

12th June 2017

Dr Fiona Godlee
Editor-in-Chief
The BMJ

Re: Effects of diet and physical activity based interventions in pregnancy on gestational weight gain and pregnancy outcomes: Individual patient data (IPD) meta-analysis of randomised trials

Dear Dr Godlee,

Thank you for considering our manuscript for publication in the BMJ. We have taken into account the suggestions of the peer reviewer, made the required revisions and uploaded amended manuscript (Revised_manuscript_SP_Jun17). We are in the process of collecting ICMJE disclosure forms and anticipate to have all until the end of the week.

In the table below we have enclosed our response to the editors and the referees' comments. We have uploaded the revised manuscript. Please do not hesitate to contact for any queries.

Yours sincerely

Prof Shakila Thangaratinam on behalf of the authors
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Comments

Reviewer: 1

Recommendation:

Comments:

The study addresses an important policy question on whether diet and /or physical activity (PA) - related interventions in pregnancy influence gestational weight gain and pregnancy outcomes. This large meta-analysis pools data from several countries using IPD data (36 trials) and study level data (67 trials). Overall effects are analysed and for IPD and non-IPD data separately overall and for pre-selected subgroups. 45 trials have been published since the work was carried out. The authors found a small (0.7kg) but the clinically important reduction in gestational weight gain in the intervention groups overall and across all the subgroups examined. Overall the paper is well laid

Response

We thank the reviewer for the comment.

out, and well structured.

Comments

Although the paper is entitled diet and physical activity, there is a much greater number of PA trials (IPD 15, total 52), than primarily diet-related trials (IPD 4 total 16).

Introduction:

Because of the potential effect of smoking on gestational weight, in my view this should be one of the subgroups examined and its influence reported.

Methods:

Design, data synthesis and quality control overall are satisfactory and appropriate.

Results

Sample sizes for some of the subgroups are small. The lack of effect of dietary interventions on gestational diabetes needs discussion. Only four studies (490 participants) are included here, hence the lack of effect may be due to small sample size.

Regarding ethnicity, the proportion of non-Caucasian, (<650), to Caucasians is very small, hence it is more difficult to show difference. Again this needs further elaboration.

Discussion

Implications for clinical practice p29.

“Healthcare professionals should avoid variations in care and lifestyle advice provided to mothers based on ethnicity, age and underlying medical conditions since no differential effects were found”

This sentence should be removed /reworded as this conclusion is not justified cf. comments under Results above. Advice and care will always need to be tailored according to the presence of an underlying medical condition, ethnicity and age.

Box p33

The last sentence is incomplete.

Table 1- Format numbers need to be aligned to the right.

Summary

The study is an important contribution to the literature in this area and with these amendments is worthy of publication.

Items to include with your revision

1. What this paper adds/what is already known box

Response

We agree with this observation. The mixed interventions are comprised of dietary and physical activity components, and hence we consider our title to be relevant.

We were limited by the variations in definitions and reporting of smoking status in pregnancy and hence refrained from examining the effect.

We thank the reviewer for the comment.

We agree with this. We have now added in the discussion that ‘The relatively small numbers of women in the diet only intervention may have contributed to the imprecision in estimates’. (page 28, lines 14 – 15)

We have acknowledged this limitation in the Discussion section as follows ‘Our findings were limited by the smaller number of non-caucasians compared to Caucasian mothers.’ (page 26, lines 14 – 15)

Our interpretation was based on the findings that no subgroup effects were observed for either gestational weight gain, or composite maternal and fetal outcomes irrespective of maternal BMI, age, parity, ethnicity or underlying medical conditions. Given these findings, we refrained from making recommendations for variation in care.

We have now corrected this sentence as:

“Interventions significantly lower the odds of caesarean section, and have no effect on offspring outcomes.”

The alignment of Table 1 has been corrected.

We thank the reviewer for this comment.

The Box is already present on the manuscript

Comments

2. Name of the ethics committee or IRB, ID# of the approval, and a statement that participants gave informed consent before taking part. If ethics committee approval was not required, please state so clearly and explain the reasons why

4. Competing interests statement

5. Contributorship statement + guarantor

7. Copyright statement/licence for publication

8. Data sharing statement (see <http://www.bmj.com/about-bmj/resources-authors/article-types/research>)

9. Funding statement and statement of the independence of researchers from funders (see <http://resources.bmj.com/bmj/authors/article-submission/article-requirements>).

10. Patient involvement statement (see <http://www.bmj.com/about-bmj/resources-authors/article-types/research>)

11. Please ensure the paper complies with The BMJ's style, as detailed below:

Response

The statement is already present on the manuscript

The statement has been amended as follows:

"Competing interests: Mixed

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/doi_disclosure.pdf and declare: no support from any

organisation for the submitted work; HH reports grants from the German Ministry of Education and Research, the Bavarian Ministry of Agriculture and Nutrition, the Bavarian Ministry of Health, the Helmholtz Center Munich, the Else Kröner-Fresenius Foundation, AOK Bavaria, Amway and the German Research Foundation outside the submitted work. BBWM reports other from ObsEva during the conduct of the study."

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non-exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd to permit this article (if accepted) to be published in BMJ editions and any other BMJPG products and sublicences such use and exploit all subsidiary rights, as set out in our licence. The statement has been added to the manuscript. Following statement has been added to the manuscript:

"Data sharing

Full dataset or its subset and technical appendix are available at from the data custodian (Queen Mary University of London) at smd-iwipdata@qmul.ac.uk. The access is regulated by terms and conditions available at request at the same email address. The presented data are anonymised, and risk of identification is low."

The statement has been added to the manuscript

The statement already present on the manuscript

- a. Title: this should include the study design eg "systematic review and meta-analysis."
- b. Abstract: Please include a structured abstract with key summary statistics, as explained below.
- c. Introduction: This should cover no more than three paragraphs, focusing on the research question and your reasons for asking it now.
- d. Methods: For an intervention study the manuscript should include enough information about the intervention(s) and comparator(s) (even if this was usual care) for reviewers and readers to understand fully what happened in the study. To enable readers to replicate your work or implement the interventions in their own practice please also provide (uploaded as one or more supplemental files, including video and audio files where appropriate) any relevant detailed descriptions and materials. Alternatively, please provide in the manuscript urls to openly accessible websites where these materials can be found.
- e. Results: Please report statistical aspects of the study in line with the Statistical Analyses and Methods in the Published Literature (SAMPL) guidelines <http://www.equator-network.org/reporting-guidelines/sampl/>. Please include in the results section of your structured abstract (and, of course, in the article's results section) the following terms, as appropriate:
- v. For a systematic review and/or meta-analysis: Point estimates and confidence intervals for the main results; one or more references for the statistical package(s) used to analyse the data, eg RevMan for a systematic review. There is no need to provide a formal reference for a very widely used package that will be very familiar to general readers eg STATA, but please say in the text which version you used. For articles that include explicit statements of the quality of evidence and strength of recommendations, we prefer reporting using the GRADE system.
- f. Discussion: To minimise the risk of careful explanation giving way to polemic, please write the discussion section of your paper in a structured way. Please follow this structure: i) statement of principal findings of the study; ii) strengths and weaknesses of the study; iii) strengths and weaknesses in relation to other studies, discussing important differences in results; iv) what your study adds (whenever possible please discuss your study in the light of relevant systematic reviews and meta-analyses); v) meaning of the study, including possible

The manuscript complies with these requirements.

explanations and implications for clinicians and policymakers and other researchers; vi) how your study could promote better decisions; vi) unanswered questions and future research