk of bias.

**Data extraction and assessment of IPD integrity**

Two independent reviewers (ER and NM) undertook data extraction at study level for inclusion and exclusion criteria, the characteristics of the intervention, and the reported outcomes. We sought to obtain IPD from relevant studies published until July 2015, which was the endpoint for IPD acquisition, to allow sufficient time for data cleaning, standardisation, and amalgamation of datasets. We also extracted the published study level data for all relevant studies published until February 2017, including those published beyond the individual data acquisition timeline, and those for which IPD were not provided by study authors.

We obtained IPD for individual maternal characteristics that were determined a priori, such as BMI, age, parity, ethnicity, socioeconomic status, and pre-existing medical conditions. Continuous variables were kept continuous, but some were also categorised when considered to be clinically useful. These included categorisations based on BMI (normal 18.5-24.9 kg/m², overweight 25-29.9 kg/m², obese ≥30 kg/m²) and age (cut-off 20 years). Mother’s ethnicity was classified as white or non-white. We used the mother’s educational status to indicate socioeconomic status; low status if the mother did not complete secondary education to A level, medium if she completed secondary education (A level equivalent), and high if she completed any further higher education. We defined pre-existing medical conditions as diabetes mellitus, early onset of gestational diabetes, or hypertension.

We considered participants to be adherent to the intervention based on the following criteria: completion of at least 70% of the intervention protocol, dataset provided information on adherence in a yes or no format, or participant was deemed to be adherent as per the study criteria. We performed range and consistency checks on all IPD and produced summary tables. The randomisation ratio, baseline characteristics, and method of analysis in the IPD dataset were compared with the published information. Any discrepancies, missing data, obvious errors, and inconsistencies between variables or outlying values were queried and rectified as necessary with input from the original authors.

**Data synthesis**

To obtain summary estimates (mean difference for gestational weight gain and odds ratios for binary outcomes) and 95% confidence intervals for the intervention effects for each primary outcome we undertook a two stage IPD meta-analysis.27 We assessed the effects across all interventions overall and for individual interventions. A two stage IPD meta-analysis was used to obtain summary estimates of the subgroup effects (interactions) of interest, which compared differential effects.
of interventions across the primary outcomes. Additionally we
evaluated whether there are any differential effects of
interventions for individual complications, according to BMI
(normal, overweight, obese). All analyses were designed to
preserve the intention to treat principle.

The first stage of the two stage meta-analysis involved analysing
the IPD in each trial separately, to account for the clustering of
participants within trials, and to obtain the estimates of interest
and their variances. For the cluster randomised trials, we
included a random intercept for a unit of randomisation to
account for this further clustering. For the outcome of gestational
weight gain, we used analysis of covariance in each trial to
regress the final weight value against the intervention while
adjusting for baseline weight and centres in cluster randomised
trials. For maternal and offspring outcomes, we used a logistic
regression model for each trial separately, with the intervention
as a covariate. We excluded women with confirmed glucose
intolerance or a hypertensive disorder at baseline, as defined by
the primary authors, in the analysis of composite adverse
pregnancy outcomes. To assess potential intervention effect
modifiers, we extended the aforementioned models to include
interaction terms between participant level covariates and the
intervention (ie, treatment-covariate interaction terms).

In the second stage, we pooled the derived effect estimates (ie,
treatment effects or treatment-covariate interactions) across
trials using a random effects model fitted using restricted
maximum likelihood. The random effects approach allowed us
to account for unexplained interstudy heterogeneity in effects
across studies. This produced summary estimates and 95%
confidence intervals for the intervention effects and the
interactions (subgroup effects). The Hartung-Knapp correction
was applied when subsequently deriving 95% confidence
intervals for the true mean effect, to help account for the
uncertainty of the estimate of interstudy heterogeneity.

We included studies that did not contribute IPD, by
incorporating their extracted study level data within the second
stage of the IPD meta-analysis framework, to obtain summary
estimates of intervention effects that combined IPD and non-IPD
studies. Sensitivity analyses were also performed by excluding
studies with high risk of bias, analysing the primary outcomes
separately for each intervention type (diet, physical activity,
and mixed), excluding participants not adherent to the
intervention, by analysing change in BMI instead of weight
gain, and excluding maternal weight gain estimates from
pregnancies that ended before 37 completed weeks of gestation
to avoid systematic differences.

Heterogeneity was summarised using the I² statistic, the
estimated interstudy variance (τ²), and approximate 95%
prediction intervals, which indicate the potential intervention
(or interaction) effect in a new population similar to those
included in the meta-analysis.

Small study effects (potential publication bias) were investigated
by using contour enhanced funnel plots alongside visual
examination and statistical tests for asymmetry (Egger’s test
for continuous outcomes or Peter’s test for binary outcomes).

We assessed for IPD availability bias by comparing the summary
results when including non-IPD studies with those from IPD
studies. Furthermore, we compared the symmetry of funnel
plots before and after inclusion of non-IPD studies. All
meta-analyses were undertaken using Stata software version
12.1 (StataCorp, College Station, TX, USA), and statistical
significance was considered at the 5% level.

Patient involvement
No patients were involved in setting the research question or
the outcome measures, nor were they involved in developing
plans for recruitment, design, or implementation of the study.
A patient representative provided an input to the interpretation
and writing up of results. There are no plans to disseminate
the results of the research to study participants or the relevant patient
community. It was not evaluated whether the studies included
in the review had any patient involvement.

Results
Study selection
We identified 58 trials published up to June 2015, of which 36
studies (62%) provided individual participant data
(IPD). Twenty studies (36%) were from Europe, four each from
North America, Australia, and Brazil, and each from Egypt and Iran.

Twenty three IPD studies included women of any body mass
index (BMI), 34 studies (61%) included only obese women, 39
studies (68%) included obese and overweight women, and 40
studies (69%) included obese, overweight and normal women.

The interventions included those mainly based on diet (four IPD
studies),16 43 64 65 or physical activity (16 IPD studies),34
and those based on a mixed approach of diet, physical activity,
or behaviour modifying techniques, or all three together (15 IPD
studies).16 17 34 39 40 41 43 44 45 46 47 48 54 55 56 58
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Characteristics of included studies and participants
IPD were available from 36 trials in 166 studies. Twenty two
studies (32%) were from Europe, four each from North America,44
Australia, and Brazil,34 49 51 53 57 and one study each from Egypt16
and Iran.46 Twenty three IPD studies included women of any body mass
index (BMI), 34 studies (61%) included only obese women, 39
studies (68%) included obese and overweight women, and 40
studies (69%) included obese, overweight and normal women.

The web appendix provides the characteristics of all IPD
studies, and also those that did not contribute IPD.

More than 80% of women in the IPD meta-analyses were of
white origin, and at least half were classified as of high
socioeconomic status. Around 45% of women were nulliparous,
40% were obese, and a similar proportion was classified as
having sedentary status with no exercise at baseline (table 1).IPD
were available to assess the effects of interventions on
gestational weight gain (33 studies, 9320 women), maternal
composite outcomes (24 studies, 8852 women), and offspring
composite outcomes (18 studies, 7981 women). The largest IPD
were available for the outcome of large for gestational age fetus
(34 studies, 12 047 women), followed by preterm delivery (32
studies, 11 676 women), small for gestational age fetus (33
studies, 11 666 women), any caesarean section (32 studies, 11
410 women), hypertensive disorders of pregnancy (22 studies,
9618 women), and gestational diabetes (27 studies, 9427
women). We did not have access to IPD for 51% of all eligible
women (12 960/25 486) from 67 studies (fig 1).

Quality of included studies
Overall, trials had a low risk of bias in random sequence
generation (71%, 73/103). More than 90% (34/36) of studies
that contributed to the IPD were assessed as low risk of bias in this domain compared with 58% (28/67) of the non-IPD studies. Two IPD studies (2/36) and one non-IPD study (3/67) were considered high risk for allocation concealment. Blinding of outcome assessment was appropriate in 44% (16/36) of IPD and 33% (22/67) of non-IPD studies (fig 2). Fewer IPD studies (5/36) were assessed as high risk of bias for incomplete outcome data than non-IPD studies (15/67). Figure 2) shows the summary of the risk of bias estimates for all eligible studies and those that did and did not contribute to IPD. We did not encounter any issues that we were not able to clarify with the IPD contributor during the IPD integrity check.

Effects of interventions on pregnancy outcomes

Gestational weight gain

Based on IPD meta-analysis (33 studies, 9320 women), diet and physical activity based interventions resulted in significantly less gestational weight gain compared with control (summary mean difference −0.70 kg, 95% confidence interval −0.92 to −0.48 kg, I²=14.1%), after adjusting for baseline weight and clustering. The approximate 95% prediction interval for the intervention effect in a new setting was −1.24 to −0.16 kg (table 2).

Differential effects in subgroups

No strong evidence was found of a treatment-covariate interaction for baseline BMI when treated as a continuous covariate (−0.02 kg change in intervention effect per one unit increase in BMI, 95% confidence interval −0.08 to 0.04 kg), or when compared as overweight versus normal (−0.11 kg, −0.77 to 0.55 kg), obese versus normal (0.06 kg, −0.90 to 1.01 kg), and obese versus overweight (−0.09 kg, −1.05 to 0.86 kg). We also did not observe evidence of a subgroup effect for age (−0.03 kg per one year increase in age, 95% confidence interval −0.08 to 0.02 kg), parity (0.10 kg change in effect for multiparity versus nulliparity, 95% confidence interval −0.39 to 0.60 kg), ethnicity (0.05 kg change in effect for non-white versus white, 95% confidence interval −1.27 to 1.37 kg), and underlying medical condition (1.51 kg change in effect for women with at least one condition versus none, 95% confidence interval −2.01 to 5.02 kg). The findings were consistent when continuous covariates were analysed as categorical measures based on clinically relevant cut points (table 3).

Sensitivity analyses

The reduction in gestational weight gain owing to the intervention was consistently observed when the analysis was restricted to studies with low risk of bias (−0.67 kg, 95% confidence interval −0.95 to −0.38 kg; 15 studies, 5585 women), women adherent to the intervention (−0.76 kg, −1.00 to −0.52 kg; 33 studies, 8565 women), women followed up until more than 37 weeks’ gestation (−0.91 kg, −1.17 to −0.66 kg; 28 studies, 5324 women), and for BMI instead of maternal weight as an outcome (−0.30 kg/m², −0.39 to −0.21 kg/m²; 31 studies, 9238 women).

Addition of studies that did not contribute IPD

In meta-analysis undertaken by supplementing the IPD with study level data from studies (48 studies, 8210 women) that did not contribute IPD, we observed a larger beneficial intervention effect for weight gain (summary mean difference −1.1 kg; 95% confidence interval −1.46 to −0.74 kg; 81 studies, 17 530 women). The benefit was also consistently observed for individual interventions based on diet, physical activity, or mixed approach (table 2).

Maternal and offspring composite outcomes

In the IPD meta-analyses, the summary estimates favoured the intervention group for reduction in odds of maternal (odds ratio 0.90, 95% confidence interval 0.79 to 1.03, I²=26.7%; 24 studies, 8851 women) and offspring composite outcomes (0.94, 0.83 to 1.08, I²=0%; 18 studies, 7981 women), but these were not statistically significant (table 4).

Differential effects across subgroups

We observed no strong evidence of differential subgroup effects for maternal composite outcome according to either baseline BMI (treatment-covariate interaction 1.00, 95% confidence interval 0.98 to 1.02, age (1.01, 0.99 to 1.03), parity (1.03, 0.75 to 1.39), ethnicity (0.93, 0.63 to 1.37), and underlying medical condition (1.44, 0.15 to 13.74) (table 5). A similar lack of differential effect was observed for offspring composite outcome in mothers grouped according to baseline BMI (interaction 0.98, 95% confidence interval 0.95 to 1.00), age (1.01, 0.98 to 1.04), parity (0.94, 0.64 to 1.37), ethnicity (1.12, 0.75 to 1.68), and underlying medical condition (0.58, 0.03 to 9.81) (table 4). The findings did not change for maternal and offspring composite outcomes when BMI and age were analysed as continuous instead of categorical variables.

Individual maternal outcomes

Overall, in the IPD meta-analysis we observed a significant reduction in caesarean section (odds ratio 0.91, 95% confidence interval 0.83 to 0.90, I²=0%; 32 studies, 11 410 women) for interventions compared with routine care. The reduction in other individual outcomes such as gestational diabetes (0.89, 0.72 to 1.10, I²=23.8%; 27 studies, 9427 women), hypertensive disorders of pregnancy (0.95, 0.78 to 1.16, I²=24.2%; 22 studies, 9618 women), and preterm delivery (0.94, 0.78 to 1.13, I²=17.3%; 32 studies, 11 676 women) were not statistically significant in IPD meta-analyses (table 5). We did not observe any differential effect according to baseline BMI category (normal, overweight, obese) for any of the individual maternal outcomes (see web appendix 3). The findings were consistent when study level data from non-IPD studies were meta-analysed with IPD, but with a stronger evidence of benefit for gestational diabetes. The reduction in gestational diabetes (0.76, 0.65 to 0.89, 36.8%; 59 studies, 16 885 women) became significant (table 5). Among individual interventions, those based mainly on physical activity showed a reduction in gestational diabetes in both IPD (odds ratio 0.67, 95% confidence interval 0.46 to 0.90, I²=0%; 10 studies, 2700 women) and in combined (IPD and non-IPD) meta-analyses (0.66, 0.53 to 0.83, I²=0%; 27 studies, 6755 women). While the summary estimates for physical activity based interventions favoured caesarean section (0.82, 0.67 to 1.01, I²=0%; 13 studies, 3046 women) and hypertensive disorders of pregnancy (0.74, 0.42 to 1.33, I²=6.0%; 7 studies, 2565 women) in IPD meta-analyses, the addition of non-IPD studies resulted in stronger evidence of benefit for these complications, with reduction in the respective odds by 17% (0.83, 0.73 to 0.95, I²=0%; 32 studies, 6587 women) and 32% (0.68, 0.49 to 0.93, I²=0%; 20 studies, 5125 women). A strong effect was observed for preterm birth with diet based interventions in both IPD (odds ratio 0.28, 95% confidence interval 0.08 to 0.96, I²=0%; 4 studies, 1344 women) and combined analyses (0.32, 0.14 to 0.70, I²=0%; 7 studies, 1696 women), but the overall sample sizes were relatively small (table 4).
There was no evidence of benefit with mixed interventions for any maternal outcomes.

**Individual offspring outcomes**

No strong evidence was found that interventions had an effect on individual offspring outcomes such as stillbirth (odds ratio 0.81, 95% confidence interval <0.01 to 256.69, I²=0%; 2 studies, 3719 women), small for gestational age fetus (1.06, 0.94 to 1.20, I²=0%; 33 studies, 11 666 women), large for gestational age fetus (0.90, 0.76 to 1.07, I²=38.0%; 34 studies, 12 047 women), and admission to a neonatal intensive care unit (1.01, 0.84 to 1.23, I²=0%; 16 studies, 8140 women) based on the IPD meta-analyses. The significance of the findings did not change when non-IPD studies were added to the IPD meta-analyses (table 5⇓). The numbers of eligible participants for whom data were obtained, effect estimates, and confidence intervals for all above analyses are available from the study authors on request. There was no differential effect for any individual offspring outcome according to the BMI category (see web appendix 3).

**Small study effects**

We found visual and statistical evidence (Egger’s test P=0.04) of small study effects in the contour enhanced funnel plots for the IPD meta-analysis of the overall effect on gestational weight gain. The asymmetry of the plot was not improved by the addition of study level data from non-IPD studies to the meta-analysis. When studies with high risk of bias were excluded from the analysis, the symmetry of the funnel plot improved (Egger’s test P=0.61). We found significant evidence of small study effects for the maternal composite outcome (Peter’s test P=0.04), but not for the offspring composite outcome (P=0.85) (see web appendix 4).

**Discussion**

Our large, collaborative individual participant data (IPD) meta-analysis confirms that diet and physical activity based interventions in pregnancy reduce gestational weight gain. This beneficial effect was consistently observed irrespective of maternal body mass index (BMI), age, parity, ethnicity, or pre-existing medical condition; and remained when studies at high risk of bias were excluded. The findings are generalisable, with the 95% prediction interval suggesting a beneficial effect on gestational weight gain when the intervention is applied in a new population or setting. There is no strong evidence that interventions reduce the risk of maternal and offspring composite outcomes, with no variation in effect observed across the subgroups.

For individual outcomes, interventions reduce caesarean section without a statistically significant reduction in other maternal and offspring complications. The effects of interventions for individual maternal and offspring complications are consistent irrespective of the BMI of the mother. Addition of study level data from non-IPD studies to the IPD meta-analysis increased the precision of estimates, without a change in the direction of effect, and showed additional benefit for gestational diabetes. Among individual interventions, those mainly based on physical activity lowered the odds of gestational diabetes.

**Strengths and weaknesses of this study**

To our knowledge this is the first IPD meta-analysis to assess the differential effects of diet and physical activity based interventions for important, clinically relevant outcomes, in subgroups of women who were identified a priori. Establishment of the International Weight Management in Pregnancy IPD Collaborative Group facilitated the collaboration of key researchers in this area and provided access to the largest IPD in this specialty. This allowed us to extract data that were not published, with larger sample sizes for outcomes such as preterm birth, small and large for gestational age fetuses, and admission to the neonatal intensive care unit for IPD than for study level meta-analysis. Furthermore, we were able to minimise the heterogeneity in the population by excluding individual women who did not fulfil the inclusion criteria. We compared the quality of studies that contributed to the IPD, which were generally of higher quality than those that did not contribute IPD.

Access to IPD provided us with substantially increased power (compared with individual trials) to robustly estimate treatment covariate interactions and to avoid the ecological bias observed in aggregate meta-regression of study level covariates. It also allowed us to adjust for baseline weight using analysis of covariance in each trial, which is the best approach to analysing continuous outcomes, although rarely used in individual trials. Our reporting of 95% prediction intervals for the overall and differential effects of interventions across subgroups allowed us to quantify the range of effects across populations of interest.

The subgroups were chosen in response to the call by the National Institute for Health and Care Excellence for assessment of the effectiveness of lifestyle interventions in pregnancy for specific groups of women considered to be at high risk of complications, such as teenagers, those from ethnic minorities, and women who enter pregnancy obese. We assessed treatment-covariate interactions for subgroups as both continuous and categorical variables. We chose 20 years as the cut-off for age, as it allowed us to assess the effect of intervention in young adults, where pregnancy may alter normal growth processes and increase the women’s risk of becoming overweight or obese. Adolescent mothers also retain more weight post partum than mature control participants.

Owing to the variation in reporting, we were only able to broadly classify the ethnicity of women as white or non-white. Our findings were limited by the smaller number of non-white compared with white mothers. We combined diet based, physical activity based, and mixed approach interventions to provide an overall estimate, and also reported their individual effects. Since more than one clinical outcome is considered to be important to clinical care, we assessed the effects of interventions on maternal and offspring composite outcomes, the individual components of which were identified through a robust Delphi process. The varying definitions may have an impact on findings for gestational diabetes and pre-eclampsia, where the cut-offs and the criteria for diagnosis differed. Another limitation is that the majority of our population has a medium to high education status, a factor favouring compliance with interventions.

**IPD repository**

By establishing the International Weight Management in Pregnancy IPD live repository through the support of the individual research teams, we ensured that in addition to the standardisation, data were robustly safeguarded. The continuing growth of the repository is crucial for future research in this area and will accelerate update of the meta-analysis for the various relevant outcomes as new studies are published. We were successful in obtaining individual data from 80% of all participants within the IPD acquisition timeline. While every...
Effort was made to include IPD from the latest studies identified in the updated search, we were limited by the time needed to prepare the IPD datasets, which involved data access, setting up of institutional contracts, cleaning and formatting of accessed data, resolution of queries with individual researchers, and standardisation and merging of the data. This restricted our ability to include studies published after the agreed data acquisition timeline in the IPD meta-analysis. In a high priority area such as obesity and weight gain in pregnancy, the number of published studies has increased rapidly, with at least 10 trials published each year since 2011, and 16 published in 2016. We sought to maximise the information needed to inform the findings by combining study level data from non-IPD studies with the IPD meta-analyses. The conclusions appeared to be robust for nearly all outcomes. Furthermore, the non-availability of IPD from these studies did not appear to contribute to the observed small study effects, since the asymmetry of the funnel plot was not altered when the non-IPD studies were added. Non-IPD studies were also generally at a higher risk of bias.

**Gestational weight gain**

Diet and physical activity based interventions reduce gestational weight gain. We have shown that this beneficial effect is observed in all women irrespective of maternal characteristics. The findings are consistent for any type of intervention, even when restricted to only high quality studies and to women adherent to the intervention, and when non-IPD are added to IPD. Mothers with excess weight gain in pregnancy are at increased risk of postpartum weight retention. This increase in interpregnancy BMI may contribute to risks of entering subsequent pregnancies as overweight or obese, with adverse outcomes in subsequent pregnancy. Furthermore, this may increase women’s risk of cardiovascular morbidity and mortality in later life. Compared with published evidence, we identified a smaller reduction in gestational weight gain of 0.7 kg with interventions. The effect of such a reduction in gestational weight gain (compared with routine care) on postpartum weight retention and long term outcomes is not known.

**Maternal and offspring outcomes**

Despite the summary effect estimates favouring the interventions for maternal and offspring composite outcomes, these were not statistically significant. Interventions significantly reduced the odds of caesarean section. Previous systematic reviews showed a trend towards reduction in this risk overall, and for individual interventions (diet, physical activity, or mixed approach), but were limited by the small sample sizes and paucity of reporting, compared with the 11 000 women included in our IPD meta-analysis. Of the individual interventions, primary activity in pregnancy showed a trend towards reduction in caesarean section in IPD meta-analysis, which became statistically significant with minimal heterogeneity when non-IPD were added. The physical activity component in most studies involved a structured exercise of moderate intensity (eg, aerobic classes or stationary cycling) with resistance training that varied in frequency (see web appendix 5). The relatively small numbers of women in the diet only intervention may have contributed to the imprecision in estimates.

Although the direction of effect appeared to favour the intervention for other maternal outcomes, they were not statistically significant. Addition of non-IPD to the IPD meta-analysis resulted in a statistically significant reduction in gestational diabetes. However, unlike our IPD analysis, we were not able to implement the strict inclusion and exclusion criteria, standardise the analysis strategy (eg, adjust for baseline), or ascertain occurrence of outcome in the combined analysis with study level data. Physical activity based interventions statistically significantly reduced the odds of gestational diabetes in IPD meta-analysis, and also when combined with non-IPD. This benefit could be mediated through mechanisms that resulted in improved glycaemic variables and outcomes in type 4 and type 2 diabetes, through increased insulin sensitivity and reduced oxidative stress. Exercise in pregnancy may also have a potential role in preventing hypertensive disorders of pregnancy. The effects of diet and physical activity on maternal and offspring outcomes did not vary according to the BMI of the woman, highlighting the potential benefits for all and not selected groups of mothers.

Interventions based on diet showed a reduction in preterm birth, although the analysis included relatively small numbers of women. We did not identify any benefits with interventions in preventing any adverse offspring outcome, despite a sample size that was twofold to threefold more than published data for some outcomes, consistent with previous findings. The lack of adverse effects such as small for gestational age and preterm birth with diet and physical activity in pregnancy should reassure mothers who have traditionally been advised not to undertake structured exercise or manage their diet in pregnancy.

**Implications for clinical practice**

Currently in the UK, only obese women are offered access to a dietician and specific antenatal classes for advice on diet and lifestyle, to minimise gestational weight gain. Based on our work, it is likely that women of all BMI groups could benefit from specific advice on diet and physical activity for weight gain, and some maternal outcomes. Healthcare professionals should avoid variations in care and lifestyle advice provided to mothers based on ethnicity, age, and underlying medical conditions, as no differential effects were found.

Discussions about diet and physical activity in pregnancy, which are delivered as part of antenatal care, should incorporate specific estimates of benefit for caesarean section and gestational weight gain, and the likelihood of preventing gestational diabetes. Mothers should be reassured about the safety of the interventions, particularly on physical activity and structured exercise in pregnancy, by highlighting the benefits and lack of harm. This may improve engagement and compliance with the intervention. Importantly, such interventions in pregnancy could be considered in global efforts to reduce caesarean section in relevant populations.

**Implications for further research**

Whether the observed benefit in gestational weight gain with diet and physical activity translates to long term benefits to the mother and child needs to be assessed. Evaluation of any differential effects according to the individual components of the intervention, such as duration, frequency, provider, and setting, on individual outcomes is required to provide detailed recommendations. The effects of these interventions on mothers in low and middle income countries, particularly in those countries with high rates of caesarean section and gestational diabetes, need to be ascertained from large randomised trials. There is a need to develop a harmonised core outcome set for future reporting of clinical trials in this area, to maximise the meaningful interpretation of published data. This is particularly relevant for rare but important outcomes such as shoulder dystocia, birth trauma, and venous thromboembolic events.
Conclusion

Diet and physical activity based interventions in pregnancy limit gestational weight gain, with no evidence that this effect differs across subgroups defined by maternal characteristics. The odds for caesarean section are also reduced.

We thank all researchers, research nurses, and staff of the participating centres in the trials contributing to this IPD meta-analysis. We thank Erica Harris for her input as a patient group representative.

Members of the International Weight Management in Pregnancy (i-WIP) Collaborative Group: Ewelina Rogozinska, doctoral researcher, Nadine Marlin, statistician, Anika Pilar Bétrán, medical officer, Anne Astrup, professor, Ruben Barakat, professor, Annick Bogaerts, assistant professor, Jose G Coticcio, professor, Roland Devlieger, associate professor, Jodie M Dodd, professor, Nermeen El Beltagy, associate professor, Fabio Facchinetti, professor, chairman of the unit, Nina RW Geiker, senior researcher, Kym J Gueff, senior lecturer, Lene AH Haakstad, associate professor, Chereyce L Harrison, research fellow, Hans Hauner, professor, Dorte M Jensen, consultant, assistant professor, Tarja I Kinnunen, lecturer, Janette Khoury, researcher, Riitta Luoto, research director, associate professor, Fionnuala McAuliffe, professor, Narges Motahari, researcher, Siv Merkved, professor, Julie Owens, professor, Maria Perales, research fellow, Elisabetta Petrella, medical doctor, Suzanne Phelan, professor, Lucilla Poston, professor, Kathrin Rauh, research fellow, Kristina M Renault, obstetrician, Linda R Sagedal, physician, Kjell Á Salvesen, professor, Garry X Shen, professor, Alexis Shub, obstetrician, senior lecturer, Tania Scudeller, professor, Fernanda G Suria, associate professor, Signe N Staafne, postdoctoral research fellow, Helena Teede, director, professor, Serena Tonstad, head physician, Mireille NM van Poppel, professor, Christina A Vinter, obstetrician, Ingvild Vistad, consultant, Seon Ae Yeo, professor, Julie Dodds, senior research manager, Sally Kerry, reader, Louise Jackson, research fellow, Pelham Barton, reader, Emma Molyneaux, postdoctoral research fellow, Alba A Martin, research fellow, Girish Rayanagoudar, researcher fellow, Anneloes E Ruttko, resident, Tracy Roberts, professor, Christianne JM de Groot, professor, Anri Coomarasamy, professor, Ben WJ Mol, professor, Javier Zamora, senior lecturer, Khalid S Khan, professor, Richard D Riley, professor, Shakila Thangaratinam, professor (see web appendix 6).

Contributors: ST, RDR, CdG, AER, and SK developed the protocol. JD oversaw the project and drafted the manuscript. ST, ER, and NM conducted the review, drafted the manuscript, and led the project. KSK and BWJM provided input into the development of the protocol and drafting of the initial manuscript. ER, EM, and AOKB developed the manuscript. JW undertook the literature search and studies selection. AER, ER, ST, EM, and GR acquired IPD. MV, LP, CAV, FMCA, JMD, JO, RB, MP, JGc, FGS, SY, AB, RD, HT, CLH, LH, GXS, AS, NEB, NMo, JK, STo, RL, TlK, KjG, FF, EP, SP, TS, KR, HH, KM, LRS, IV, SNS, SM, KAS, DMJ, MvP, AA, and NWRG contributed data to the project and provided input at all stages of the project. ER, GR, and NM mapped the variables in the available datasets. ER and NM cleaned and quality checked data. DM harmonised the data. NM, SK, and RDR conducted the data analysis. TR, LJ, and PB provided input into the protocol. APB provided input into the conduct of study. JZ provided methodological support. KSK, AC, and BWJM were involved in project development and provided input at all stages. All authors critically appraised the final draft of the report. ST is the guarantor.

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Ethical approval: Not required.

Data sharing: The full dataset or its subset and technical appendix are available from the data custodian (Queen Mary University of London) at smd-wipdata@qmul.ac.uk. Access to the dataset is regulated by terms and conditions available on request. The presented data are anonymised and risk of identification of individual participants is low.

Transparency: The lead author (IER) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.
What is already known on this topic

Increased weight gain in pregnancy is associated with maternal and fetal complications. Interventions based on diet or physical activity or both in pregnancy minimise gestational weight gain.

Interventions based on diet and physical activity may have a potential role in preventing adverse pregnancy outcomes.

What this study adds

Diet and physical activity-based interventions consistently reduce gestational weight gain across various subgroups of women categorised by age, parity, body mass index, ethnicity, and pre-existing medical condition. The reduction in odds of adverse maternal and offspring composite outcomes with diet and physical activity is significant, and does not vary across various subgroups of women.

Interventions significantly lower the odds of caesarean section and have no effect on off-spring outcomes.

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What this study adds

Diet and physical activity-based interventions consistently reduce gestational weight gain across various subgroups of women categorised by age, parity, body mass index, ethnicity, and pre-existing medical condition. The reduction in odds of adverse maternal and offspring composite outcomes with diet and physical activity is significant, and does not vary across various subgroups of women.

Interventions significantly lower the odds of caesarean section and have no effect on off-spring outcomes.


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## Tables

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No of studies (No of women)</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age (years)</td>
<td>35 (12 006)</td>
<td>30.0 (5.1)</td>
<td>30.1 (5.2)</td>
</tr>
<tr>
<td>Weight (body mass index):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (18.5-24.9 kg/m²)</td>
<td></td>
<td>1974 (31.7)</td>
<td>1842 (31.8)</td>
</tr>
<tr>
<td>Overweight (25-29.9 kg/m²)</td>
<td></td>
<td>1578 (25.3)</td>
<td>1523 (26.3)</td>
</tr>
<tr>
<td>Obese (≥30 kg/m²)</td>
<td></td>
<td>2680 (43.0)</td>
<td>2434 (42.0)</td>
</tr>
<tr>
<td>Race/ethnicity:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (including Russians and Australians)</td>
<td>4562 (88.0)</td>
<td>4217 (87.2)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>157 (3.0)</td>
<td>156 (3.2)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>292 (5.6)</td>
<td>292 (6.0)</td>
<td></td>
</tr>
<tr>
<td>Central and South American</td>
<td>67 (1.3)</td>
<td>64 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Middle Eastern (including Iranian and Turkish)</td>
<td>37 (0.7)</td>
<td>37 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>71 (1.4)</td>
<td>68 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Educational status of mother†:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>722 (15.6)</td>
<td>724 (16.9)</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>1372 (29.6)</td>
<td>1292 (30.2)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>2536 (54.8)</td>
<td>2268 (52.9)</td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>29 (10 958)</td>
<td>875 (15.4)</td>
<td>865 (16.4)</td>
</tr>
<tr>
<td>Parity</td>
<td>33 (11 805)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>3027 (49.5)</td>
<td>2692 (47.3)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2136 (34.9)</td>
<td>2083 (36.6)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>647 (10.6)</td>
<td>634 (11.1)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>179 (2.9)</td>
<td>165 (2.9)</td>
<td></td>
</tr>
<tr>
<td>≥4</td>
<td>129 (2.1)</td>
<td>113 (2)</td>
<td></td>
</tr>
<tr>
<td>No exercise or sedentary</td>
<td>27 (7583)</td>
<td>1761 (44.6)</td>
<td>1731 (47.6)</td>
</tr>
<tr>
<td>Pre-existing diabetes mellitus</td>
<td>25 (9589)</td>
<td>6 (0.1)</td>
<td>9 (0.2)</td>
</tr>
<tr>
<td>Pre-existing hypertension</td>
<td>23 (5494)</td>
<td>73 (2.5)</td>
<td>54 (2.1)</td>
</tr>
</tbody>
</table>

*Proportion out of observations in control or intervention arms, respectively.
†Low=not completed secondary education to A level; medium=completed secondary education (A level equivalent); high=any further or higher education.
Table 2 | Effects of diet and physical activity based interventions on gestational weight gain summarised using individual participant data (IPD) alone, and by supplementing IPD with study level data from studies that did not contribute IPD. Values are means (standard deviations) unless stated otherwise

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>No of studies (No of women)</th>
<th>Intervention</th>
<th>Control</th>
<th>Mean difference (95% CI)</th>
<th>$I^2$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IPD</td>
<td>IPD and non-IPD</td>
<td>IPD</td>
<td>IPD and non-IPD</td>
<td>IPD</td>
</tr>
<tr>
<td>Overall</td>
<td>33 (9320)</td>
<td>81 (17 530)</td>
<td>10.1 (5.4)</td>
<td>10.6*</td>
<td>10.8 (5.4)</td>
</tr>
<tr>
<td>Diet</td>
<td>4 (1168)</td>
<td>12 (2017)</td>
<td>10.2 (4.4)</td>
<td>9.2*</td>
<td>11.0 (4.8)</td>
</tr>
<tr>
<td>Physical activity</td>
<td>15 (2915)</td>
<td>37 (7355)</td>
<td>9.8 (4.4)</td>
<td>11.3*</td>
<td>10.8 (4.8)</td>
</tr>
<tr>
<td>Mixed approach</td>
<td>15 (5369)</td>
<td>35 (8448)</td>
<td>10.2 (6.0)</td>
<td>10.3*</td>
<td>10.6 (5.9)</td>
</tr>
</tbody>
</table>

*Recalculation using DerSimonian-Laird.
### Table 3: Differential effects of diet and physical activity based interventions on gestational weight gain in subgroups of pregnant women

<table>
<thead>
<tr>
<th>Maternal characteristics</th>
<th>No of studies (No of women)</th>
<th>Mean difference kg (95% CI)</th>
<th>Treatment covariate interaction Mean difference kg (95% CI)</th>
<th>Coefficient; 95% CI (95% PI)</th>
<th>I² (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline body mass index:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>21 (3376)</td>
<td>−0.77 (−1.15 to −0.39)</td>
<td>−0.02; −0.08 to 0.04 (−0.21 to 0.17)††</td>
<td>−0.77 (−1.15 to −0.39)</td>
<td>39.8</td>
</tr>
<tr>
<td>Overweight</td>
<td>28 (2574)</td>
<td>−0.75 (−1.22 to −0.27)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>31 (3335)</td>
<td>−0.85 (−1.41 to −0.29)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parity:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>27 (4513)</td>
<td>−0.80 (−1.17 to −0.43)</td>
<td>0.10; −0.39 to 0.60 (−0.83 to 1.04)‡‡</td>
<td>−0.80 (−1.17 to −0.43)</td>
<td>4.6</td>
</tr>
<tr>
<td>Multiparous</td>
<td>27 (4546)</td>
<td>−0.62 (−0.88 to −0.37)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethnicity:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>21 (6814)</td>
<td>−0.74 (−1.07 to −0.42)</td>
<td>0.05; −1.27 to 1.37 (−1.28 to 1.39)§††</td>
<td>−0.74 (−1.07 to −0.42)</td>
<td>26.1</td>
</tr>
<tr>
<td>Non-white</td>
<td>15 (621)</td>
<td>−0.42 (−1.12 to 0.28)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥20</td>
<td>32 (9045)</td>
<td>−0.72 (−0.95 to −0.50)</td>
<td>−0.03; −0.08 to 0.02 (−0.14 to 0.09)¶††</td>
<td>−0.72 (−0.95 to −0.50)</td>
<td>25.9</td>
</tr>
<tr>
<td>&lt;20</td>
<td>13 (232)</td>
<td>0.05 (−1.34 to 1.44)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-existing medical conditions**:</td>
<td></td>
<td></td>
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<tr>
<td>None</td>
<td>18 (4335)</td>
<td>−0.62 (−0.90 to −0.34)</td>
<td>1.51; −2.01 to 5.02 (−4.13 to 7.15)††</td>
<td>−0.62 (−0.90 to −0.34)</td>
<td>28.4</td>
</tr>
<tr>
<td>≥1</td>
<td>6 (128)</td>
<td>0.40 (−1.92 to 2.71)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

PI=prediction interval.

*Model accounted for baseline weight and clustering effect.
†Per unit of body mass index.
‡Multiparous versus nulliparous.
§Non-white versus white.
¶Per year of age.
**Diabetes mellitus or hypertension.
††≥1 medical condition versus none.
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>No of studies (No of women)</th>
<th>Intervention: event/No event</th>
<th>Control: event/No event</th>
<th>Odds ratio (95% CI)</th>
<th>$I^2$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IPD and non-IPD</td>
<td>IPD and non-IPD</td>
<td>IPD and non-IPD</td>
<td>IPD and non-IPD</td>
<td>IPD and non-IPD</td>
</tr>
<tr>
<td>Maternal</td>
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<td>Composite outcome:</td>
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<tr>
<td>Overall</td>
<td>24 (8851)</td>
<td>NA</td>
<td>1896/2728</td>
<td>0.90 (0.79 to 1.03)</td>
<td>NA</td>
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<tr>
<td>Diet</td>
<td>3 (397)</td>
<td>NA</td>
<td>42/137</td>
<td>0.60 (0.20 to 1.75)</td>
<td>NA</td>
</tr>
<tr>
<td>Physical activity</td>
<td>9 (2311)</td>
<td>NA</td>
<td>346/850</td>
<td>0.81 (0.61 to 1.09)</td>
<td>NA</td>
</tr>
<tr>
<td>Mixed approach</td>
<td>13 (6259)</td>
<td>NA</td>
<td>1508/1742</td>
<td>0.97 (0.84 to 1.12)</td>
<td>NA</td>
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<tr>
<td>Gestational diabetes:</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>27 (9427)</td>
<td>59 (16 885)</td>
<td>584/4333</td>
<td>0.89 (0.72 to 1.10)</td>
<td>0.76 (0.65 to 0.89)</td>
</tr>
<tr>
<td>Diet</td>
<td>4 (490)</td>
<td>8 (1106)</td>
<td>13/208</td>
<td>1.03 (0.30 to 3.61)</td>
<td>0.74 (0.37 to 1.69)</td>
</tr>
<tr>
<td>Physical activity</td>
<td>10 (2700)</td>
<td>27 (6755)</td>
<td>90/1300</td>
<td>0.67 (0.46 to 0.99)</td>
<td>0.66 (0.53 to 0.83)</td>
</tr>
<tr>
<td>Mixed approach</td>
<td>14 (6355)</td>
<td>27 (9342)</td>
<td>481/2825</td>
<td>1.02 (0.79 to 1.32)</td>
<td>0.86 (0.72 to 1.07)</td>
</tr>
<tr>
<td>Hypertensive disorders of pregnancy:</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>22 (9618)</td>
<td>45 (14 849)</td>
<td>432/4586</td>
<td>0.95 (0.78 to 1.16)</td>
<td>0.85 (0.71 to 1.00)</td>
</tr>
<tr>
<td>Diet</td>
<td>3 (397)</td>
<td>5 (729)</td>
<td>18/161</td>
<td>0.59 (0.07 to 4.65)</td>
<td>0.57 (0.18 to 1.79)</td>
</tr>
<tr>
<td>Physical activity</td>
<td>7 (2565)</td>
<td>20 (5125)</td>
<td>55/1242</td>
<td>0.74 (0.42 to 1.33)</td>
<td>0.18 (0.49 to 0.93)</td>
</tr>
<tr>
<td>Mixed approach</td>
<td>13 (6797)</td>
<td>21 (9136)</td>
<td>359/3183</td>
<td>1.05 (0.86 to 1.28)</td>
<td>1.01 (0.87 to 1.17)</td>
</tr>
<tr>
<td>Preterm birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>32 (11 676)</td>
<td>49 (14 339)</td>
<td>332/5713</td>
<td>0.94 (0.78 to 1.13)</td>
<td>0.92 (0.79 to 1.08)</td>
</tr>
<tr>
<td>Diet</td>
<td>4 (1344)</td>
<td>7 (1696)</td>
<td>9/647</td>
<td>0.28 (0.08 to 0.96)</td>
<td>0.32 (0.14 to 0.70)</td>
</tr>
<tr>
<td>Physical activity</td>
<td>13 (3249)</td>
<td>23 (5149)</td>
<td>95/1541</td>
<td>1.29 (0.90 to 1.85)</td>
<td>1.09 (0.84 to 1.41)</td>
</tr>
<tr>
<td>Mixed approach</td>
<td>16 (7219)</td>
<td>20 (7630)</td>
<td>228/3525</td>
<td>0.91 (0.73 to 1.12)</td>
<td>0.92 (0.75 to 1.12)</td>
</tr>
<tr>
<td>Caesarean section:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>32 (11 410)</td>
<td>66 (18 041)</td>
<td>1525/4385</td>
<td>0.91 (0.83 to 0.99)</td>
<td>0.89 (0.83 to 0.96)</td>
</tr>
<tr>
<td>Diet</td>
<td>4 (1340)</td>
<td>7 (1732)</td>
<td>117/535</td>
<td>0.78 (0.50 to 1.22)</td>
<td>0.88 (0.65 to 1.17)</td>
</tr>
<tr>
<td>Physical activity</td>
<td>13 (3046)</td>
<td>32 (6587)</td>
<td>306/1230</td>
<td>0.82 (0.67 to 1.01)</td>
<td>0.83 (0.73 to 0.95)</td>
</tr>
<tr>
<td>Mixed approach</td>
<td>16 (7160)</td>
<td>28 (9858)</td>
<td>1102/2620</td>
<td>0.95 (0.84 to 1.08)</td>
<td>0.92 (0.80 to 1.06)</td>
</tr>
</tbody>
</table>

Offspring
## Table 4 (continued)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>No of studies (No of women)</th>
<th>Intervention: event/No event</th>
<th>Control: event/No event</th>
<th>Odds ratio (95% CI)</th>
<th>f (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IPD</td>
<td>IPD and non-IPD</td>
<td>IPD</td>
<td>IPD and non-IPD</td>
<td>IPD</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>0.94 (0.83 to 1.08)</td>
<td>NA</td>
</tr>
<tr>
<td>Composite outcome:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>18 (7981)</td>
<td>NA</td>
<td>1007/3172</td>
<td>951/2851</td>
<td>NA</td>
</tr>
<tr>
<td>Diet</td>
<td>2 (346)</td>
<td>NA</td>
<td>34/132</td>
<td>48/132</td>
<td>NA</td>
</tr>
<tr>
<td>Physical activity</td>
<td>5 (1274)</td>
<td>NA</td>
<td>138/495</td>
<td>143/498</td>
<td>NA</td>
</tr>
<tr>
<td>Mixed approach</td>
<td>12 (6494)</td>
<td>NA</td>
<td>835/2545</td>
<td>797/2317</td>
<td>NA</td>
</tr>
<tr>
<td>Stillbirth:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>2 (3719)</td>
<td>4 (4534)</td>
<td>9/1858</td>
<td>11/1841</td>
<td>14/2247</td>
</tr>
<tr>
<td>Small for gestational age:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>33 (1166)</td>
<td>44 (12 937)</td>
<td>709/5324</td>
<td>632/5001</td>
<td>685/5461</td>
</tr>
<tr>
<td>Diet</td>
<td>4 (1337)</td>
<td>6 (1628)</td>
<td>41/610</td>
<td>50/746</td>
<td>47/639</td>
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<tr>
<td>Physical activity</td>
<td>14 (3272)</td>
<td>21 (3955)</td>
<td>243/1402</td>
<td>232/1395</td>
<td>271/1670</td>
</tr>
<tr>
<td>Mixed approach</td>
<td>16 (7193)</td>
<td>20 (7670)</td>
<td>425/3312</td>
<td>370/3086</td>
<td>386/3309</td>
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<tr>
<td>Large for gestational age:</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Overall</td>
<td>34 (12 047)</td>
<td>45 (13 348)</td>
<td>744/5492</td>
<td>759/5052</td>
<td>833/5510</td>
</tr>
<tr>
<td>Diet</td>
<td>4 (1408)</td>
<td>6 (1699)</td>
<td>155/529</td>
<td>172/663</td>
<td>176/548</td>
</tr>
<tr>
<td>Physical activity</td>
<td>15 (3330)</td>
<td>21 (3930)</td>
<td>121/1557</td>
<td>124/1528</td>
<td>161/1768</td>
</tr>
<tr>
<td>Mixed approach</td>
<td>16 (7450)</td>
<td>21 (8040)</td>
<td>468/3406</td>
<td>489/3680</td>
<td>481/3905</td>
</tr>
<tr>
<td>Admission to neonatal intensive care unit:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>16 (8140)</td>
<td>21 (9498)</td>
<td>302/3973</td>
<td>279/3568</td>
<td>400/4149</td>
</tr>
<tr>
<td>Diet</td>
<td>1 (289)</td>
<td>2 (389)</td>
<td>3/137</td>
<td>11/179</td>
<td>13/136</td>
</tr>
<tr>
<td>Physical activity</td>
<td>3 (1166)</td>
<td>4 (1240)</td>
<td>31/552</td>
<td>34/586</td>
<td>40/543</td>
</tr>
<tr>
<td>Mixed approach</td>
<td>13 (6818)</td>
<td>15 (7771)</td>
<td>268/3284</td>
<td>360/3626</td>
<td>332/3453</td>
</tr>
</tbody>
</table>

*Recalculation using DerSimonian-Laird.
†All data come from studies with mixed approach interventions.
‡Not possible to estimate standard deviations.
<table>
<thead>
<tr>
<th>Composite outcomes</th>
<th>No of studies (No of women)</th>
<th>Odds ratio (95% CI)</th>
<th>Treatment covariate interaction</th>
</tr>
</thead>
</table>
|                    |                             |                     | Coefficient; 95% CI (95% PI)     | I² (%) |}

**Maternal**

Baseline body mass index:

|                     |  |  |  |       |  |  |  |  |  |  |
|---------------------|-----------------------------|---------------------|----------------------------------|
| Normal              | 12 (2445)                   | 0.91 (0.85 to 1.28) | 1.00; 0.98 to 1.02 (0.98 to 1.02)† | 0 |
| Overweight          | 19 (2222)                   | 1.04 (0.86 to 1.26) |                                 |
| Obese               | 20 (4181)                   | 0.92 (0.80 to 1.05) |                                 |

Parity:

Nulliparous         | 21 (4613)                   | 0.87 (0.71 to 1.07) | 1.03; 0.75 to 1.39 (0.53 to 2.00)‡ | 34.0 |

Multiparous         | 22 (4186)                   | 0.92 (0.78 to 1.07) |                                 |

Ethnicity:

White               | 15 (6510)                   | 0.92 (0.79 to 1.07) | 0.93; 0.63 to 1.37 (0.62 to 1.38)§ | 0 |

Non-white           | 11 (917)                    | 0.86 (0.63 to 1.17) |                                 |

Age (years):

≥20                 | 24 (8656)                   | 0.91 (0.81 to 1.02) | 1.01; 0.99 to 1.03 (0.99 to 1.03)¶ | 0 |

<20                 | 9 (172)                     | 1.57 (0.66 to 3.71) |                                 |

Pre-existing medical condition**:

None                | 15 (3135)                   | 0.85 (0.66 to 1.09) | 1.44; 0.15 to 13.74 (0.03 to 76.75)†† | 24.9 |

≥1                  | 5 (69)                      | 1.65 (0.36 to 7.51) |                                 |

**Offspring**

Baseline body mass index:

|                     |  |  |  |       |  |  |  |  |  |  |
|---------------------|-----------------------------|---------------------|----------------------------------|
| Normal              | 7 (1843)                    | 0.93 (0.60 to 1.43) | 0.98; 0.95 to 1.00 (0.94 to 1.02)† | 18.5 |
| Overweight          | 12 (2065)                   | 0.83 (0.61 to 1.13) |                                 |
| Obese               | 13 (4327)                   | 0.92 (0.72 to 1.19) |                                 |

Parity:

Nulliparous         | 16 (4152)                   | 0.97 (0.80 to 1.17) | 0.94; 0.64 to 1.37 (0.39 to 2.28)‡ | 35.5 |

Multiparous         | 15 (4048)                   | 0.91 (0.72 to 1.15) |                                 |

Ethnicity:

White               | 11 (6018)                   | 0.93 (0.79 to 1.08) | 1.12; 0.75 to 1.68 (0.74 to 1.69)§ | 0 |

Non-white           | 9 (939)                     | 1.10 (0.78 to 1.54) |                                 |

Age (years):

≥20                 | 16 (8061)                   | 0.95 (0.82 to 1.09) | 1.01; 0.98, 1.04 (0.97 to 1.05)¶ | 4.1 |

<20                 | 7 (162)                     | 1.01 (0.34 to 2.98) |                                 |

Pre-existing medical condition**:

None                | 12 (3407)                   | 0.89 (0.74 to 1.08) | 0.58; 0.03, 9.81 (<0.001 to 2440.15)†† | 0 |

≥1                  | 3 (63)                      | 0.54 (0.04 to 7.52) |                                 |

PI = prediction interval.

*Model accounted for baseline weight and clustering effect.
†Per unit of body mass index.
‡Multiparous versus nulliparous.
§Non-white versus white.
¶Per year of age.
**Diabetes mellitus or hypertension.
††≥1 medical condition versus none.
Figures

Citations from electronic databases search from Jan 2012 to Feb 2017* (n=11 815) → Citations from previous systematic review (inception to Jan 2012) and other sources† (n=105)

Records available after duplicates removed (n=7038) → Citations excluded (n=6820)

Full text studies assessed for eligibility (n=218) → Excluded (n=115):
- Published before 1990 (n=4)
- Pilot trial incorporated into main trial (n=2)
- Protocol (ongoing recruitment) (n=37)
- Irrelevant study objective or intervention (n=15)
- Active comparison (n=28)
- No obstetric outcomes (n=11)
- Wrong study population (n=14)
- Full text or abstract not available (n=4)

Eligible studies (n=103)

Studies for which IPD were sought (n=58) → Eligible studies identified beyond data acquisition timeline (n=45; 9945 women)

Studies that did not provide IPD (n=22):
- Conflict of interest (n=2; 610 women)
- Lack of time (n=2; 286 women)
- Data sharing issue (n=1; 132 women)
- Data loss (n=2; 421 women)
- Contact loss (n=4; 531 women)
- No response (n=11; 1035 women)

Studies that provided IPD (n=36; 12 526 women)

Gestational weight gain (n=33; 9320 women)
- Maternal composite (n=34; 8852 women)
- Gestational diabetes (n=27; 9427 women)
- Hypertensive disorder of pregnancy (n=22; 9618 women)
- Preterm birth (n=32; 11 676 women)
- Caesarean section (n=12; 11 410 women)

Offspring composite (n=18; 7981 women)
- Stillbirth (n=2; 3719 women)
- Small for gestational age (n=33; 16 666 women)
- Large for gestational age (n=34; 12 047 women)
- Admission to NICU (n=16; 8140 women)

Studies for which IPD data were not available (n=67; 12 960 women)

Gestational weight gain (n=48; 8210 women)
- Maternal outcomes
  - Gestational diabetes (n=32; 8033 women)
  - Hypertensive disorder of pregnancy (n=23; 5231 women)
  - Preterm birth (n=17; 2663 women)
  - Caesarean section (n=34; 6631 women)
  - Offspring outcomes
    - Stillbirth (n=2; 815 women)
    - Small for gestational age (n=11; 1271 women)
    - Large for gestational age (n=11; 1301 women)
    - Admission to NICU (n=5; 1358 women)

Studies with IPD and without IPD availability

Maternal outcomes: gestational weight gain (n=81; 17 530 women), gestational diabetes (n=59; 16 1885 women), hypertensive disease (n=54; 14 819 women), preterm birth (n=49; 14 339 women), caesarean section (n=66; 18 041 women)

Offspring outcomes: Stillbirth (n=6; 4534 women), small for gestational age (n=44; 12 937 women), large for gestational age (n=45; 13 348 women), admission to NICU (n=21; 9498 women)

NICU = neonatal intensive care unit
*Database search was updated in October 2013 (9159 records), March 2015 (3551 records), January 2016 (1733 records), and February 2017 (1547 records)
†Other sources: reference search, personal communication, and Google search

Fig 1 Identification and selection of studies in individual participant data (IPD) meta-analysis of diet and physical activity based interventions on pregnancy outcomes after gestational weight gain.
Fig 2 Assessment of risk of bias in all eligible studies (n=103), studies with individual participant data (IPD) (n=36), and studies without access to IPD (n=67)