Effects of antenatal diet and physical activity on maternal and fetal outcomes: individual patient data meta-analysis and health economic evaluation

Ewelina Rogozińska,[1,2] Nadine Marlin,[3] Louise Jackson,[4] Girish Rayanagoudar,[1] Anneloes E Ruifrok,[5,6] Julie Dodds,[1] Emma Molyneaux,[7] Mireille NM van Poppel,[8,9] Lucilla Poston,[10] Christina A Vinter,[11] Fionnuala McAuliffe,[12] Jodie M Dodd,[13,14] Julie Owens,[13] Ruben Barakat,[15] Maria Perales,[15] Jose G Cecatti,[16] Fernanda Surita,[16] SeonAe Yeo,[17] Annick Bogaerts,[18,19] Roland Devlieger,[20] Helena Teede,[21] Cheryce Harrison,[21] Lene Haakstad,[22] Garry X Shen,[23] Alexis Shub,[24] Nermeen El Beltagy,[25] Narges Motahari,[26] Janette Khoury,[27] Serena Tonstad,[27] Riitta Luoto,[28] Tarja I Kinnunen,[29] Kym Guelfi,[30] Fabio Facchinetti,[31] Elisabetta Petrella,[31] Suzanne Phelan,[32] Tânia T Scudeller,[33] Kathrin Rauh,[34,35] Hans Hauner,[34] Kristina Renault,[11,36] Christianne JM de Groot,[6] Linda R Sagedal,[37] Ingvild Vistad,[37] Signe Nilssen Stafne,[38,39] Siv Mørkved,[38,39] Kjell Å Salvesen,[40,41] Dorte M Jensen,[42] Márcia Vitolo,[43] Arne Astrup,[44] Nina RW Geiker,[45] Sally Kerry,[3] Pelham Barton,[4] Tracy Roberts,[4] Richard D Riley,[46] Arri Coomarasamy,[47] Ben Willem Mol,[48] Khalid S Khan[1,2] and Shakila Thangaratinam,[1,2]* on behalf of the International Weight Management in Pregnancy (i-WIP) Collaborative Group

[1]Women's Health Research Unit, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK
[2]Multidisciplinary Evidence Synthesis Hub, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK
[3]Pragmatic Clinical Trials Unit, Blizard Institute, Barts and the London School of Medicine and Dentistry, London, UK
[4]Health Economics Unit, School of Health and Population Sciences, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK
[5]Department of Obstetrics and Gynecology, Academic Medical Centre, Amsterdam, the Netherlands
[6]Department of Obstetrics and Gynaecology, Faculty of Medicine, VU University Medical Center, Amsterdam, the Netherlands
[7]Section of Women's Mental Health, Health Service and Population Research Department, Institute of Psychiatry, King's College London, London, UK
[8]Department of Public and Occupational Health, EMGO Institute for Health and Care Research (EMGO+), VU University Medical Center, Amsterdam, the Netherlands
[9]Institute of Sport Science, University of Graz, Graz, Austria
[10]Division of Women's Health, Women's Health Academic Centre, King's College London, St Thomas' Hospital, London, UK
[11]Department of Obstetrics and Gynecology, Odense University Hospital, University of Southern Denmark, Odense, Denmark
[12]School of Medicine & Medical Science, UCD Institute of Food and Health, Dublin, Ireland
[13]The Robinson Research Institute, School of Medicine, Department of Obstetrics & Gynaecology, University of Adelaide, SA, Australia
[14]Women's and Children's Health Network, Women's and Babies Division, North Adelaide, SA, Australia
[15]Facultad de Ciencias de la Actividad Física y del Deporte, Universidad Politecnica de Madrid, Madrid, Spain
[16]Department of Obstetrics and Gynecology, School of Medical Sciences, University of Campinas, Campinas, Brazil
[17]School of Nursing, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
[18]Research Unit Healthy Living, University Colleges Leuven-Limburg, Leuven, Belgium
[19]Centre for Research and Innovation in Care, University of Antwerp, Antwerp, Belgium
[20]Division of Mother and Child, Department of Obstetrics and Gynaecology, University Colleges Leuven-Limburg, Hasselt and University Hospitals KU Leuven, Leuven, Belgium
[21]Monash Centre for Health Research and Implementation, School of Public Health, Monash University, Melbourne, VIC, Australia
[22]Norwegian School of Sport Sciences, Department of Sports Medicine, Oslo, Norway
[23]Department of Internal Medicine, University of Manitoba, Winnipeg, MB, Canada
[24]Department of Obstetrics and Gynaecology, University of Melbourne, Melbourne, VIC, Australia

[25]Department of Obstetrics and Gynecology, Alexandria University, Alexandria, Egypt
[26]Department of Sport Physiology, Faculty of Physical Education and Sport Sciences, Mazandaran University, Babolsar, Iran
[27]Department of Obstetrics and Gynecology, Oslo University Hospital, Oslo, Norway
[28]UKK Institute for Health Promotion Research, Tampere, Finland
[29]School of Health Sciences, University of Tampere, Tampere, Finland
[30]School of Sport Science, Exercise and Health, University of Western Australia, Perth, WA, Australia
[31]Mother-Infant Department, University of Modena and Reggio Emilia, Modena, Italy
[32]Kinesiology Department, California Polytechnic State University, San Luis Obispo, CA, USA
[33]Department of Management and Health Care, São Paulo Federal University, Santos, Brazil
[34]Else Kröner-Fresenius-Center for Nutritional Medicine, Technische Universität München, Munich, Germany
[35]Competence Centre for Nutrition, Freising, Germany
[36]Departments of Obstetrics and Gynecology, Hvidovre Hospital, University of Copenhagen, Copenhagen, Denmark
[37]Department of Obstetrics and Gynecology, Sorlandet Hospital Kristiansand, Kristiansand, Norway
[38]Department of Public Health and General Practice, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway
[39]Clinical Services, St Olavs Hospital, Trondheim University Hospital, Trondheim, Norway
[40]Department of Obstetrics and Gynaecology, Clinical Sciences, Lund University, Lund, Sweden
[41]Department of Laboratory Medicine Children's and Women's Health, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway
[42]Department of Endocrinology, Odense University Hospital, Odense, Denmark
[43]Department of Nutrition and the Graduate Program in Health Sciences, Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil
[44]Department of Nutrition, Exercise and Sports, University of Copenhagen, Copenhagen, Denmark
[45]Nutritional Research Unit, Copenhagen University Hospital Herlev, Copenhagen, Denmark
[46]Research Institute for Primary Care and Health Sciences, Keele University, Keele, UK
[47]School of Clinical and Experimental Medicine, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK
[48]The South Australian Health and Medical Research Institute, Adelaide, SA, Australia

*Corresponding author s.thangaratinam@qmul.ac.uk

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Scientific summary

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Scientific summary

Background

Obesity and excess weight gain in pregnancy are associated with adverse maternal and fetal outcomes. Maternal age, parity, ethnicity and underlying medical conditions influence the risk of complications. Diet and physical activities have the potential to reduce weight gain and alter pregnancy outcomes. Variation in the effect of these interventions across subgroups of women may have implications for clinical management and provision of care. The association of gestational weight gain (GWG) with complications in pregnancy needs evaluation using robust data.

Objectives

Primary

1. To assess if the effects of diet- and physical activity-based interventions on (1) GWG, (2) composite maternal outcomes and (3) composite fetal/neonatal outcomes vary in subgroups of women based on body mass index (BMI) at booking, age, parity, ethnicity and underlying medical conditions.

Secondary

1. To evaluate the association of GWG and adverse pregnancy outcomes in women and their infants.
2. To assess adherence to the Institute of Medicine (IOM)-recommended weight-gain targets in normal weight, overweight and obese pregnant women and rates of maternal and fetal complications.
3. To identify the predictors of GWG in pregnancy based on maternal characteristics such as parity, pre-pregnancy or early pregnancy BMI, ethnicity, smoking, diet, physical activity and socioeconomic status.
4. To evaluate the cost-effectiveness of interventions.
5. To undertake network meta-analysis to determine the rank order of interventions based on effectiveness.

Methods

We undertook individual participant data (IPD) meta-analysis by using a prospective protocol in line with existing recommendations, and complied with the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines for IPD meta-analysis in reporting our work. We searched MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Database of Abstracts of Reviews of Effects and Health Technology Assessment database, from October 2013 to March 2015, for relevant studies (to update a previous search). Randomised trials that assessed the effects of diet, physical activity or mixed-approach interventions on GWG, composite maternal and fetal/neonatal outcomes were included. The composite maternal outcome included gestational diabetes mellitus (GDM), pre-eclampsia (PE) or pregnancy-induced hypertension (PIH), preterm delivery and Caesarean section. The composite fetal outcomes included intrauterine death, small for gestational age, large for gestational age and admission to the neonatal intensive care unit (NICU). Researchers from the International Weight Management in Pregnancy Collaborative Network shared the primary data.

We obtained summary estimates of effects and 95% confidence intervals (CIs) for each intervention type and outcome, with a two-step IPD random-effects meta-analysis, for all women combined and for each

subgroup of interest. We synthesised the differences in effects between subgroups in a two-step IPD random-effects meta-analysis. In the first stage, we either fitted a linear regression adjusted for baseline (for continuous outcomes) or a logistic regression model (for binary outcomes) in each study separately; in the second stage, the pertinent effect estimates were then combined across studies using a random-effects meta-analysis model estimating via restricted maximum likelihood. We quantified the relationship between weight gain and pregnancy complications. A model-based economic evaluation was undertaken to assess the cost-effectiveness of the interventions.

Results

Of the 74 eligible studies (17,727 women), 36 (12,434 women) contributed data to the IPD meta-analysis: 33 (9320 women) evaluated GWG, 24 (8852 women) reported all four components of the composite maternal outcomes and 18 (7981 women) assessed all four components of the fetal/neonatal composite outcomes.

Effect of diet- and physical activity-based interventions on maternal and fetal outcomes

Diet- and physical activity-based interventions reduced GWG by an average of –0.70 kg [95% CI –0.92 to –0.48 kg, 95% prediction interval (PI) –1.24 to –0.16 kg; 33 studies, 9320 women] compared with the control group in the IPD meta-analysis. The odds of composite adverse maternal outcome were not significantly reduced by the interventions [summary odds ratio (OR) 0.90, 95% CI 0.79 to 1.03, 95% PI 0.68 to 1.20]. The interventions had no effect on fetal/neonatal outcomes (summary OR 0.94, 95% CI 0.83 to 1.08, 95% PI 0.74 to 1.21).

The IPD meta-analysis showed a significant reduction in rates of Caesarean section (OR 0.91, 95% CI 0.83 to 0.99; 32 studies contributing data, 11,410 women). The decreases in rates of other individual maternal outcomes [such as GDM (OR 0.89, 95% CI 0.72 to 1.10; 27 studies contributing data, 9427 women), PE or PIH (OR 0.95, 95% CI 0.78 to 1.16; 22 studies, 9618 women) and preterm birth (OR 0.94, 95% CI 0.78 to 1.13; 32 studies contributing data, 116,876 women)] were not significant.

Sensitivity analysis showed that the beneficial effect on weight gain persisted after adding non-IPD data (summary mean difference –1.13 kg, 95% CI –1.58 to –0.68 kg; 60 studies, 12,895 women). Meta-analysis of published aggregate data showed a significant reduction only in GDM (OR 0.78, 95% CI 0.64 to 0.95; 29 studies, 11,118 women) and Caesarean section (OR 0.90, 95% CI 0.82 to 0.99; 37 studies, 11,340 women) compared with the control group. There were no significant reductions in preterm birth (OR 0.80, 95% CI 0.63 to 1.01; 23 studies, 7480 women) and PE or PIH (OR 0.89, 95% CI 0.75 to 1.05; 20 studies, 9198 women). Both aggregate and IPD meta-analyses did not have an effect on fetal/neonatal outcomes.

Differential effect of interventions on gestational weight gain and pregnancy outcomes

The effect of interventions on GWG did not significantly vary with maternal BMI (–0.02 kg change in intervention effect per 1 kg/m^2 increase in BMI, 95% CI –0.08 to 0.04 kg), age (–0.03 kg change in intervention effect per 1-year increase in age, 95% CI –0.08 to 0.02 kg), parity (0.10 kg change in intervention effect for multiparity vs. nulliparity, 95% CI –0.39 to 0.60 kg), ethnicity (0.05 kg change in intervention effect for non-Caucasian vs. Caucasian, 95% CI –1.27 to 1.37 kg) or underlying medical conditions (1.51 kg change in intervention effect for women with at least one condition vs. none, 95% CI –2.01 to 5.02 kg).

We did not identify any significant change in treatment effect for composite maternal outcomes in subgroups based on maternal BMI (no change in effect for every 1 kg/m^2 increase in BMI, OR 1.00, 95% CI 0.98 to 1.02), age (1% increase in effect for every 1-year increase in age, OR 1.01, 95% CI 0.99 to 1.03), parity (3% increase in effect for multiparity vs. nulliparity, OR 1.03, 95% CI 0.75 to 1.39), ethnicity (7% decrease in effect for non-Caucasian vs. Caucasian, OR 0.93, 95% CI 0.63 to 1.37) or underlying

medical conditions (44% increase in effect for women with at least one condition vs. none, OR 1.44, 95% CI 0.15 to 13.74). For composite fetal/neonatal outcome we observed a 2% lowered effect (OR 0.98, 95% CI 0.95 to 1.00) for every 1 kg/m^2 increase in booking BMI, which was of borderline significance. There was no significant treatment–covariate interaction for other factors and composite fetal/neonatal outcome. There was significant evidence of small-study effects for GWG (Egger's test, $p = 0.038$) and the composite maternal outcome (Peter's test, $p = 0.036$), but not for fetal/neonatal composite outcome ($p = 0.398$).

Gestational weight gain and pregnancy outcomes

We did not identify an association between GWG, booking BMI and risk of maternal (summary OR 1.03, 95% CI 0.93 to 1.15) or fetal/neonatal complications (summary OR 1.02, 95% CI 0.91 to 1.15). Adherence to IOM criteria for GWG did not significantly reduce GWG. Increase in maternal age (–0.1 kg, 95% CI –0.14 to –0.06 kg) and multiparity (–0.73 kg, 95% CI –1.24 to –0.23 kg) were significantly associated with GWG.

We refrained from undertaking network meta-analysis, as there were no differences in estimates of effect for GWG between diet-based, physical activity-based and mixed-approach interventions.

Cost-effectiveness of the intervention

Diet- and physical activity-based interventions in pregnancy are not cost-effective compared with usual care. Although the primary base-case analysis indicated a small reduction in pregnancy-related complications, the probabilistic sensitivity analysis showed no evidence of significant difference between the intervention and the control arms for either cost or clinical effectiveness. Similarly, the results of the secondary analysis for obese, overweight and normal weight women found no evidence that diet- and physical activity-based interventions are more cost-effective than usual care for any of the subgroups.

Conclusions

Interventions based on diet and physical activity in pregnancy reduce GWG, and the effect does not vary by maternal BMI, age, parity, ethnicity or underlying medical conditions. The interventions do not confer any additional benefit for composite maternal and fetal outcomes and are not cost-effective. There is no evidence to support routine use of IOM targets for GWG.

Recommendations for further research

The impact of lifestyle interventions in pregnancy on long-term outcomes (such as postpartum weight retention, future risk of diabetes and hypertension, subsequent pregnancy outcomes and childhood obesity) needs evaluation. Randomised trials are required to evaluate the effect of interventions to optimise the pre-pregnancy health of the mother.

Study registration

This study is registered as PROSPERO CRD42013003804.

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