Lifestyle interventions for obese women before and during pregnancy: The effect on pregnancy outcomes
Ruifrok, A.E.

Citation for published version (APA):

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Association between weight gain during pregnancy and pregnancy outcomes after dietary and lifestyle interventions: A meta-analysis.
Association between weight gain during pregnancy and pregnancy outcomes after dietary and lifestyle interventions: A meta-analysis

A.E. Ruifrok
M.N.M. van Poppel
M. van Wely
E. Rogozińska
K.S. Khan
C.J.M. de Groot
S. Thangaratinam
B.W.J. Mol

American Journal of Perinatology
2013 August 5
Abstract

Objective
Lifestyle interventions in obese pregnant women reduce adverse maternal outcomes of pregnancy. However, the association between weight change due to interventions and the actual reduction in complications is unknown. The objective of this study was to determine the association between gestational weight gain (GWG) and the rate of pregnancy complications.

Study design
The authors included randomised controlled trials (RCTs) assessing the effect of lifestyle interventions during pregnancy on GWG and adverse maternal and foetal outcomes. For each outcome they assessed the association between GWG and the risk of adverse pregnancy outcomes.

Results
They analysed data of 23 RCTs (4,990 women). Increased GWG was associated with a non-significant increase in the incidence of pre-eclampsia (PE) (0.2% per gained kg, 95% confidence interval (CI) 0.5 to 0.9%, \( p > 0.05 \)), gestational diabetes (GDM) (0.3% per gained kg, 95% CI 0.5 to 1.0%, \( p > 0.05 \)), and induction of labour (IOL) (1.5% per gained kg, 95% CI 0.9 to 3.9%, \( p > 0.05 \)).

Conclusion
Reduction in GWG due to lifestyle interventions in pregnancy had statistically non-significant effects on lowering the incidence of PE, GDM, and IOL. Possibly, the beneficial effect of lifestyle interventions on pregnancy outcomes is due to an effect independent of the reduction of GWG.
Introduction

Excessive weight gain during pregnancy is associated with an increased risk of obstetric, maternal, and foetal complications\textsuperscript{1–9} and postpartum weight retention.\textsuperscript{10;11} It also increases the risk of obesity in children\textsuperscript{6;10;12} and long-term obesity related complications resulting in a significant burden on health care.\textsuperscript{10;11;13–18} Limited or no weight gain in pregnancy has been shown to be associated with favourable pregnancy outcomes by reducing the risk of pre-eclampsia (PE), caesarean delivery, and large for gestational age foetus.\textsuperscript{4;8}

Dietary and lifestyle interventions in pregnancy significantly reduce gestational weight gain (GWG).\textsuperscript{19} Dietary interventions significantly reduce the risk of pregnancy complications such as PE, gestational diabetes mellitus (GDM), pregnancy-induced hypertension (PIH), and preterm delivery without adverse effects compared with other methods.\textsuperscript{19} The Institute of Medicine\textsuperscript{20} in the United States provides target weight gain recommendations in pregnancy for normal weight, overweight, and obese women, assuming association between GWG and pregnancy outcomes based on observational data.

However, there is limited evidence from randomised trials regarding the benefit obtained with reduction in GWG. Currently, the National Institute for Health and Clinical Excellence in United Kingdom\textsuperscript{21} do not recommend specific weight gain targets in pregnancy in the absence of robust data validated in interventional trials. In an attempt to provide these data from intervention studies, the authors undertook a meta-analysis to assess the impact of GWG on the incidence of complications both in women with and without weight management interventions.

Methods

Literature Search and Study Selection

The authors searched the following databases from inception to January 2012: PubMed, MEDLINE, the Excerpta Medica database (Embase), BIOSIS, LILACS, Science Citation Index (SCI), Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE), PsychInfo, and Health Technology Assessment Database (HTA). Relevant unpublished studies and those reported in the gray literature were searched in databases including Inside Conferences, Systems for Information in Gray Literature (SIGLE), Dissertation Abstracts, and ClinicalTrials.gov. Language restrictions were not applied. They included only randomised controlled trials that evaluated the effect of interventions on GWG and pregnancy outcomes. The search term combination captured the concept “pregnancy and weight,” incorporating MeSH, free text, and word variants.

Inclusion criteria were trials with pregnant women expecting one or multiple babies (i.e., twins or triplets), who were normal weight (body mass index (BMI) 18.5-24.9 kg/m\textsuperscript{2}), overweight (BMI 25-29.9 kg/m\textsuperscript{2}), or obese (BMI ≥30 kg/m\textsuperscript{2}). Studies assessing weight reducing drugs or
surgical interventions were not included in this meta-analysis. Also, studies exclusively on pregnant women who were underweight (BMI < 18.5 kg/m²) and women with contraindications to limit GWG were excluded. GWG was defined as weight before delivery (as stated by each individual trial in this meta-analysis) minus the weight measured at booking (measurement at inclusion or self-reported pre-pregnancy weight).

Outcomes
The primary outcomes were chosen based on a Delphi survey of experts conducted for the Health Technology Assessment by Thangaratinam et al. were GDM, PIH, and PE. The authors accepted the definitions used by the authors of the primary studies (in general; PIH was defined as blood pressure exceeding 140/90 mm Hg without the presence of proteinuria and diagnosed after 20 weeks of gestation; PE as PIH with presence of proteinuria). Secondary outcomes were admission to intensive care or high dependency unit, thromboembolism, and induction of labour.

Study Quality Assessment
Quality, defined as the extent to which an estimate of effect was likely to be correct or unbiased, was evaluated with accepted contemporary standards. Two independent reviewers (A.E.R. and S.T.) performed quality assessment in duplicate using predesigned and piloted forms. The authors attempted to obtain missing information by contacting investigators. The degree of publication bias was not possible to establish, nonetheless both large and small studies were identified, as well as negative and positive studies.

Data Extraction
Study characteristics and findings were extracted in duplicate by independent reviewers (A.E.R. and E.R.) using predesigned and piloted data extraction forms. Any disagreements were resolved by consensus and/or arbitration involving a third reviewer (S.T.). Missing information was obtained from investigators if it was crucial for subsequent analysis. To avoid any biased opinion, unpublished information was treated in the same fashion as published information.

Analysis
The authors analysed the effect of GWG on obstetric and foetal outcomes. For each study, they assessed the association between the mean GWG and the incidence of relevant outcomes. The association between GWG and maternal and neonatal outcomes were analysed using a random effect meta-regression. The regression coefficient, \( \beta \), obtained from a meta-regression analysis will describe how the outcome variable (the intervention effect, i.e., the pregnancy outcome) changes with a unit increase in the explanatory variable (the potential effect modifier, i.e., GWG). The statistical significance of the regression coefficient is a test to
check whether there is a linear relationship between intervention effect and the explanatory variable or not.

Also, subgroup analyses were performed for each type of lifestyle intervention (diet, physical activity, and mixed approach). Statistical analysis was performed using STATA version 11.2 (StataCorp LP, College Station, Texas).

**Results**

**Characteristics of the Included Studies**
The authors identified 44 RCTs eligible for inclusion in this meta-analysis out of 19,852 citations. Figure 1 shows a flow chart of the search. After detailed evaluation of these articles, the authors excluded 21 RCTs as no data on GWG were available from these articles, resulting in the inclusion of 23 articles (4,990 women) in this meta-analysis (Table 1). The trials compared the effect of diet and lifestyle interventions to standard care on GWG and pregnancy outcomes. One trial included all BMI groups, three trials included normal weight–obese subjects (BMI >19 kg/m²), seven trials included only overweight or obese women (BMI >25 kg/m²), and 12 trials did not report if they used any BMI restrictions. The ethnicity of participants was reported in 16 studies with 9 studies including ethnically diverse population and 5 studies included Caucasian women only and one African–American women only.

**Quality of the Included Trials**
Out of the 23 studies included in this analysis, 17 (74%) were adequately randomised, 5 (22%) did not state their method of randomisation, and 1 was unclear. Seven (30%) studies had adequate allocation concealment, 12 (52%) did not report the allocation concealment, and four (18%) were unclear. All studies stated the number of patients lost to follow-up, if any. All but two studies stated the reasons of losses to follow-up. One study stated the statistical analyses were performed according to intention to treat approach.

**Gestational Weight Gain and Pregnancy Outcomes**
An increase in GWG was associated with a statistical non-significant increase in the risk of PE, GDM, and induction of labour (Figures 2–4). The incidence of PE increased by 0.2% (percentage points) for each kilogram gained (95% CI 0.5 to 0.9%, p>0.05) and the incidence of GDM increased with 0.3% for each kilogram gained (95% CI 0.5 to 1.0%, p>0.05).

The incidence of PIH increased by 0.2% (95% CI 1.5 to 2.0%, p>0.05) for each kilogram gained. The chance of induction of labour increased by 1.5% for each kilogram gained (95% CI 0.9 to 3.9%, p>0.05) and the incidence of preterm birth increased by 0.1% for each kilogram gained (95% CI 0.3 to 0.6%, p>0.05).
Figure 1. Identification of literature on the effect of gestational weight gain on maternal and foetal outcomes
<table>
<thead>
<tr>
<th>Study</th>
<th>Type of intervention</th>
<th>Study characteristics</th>
<th>Outcomes</th>
<th>Number of patients (N. intervention/ control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baciuk et al. (2008)</td>
<td>Physical activity</td>
<td>Race n.a., no morbid obesity, age restrictions n.a., GA at inclusion &lt;20 wks, glucose status n.a., no known pre-existing health problems</td>
<td>preterm delivery, SC, vaginal delivery, birth weight, SGA</td>
<td>71 [34/37]</td>
</tr>
<tr>
<td>Barakat et al. (2009)</td>
<td>Physical activity</td>
<td>Caucasian, BMI restrictions n.a., age 25-35 yrs, GA at inclusion n.a. (total at least 26 wks intervention), glucose status n.a., no known pre-existing health problems</td>
<td>preterm delivery, birth weight, LGA, SGA, AS, macrosomia (&gt;4000g)</td>
<td>142 [72/70]</td>
</tr>
<tr>
<td>Barakat et al. (2011)</td>
<td>Physical activity</td>
<td>Spanish (white), BMI restrictions n.a., age 23-38 yrs, GA at inclusion 1st prenatal visit, glucose status n.a., no known pre-existing health problems</td>
<td>SC, vaginal delivery, birth weight, AS</td>
<td>80 [40/40]</td>
</tr>
<tr>
<td>Briley et al. (2002)</td>
<td>Diet</td>
<td>African American, BMI restrictions n.a., age restrictions n.a., GA at inclusion &lt;24 wks, nondiabetic, no known pre-existing health problems</td>
<td>preterm delivery, birth weight</td>
<td>20 [10/10]</td>
</tr>
<tr>
<td>Crowther et al. (2005)</td>
<td>Diet</td>
<td>Ethnically diverse, BMI restrictions n.a., age restrictions n.a., GA at inclusion 16-30 wks, GDM, no known pre-existing health problems [hypertension was no exclusion criterion]</td>
<td>PE, SC, IOL, PPH, birth weight, LGA, SGA, birth trauma, hyperbilirubinemia, hypoglycemia, admission to NICU, RDS, shoulder dystocia, intra-uterine death</td>
<td>1000 [490/510]</td>
</tr>
<tr>
<td>Guelinckx et al. (2010)</td>
<td>Mixed approach</td>
<td>Caucasian, obese (&gt;29 kg/m²), age restrictions n.a., GA at inclusion &lt;15 wks, nondiabetic, no known pre-existing health problems</td>
<td>PE, PIH, SC, IOL, birth weight, LGA</td>
<td>85 [42/43]</td>
</tr>
<tr>
<td>Hui et al. (2006)</td>
<td>Mixed approach</td>
<td>Ethnically diverse, BMI restrictions n.a., age restrictions n.a., GA at inclusion &lt;26 wks, nondiabetic, no known pre-existing health problems</td>
<td>GDM, birth weight, LGA</td>
<td>45 [24/21]</td>
</tr>
<tr>
<td>Hui et al. (2011)</td>
<td>Mixed approach</td>
<td>Race n.a., BMI restrictions n.a., age restrictions n.a., GA at inclusion 20-26 wks, nondiabetic, no known pre-existing health problems</td>
<td>SC, GDM, birth weight, LGA</td>
<td>190 [88/102]</td>
</tr>
<tr>
<td>Jeffries et al. (2009)</td>
<td>Mixed approach</td>
<td>Race n.a., BMI restrictions none, age &gt;18 - &lt;45 yrs, GA at inclusion &lt;14 wks, nondiabetic, other risk factors: n.a.</td>
<td>PE, GDM, PIH, preterm delivery, SC, birth weight, LGA, SGA, hypoglycemia, shoulder dystocia</td>
<td>236 [111/125]</td>
</tr>
<tr>
<td>Khaledan et al. (2010)</td>
<td>Physical activity</td>
<td>Race n.a., BMI restrictions n.a., age restrictions n.a., GA at inclusion 24-32 wks, no Diabetes Mellitus type 1 (DM1) with poor control, no known pre-existing health problems</td>
<td>SC, birth weight</td>
<td>39 [17/22]</td>
</tr>
<tr>
<td>Khoury et al. (2005)</td>
<td>Diet</td>
<td>Caucasian, BMI 19-32 kg/m², age 21-38 yrs, GA at inclusion 17-20 wks, nondiabetic, no known pre-existing health problems</td>
<td>PE, preterm delivery, birth weight, SGA, intra-uterine death</td>
<td>290 [141/149]</td>
</tr>
<tr>
<td>Landon et al. (2009)</td>
<td>Diet</td>
<td>Ethnically diverse, BMI restrictions n.a., age restrictions n.a., GA at inclusion 24-30 wks, mild gestational diabetes, no known pre-existing health problems</td>
<td>PE, preterm delivery, SC, vaginal delivery, IOL, birth weight, LGA, SGA, birth trauma, hyperbilirubinemia, hypoglycemia, admission to NICU, RDS, shoulder dystocia</td>
<td>958 [473/485]</td>
</tr>
<tr>
<td>Luoto et al. (2011)</td>
<td>Mixed approach</td>
<td>Race n.a., BMI &gt;17 kg/m², age &gt;18 yrs, GA at inclusion 8-12 wks, nondiabetic, no known pre-existing health problems</td>
<td>PE, GDM, birth weight, LGA, SGA</td>
<td>399 [180/219]</td>
</tr>
</tbody>
</table>

(Continued)
<table>
<thead>
<tr>
<th>Study</th>
<th>Type of intervention</th>
<th>Study characteristics</th>
<th>Outcomes</th>
<th>Number of patients (N, intervention/control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marquez et al. (2000)</td>
<td>Physical activity</td>
<td>Race n.a., BMI restrictions n.a., age restrictions n.a., GA at inclusion n.a. (total 15 wks intervention), glucose status n.a., other risk factors: n.a.</td>
<td>SC, birth weight, A5</td>
<td>15 (6/9)</td>
</tr>
<tr>
<td>Phelan et al. (2011)</td>
<td>Mixed approach</td>
<td>Ethnically diverse, BMI 19.8-26.0 kg/m², age &gt;18 wks, GA at inclusion 10-16 wks, glucose status n.a., no known pre-existing health problems</td>
<td>PE, GDM, PIH, preterm delivery, SC, birth weight, macrosomia, birth weight &lt;2500g</td>
<td>186 (94/92)</td>
</tr>
<tr>
<td>Phelan et al. (2011)</td>
<td>Mixed approach</td>
<td>Ethnically diverse, BMI &gt;26.0 kg/m², age &gt;18 wks, GA at inclusion 10-16 wks, glucose status n.a., no known pre-existing health problems</td>
<td>PE, GDM, PIH, preterm delivery, SC, birth weight, macrosomia, birth weight &lt;2500g</td>
<td>177 (90/87)</td>
</tr>
<tr>
<td>Polley et al. (2002)</td>
<td>Mixed approach</td>
<td>Ethnically diverse, BMI 19.8-26 kg/m², age &gt;18 yrs, GA at inclusion &lt;20 wks, non-diabetic, no known pre-existing health problems</td>
<td>PE, GDM, PIH, preterm delivery, SC, birth weight, LGA, SGA</td>
<td>61 (31/30)</td>
</tr>
<tr>
<td>Polley et al. (2002)</td>
<td>Mixed approach</td>
<td>Ethnically diverse, BMI &gt;26 kg/m², age &gt;18 yrs, GA at inclusion &lt;20 wks, non-diabetic, no known pre-existing health problems</td>
<td>PE, GDM, PIH, preterm delivery, SC, birth weight, LGA, SGA</td>
<td>49 (22/27)</td>
</tr>
<tr>
<td>Prevedel et al. (2003)</td>
<td>Physical activity</td>
<td>Race: n.a., BMI restrictions n.a., age restrictions n.a. (primiparous or adolescents), GA at inclusion 16-20 wks, glucose status n.a., no known pre-existing health problems</td>
<td>preterm delivery, birth weight, SGA</td>
<td>41 (19/22)</td>
</tr>
<tr>
<td>Quinlivan et al. (2011)</td>
<td>Diet</td>
<td>Ethnically diverse, BMI &gt;25.0 kg/m², age restrictions n.a., inclusion at first antenatal visit, glucose status n.a., other risk factors: n.a.</td>
<td>GDM, birth weight</td>
<td>124 (61/63)</td>
</tr>
<tr>
<td>Rae et al. (2000)</td>
<td>Diet</td>
<td>Ethnically diverse, &gt;110% of ideal body weight, age restrictions n.a., GA at inclusion ≤35 wks, BMI, other risk factors: n.a.</td>
<td>PE, vaginal delivery, IOL, birth weight, LGA, hypoglycemia, shoulder dystocia</td>
<td>124 (58/66)</td>
</tr>
<tr>
<td>Santos et al. (2005)</td>
<td>Physical activity</td>
<td>Race n.a., BMI 26-31 kg/m², age ≥20 yrs, GA at inclusion ≥20 wks, non-diabetic, other risk factors: n.a. (no hypertension)</td>
<td>preterm delivery, birth weight, SGA</td>
<td>72 (35/37)</td>
</tr>
<tr>
<td>Thornton et al. (2009)</td>
<td>Diet</td>
<td>Ethnically diverse, BMI &gt;30 kg/m², age restrictions n.a., GA at inclusion 12-28 wks, non-diabetic, no known pre-existing health problems</td>
<td>PE, GDM, PIH, preterm delivery, SC, IOL, PPH, birth weight, LGA</td>
<td>232 (116/116)</td>
</tr>
<tr>
<td>Vinter et al. (2011)</td>
<td>Mixed approach</td>
<td>Caucasian, BMI 30-45 kg/m², age 18-40 yrs, GA at inclusion 10-14 wks, non-diabetic, no known pre-existing health problems</td>
<td>PE, GDM, SC, LGA, admission to NICU</td>
<td>304 (154/150)</td>
</tr>
<tr>
<td>Wolff et al. (2008)</td>
<td>Diet</td>
<td>Caucasian, BMI ≥30 kg/m², age &gt;18 - &lt;45 yrs, GA at inclusion &lt;18 wks, non-diabetic, no known pre-existing health problems</td>
<td>PE, GDM, PIH, SC, birth weight</td>
<td>50 (27/23)</td>
</tr>
</tbody>
</table>

Abbreviations: AS= Apgar score, BMI= Body mass index, DM= Diabetes mellitus, GA= Gestational age, GDM= Gestational diabetes mellitus, GWG= Gestational weight gain, PPH= Postpartum haemorrhage, IOL= Induction of labour, LGA= Large for gestational age, NICU= Neonatal intensive care unit, n.a.= not available, NW= Normal weight, OB= Obese, OW= Overweight, PIH= Pregnancy induced hypertension, PE= Pre-eclampsia, RCT= Randomised controlled trial, RDS= Respiratory distress syndrome, SC= Caesarean section, SGA= Small for gestational age.
Figure 2. Incidence of pre-eclampsia versus gestational weight gain. Note: Circle size corresponds to the number of women included in each trial. $\beta =$ regression coefficient.

Figure 3. Incidence of gestational diabetes versus gestational weight gain. Note: Circle size corresponds to the number of women included in each trial. $\beta =$ regression coefficient.
Figure 4. Incidence of induction of labour versus gestational weight gain. Note: Circle size corresponds to the number of women included in each trial. $\beta =$ regression coefficient.

Effect of Intervention on the Association between Gestational Weight Gain and Pregnancy Outcomes

A total of 12 trials assessed the effect of the intervention on PE, with a total of 4,151 women. The risk of PE increased by 0.4% (95% CI 0.6 to 1.4%, $p>0.05$) for each kilogram gained in the intervention group compared with 0.2% (95% CI 1.5 to 1.2%, $p>0.05$) in the control group. Total 10 trials assessed the effect of the intervention on gestational diabetes, including 2,053 women. The risk of GDM increased by 0.2% (95% CI 1.0 to 1.4%, $p>0.05$) for each kilogram gained in the intervention group versus 0.3% (95% CI 1.4 to 2.1%, $p>0.05$) in the control group. Six trials reported on the effect of the intervention on PIH, with a total of 1,076 women. The risk for PIH increased by 0.4% (95% CI 2.8 to 3.6%, $p>0.05$) for each kilogram gained in the intervention group compared with 0.8% (95% CI 4.5 to 3.0%, $p>0.05$) in the control group. Total 11 trials assessed the effect of the intervention on preterm birth, with a total of 2,588 women. The risk for preterm birth increased by 0.2% (95% CI 0.5 to 0.9%, $p>0.05$) for each kilogram gained in the intervention group compared with 0.03% (95% CI 0.7 to 0.7%, $p>0.05$) in the control group.
Effect of Dietary Intervention on the Association between Gestational Weight Gain and Pregnancy Outcomes

A total of eight trials compared diet versus normal care, with a total of 2,768 women. Of these, six studies assessed the effect of PE, including 2,624 women. The risk for PE increased by 1.6% (95% CI 0.5 to 3.6%, p>0.05) for each kilogram gained in the treatment arm versus 0.04% (95% CI 3.1 to 3.2%, p>0.05) in the control arm (Figures 5A and 5B). Only three trials, with a total of 406 women, assessed the effect on GDM, therefore no subgroup analysis was performed. Two trials assessed the effect on PIH, with a total of 282 women, and again no subgroup analysis was performed. Four trials assessed the effect on preterm delivery, with a total of 1,474 women. The risk for preterm delivery decreased by 1.3% (95% CI 4.1 to 1.5%, p>0.05) for each kilogram gained in the treatment arm, compared with 0.6% (95% CI 5.4 to 4.3%, p>0.05) in the control arm.

Effect of an Intervention with Physical Activity on the Association between Gestational Weight Gain and Pregnancy Outcomes

Seven trials compared physical activity versus normal care, with a total of 446 women. Of these seven studies, none assessed the effect on PE, GDM, or PIH. Four assessed the effect on preterm delivery, with a total of 325 women. The risk of preterm birth in the group participating in physical activity increased by 0.2% (95% CI 2.5 to 2.9%, p>0.05) for each kilogram gained compared with 0.4% (95% CI 1.7 to 2.5%, p>0.05) in the control group.

Effect of an Intervention with Mixed Approach on the Association between Gestational Weight Gain and Pregnancy Outcomes

A total of eight trials compared a mixed approach (both diet and physical activity) versus normal care, with a total of 1,732 women. Of these eight trials, six assessed the effect on PE, including 1,417 women. The risk of PE in the arm receiving mixed care decreased by 0.4% (95% CI 2.7 to 2.0%, p>0.05) for each kilogram gained compared with 0.3% (95% CI 2.9 to 2.3%, p>0.05) in the control group. Seven trials assessed the effect on GDM, with a total of 1,628 women. The risk of GDM in the treatment arm increased by 0.3% (95% CI 1.8 to 2.5%, p>0.05) for each kilogram gained compared with 0.2% (95% CI 1.1 to 1.5%, p>0.05) in the control arm. Four trials assessed the effect on PIH, with a total of 779 women. The risk of PIH in the treatment arm decreased by 2.9% (95% CI 10.4 to 4.5%, p>0.05) for each kilogram gained compared with 0.9% in the control group (95% CI 5.9 to 4.1%, p>0.05). Three trials, with a total of 694 women, assessed the effect on preterm delivery. The risk of preterm delivery in the treatment arm increased by 1.3% (95% CI 1.8 to 4.4%, p>0.05) for each kilogram gained compared with 1.4% (95% CI 0.5 to 3.4%, p>0.05) in the control group.

Table 2 shows a summary of the results of the subanalyses.
Figure 5a. Incidence of pre-eclampsia versus gestational weight gain, intervention: diet. Note: Circle size corresponds to the number of women included in each trial. β = regression coefficient.

Figure 5b. Incidence of pre-eclampsia versus gestational weight gain, intervention: control. Note: Circle size corresponds to the number of women included in each trial. β = regression coefficient.
Table 2. Summary of the subanalyses: Associations between GWG and pregnancy outcomes according intervention and group allocation

<table>
<thead>
<tr>
<th>Type of intervention</th>
<th>Intervention group Regression coeff. % (95% CI)</th>
<th>Control group Regression coeff. % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-eclampsia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet</td>
<td>1.6 (-0.5 to 3.6)</td>
<td>0.04 (-3.1 to 3.2)</td>
</tr>
<tr>
<td>Physical activity</td>
<td>n.a.*</td>
<td>n.a.</td>
</tr>
<tr>
<td>Mixed</td>
<td>-0.4 (-2.7 to 2.0)</td>
<td>-0.3 (-2.9 to 2.3)</td>
</tr>
<tr>
<td>Any</td>
<td>0.4 (-0.6 to 1.4)</td>
<td>-0.2 (-1.5 to 1.2)</td>
</tr>
<tr>
<td>Gestational Diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td>Physical activity</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td>Mixed</td>
<td>0.3 (-1.8 to 2.5)</td>
<td>0.2 (-1.1 to 1.5)</td>
</tr>
<tr>
<td>Any</td>
<td>0.2 (-1.0 to 1.3)</td>
<td>0.4 (-1.4 to 2.1)</td>
</tr>
<tr>
<td>Preterm birth</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet</td>
<td>-1.3 (-4.1 to 1.5)</td>
<td>-0.6 (-5.4 to 4.3)</td>
</tr>
<tr>
<td>Physical activity</td>
<td>0.2 (-2.5 to 2.9)</td>
<td>0.4 (-1.7 to 2.5)</td>
</tr>
<tr>
<td>Mixed</td>
<td>1.3 (-1.8 to 4.4)</td>
<td>1.4 (-0.5 to 3.4)</td>
</tr>
<tr>
<td>Any</td>
<td>0.2 (-0.5 to 0.9)</td>
<td>-0.03 (-0.7 to 0.7)</td>
</tr>
</tbody>
</table>

* N.a.: not available.

Discussion

Summary of Findings
Following the meta-analysis of Thangaratinam et al., that assessed the effect of lifestyle interventions on pregnancy outcomes, the authors were interested in the causal role of GWG in this process. They found that within the intervention studies meta-analysed by Thangaratinam et al., increased GWG was associated with an increased risk of PE, GDM, and induction of labour, albeit that these results were not statistical significant.

When assessing the effect of diet in the PE subanalysis; there was a remarkable difference between the intervention and control groups, in favour of the intervention group, however this result had no statistical significance.

Strengths and Limitations
This systematic review was comprehensive in its scope and search. The review was conducted in line with contemporary recommendations and complied with the PRISMA (preferred reporting items for systematic reviews and meta-analyses) statement. The authors’ search of literature aimed to minimise the risk of selection and publication bias. Most of the published reviews on effects of dietary and lifestyle interventions...
on maternal and foetal outcomes were limited to specific groups of women or types of intervention. There was no formal prioritisation of the importance of the clinical outcomes, and few assessed the quality of the evidence for the important outcomes. They undertook rigorous quality assessment and formally prioritised the outcomes for clinical importance. Reliable data were identified on clinically important outcomes related to weight and pregnancy by the Delphi survey. They explored for sources of heterogeneity when required.

The authors note the data was based on aggregated average outcomes per study, thereby limiting the statistical precision of this meta-analysis.

There was heterogeneity within and between the studies due to the aggregated data. The averages for GWG and outcomes were used per included study, and the data reported did not allow for stratifications for BMI.

Different definitions for GWG were used, ranging from “weight measured at last clinical visit before delivery minus self-reported pre-pregnancy weight” to “weight measured at last clinical visit before delivery minus weight measured at inclusion of the trial.” These differences in definitions were accepted; however we realise this increases heterogeneity.

Also there was heterogeneity in population characteristics, definitions of outcome measures, interventions and duration of interventions, and diabetic status. Furthermore, it was not stated whether the weight of women with PE or GDM was measured before or after developing this complication, hence potentially GWG in these women is overestimated as weight could increase due to other factors such as oedema or polyhydramnios.

In the review of Thangaratinam et al. 2012 dietary interventions seemed effective in reducing the incidence of PE, PIH, and preterm birth. Therefore, one might have hypothesised that these effects were due to a reduction in GWG. However, in the present meta-analysis this effect of GWG on outcomes was not found. It could be that lifestyle interventions, such as a healthy diet, do not (or not only) lead to decreased weight gain per se, but change metabolism and overall health, resulting in better pregnancy outcomes. The same theory could be used for physical activity interventions, leading to a change in body composition (with more muscle and less fat), without reducing GWG as muscle tissue weighs more than fat. Active women may thus experience less pregnancy complications and benefit in the long term.

Another reason might be that differences in GWG achieved by these interventions are too small to produce a detectable effect on the outcomes, or those causal pathways other than GWG play a role between the interventions and outcomes.

**Recommendations for Future Research**

For future research an individual patient data (IPD) meta-analysis is recommended, as statistical resolution can be enhanced by using
individual instead of aggregated average data, and as more homogenous sub groups (e.g., allocated by BMI) and large sample size within these groups can be established. This approach should provide adequate power to generate valid, reliable answers and to populate the model for decision analytic modelling for health economic evaluation. Another recommendation would be to enhance standardisation and thereby homogeneity in definitions. Often, different definitions and end-point are used, complicating the comparison of trials through normal meta-analysis. The use of end-point definitions, standardising common definitions, defining variables, baseline characteristics, and end-point measurements, consistently will facilitate and enhance the quality of meta-analyses.

Another step forward would be to assess whether the improvement in clinical outcomes is related to reduction in GWG alone or if there is any added benefit from the type of intervention resulting in weight change. This will allow us to implement those weight management interventions that show clear benefit with specific weight gain targets in pregnancy.

The paucity of descriptive information on the intensity and duration of intervention, means of provision, and patient compliance are factors that could potentially facilitate or hinder implementation. These gaps identify issues for further research. There is a need for good quality large prospective studies for the important clinical outcomes identified including long-term effects on the mother and foetus.

**Conclusion**

Overall, increased GWG was associated with a non-significant increase in the incidence of PE, GDM, and induction of labour. Based on this meta-analysis it is not possible to establish whether GWG plays a role in the causal pathway on the incidence of pregnancy complications. To date, no evidence for such a relationship was found. Additional research is recommended, for example, by IPD meta-analysis, stratifying for GWG and outcomes, and also for (pre-pregnancy) BMI. More homogeneity in endpoint definitions and a larger sample size per pregnancy outcome might help in obtaining results to refine the implementation of daily clinical care guidelines.
References


