

BMJ -
Decision on
Manuscript
ID
BMJ.2016.0
36114

Body: 06-Mar-2017

Dear Miss Rogozińska

Manuscript ID BMJ.2016.036114 entitled "Effects of lifestyle interventions in pregnancy on maternal and offspring outcomes: Individual participant data (IPD) meta-analysis of randomised trials"

Thank you for sending us your paper, and for being so patient and understanding during the unusually lengthy peer review process. We sent your paper for external peer review and discussed it at our manuscript committee meeting. We recognise its potential importance and relevance to general medical readers, but I am afraid that we have not yet been able to reach a final decision on it because several important aspects of the work still need clarifying.

We hope very much that you will be willing and able to revise your paper as explained below in the report from the manuscript meeting, so that we will be in a better position to understand your study and decide whether the BMJ is the right journal for it. We are looking forward to reading the revised version and, we hope, reaching a decision.

Kristina Fišter
kfister@bmj.com

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****Report from The BMJ's manuscript committee meeting****

These comments are an attempt to summarise the discussions at the manuscript meeting. They are not an exact transcript.

Members of the committee were: Wim Weber (chair), Rafael Perera (statistician), John Fletcher, Georg Roeggla, Jose Merino, Daoxin Yin, Amy Price, Tiago Villanueva, Sophie Cook, Kristina Fišter.

Decision: Put points

Detailed comments from the meeting:

First, please revise your paper to respond to all of the comments by the reviewers. Their reports are available at the end of this letter, below.

Please also respond to these additional comments by the committee:

- * The title should make it clearer that the paper is mostly looking at diet and activity interventions aimed at reducing weight in pregnant women.

- * As presented, the paper is not going to be of much help to clinicians who see obese pregnant women. Can you improve on this?

- * Can you be more specific about interventions and maybe decouple the composite outcomes so actions can be seen on an IPD level? There seems little point in using individual data if it is going to be lumped into composites, although we do appreciate the rationale behind this decision as well as the process used to agree on the composition of the outcomes.

- * We would like to see the contributions of the authors listed. All authors should have read the paper with track changes prior to submission to comply with COPE.

- * The major reason given for carrying out this IPD is to test if the effect seen varied by subgroups. The paper states that it did not, but the analysis and the presentation of these is not entirely transparent.

- * As one of the main objectives of this IPD was to assess the effects of the intervention in different subgroups, this analysis should be highlighted in the Methods section and

expanded slightly.

Currently it is only described in the last sentence of the second paragraph of the Data Analysis section: "To assess potential intervention effect modifiers, we extended the aforementioned models to include interaction terms between participant-level covariates and the intervention (i.e. treatment-covariate interaction terms)."

* Consider placing in a different paragraph as well as expanding how this was reported/presented in the Results section. This paragraph could also include a description of how the categories/subgroups were selected.

* The use of composite outcomes could be problematic if one of the multiple ones included dominates (i.e. is more prevalent). Can you tell us more about this?

* The search is about a year old now. We'll leave it to you to decide how to handle that, and recognise that we have partly contributed to this.

* In case the paper has been to another journal before coming to us, we would encourage you in line with the ICMJE recommendations to share the correspondence and any reviewer reports with us, in order to share expertise and improve the overall peer review process.

In your response please provide, point by point, your replies to the comments made by the reviewers and the editors, explaining how you have dealt with them in the paper.

Comments from Reviewers

Reviewer: 1

Recommendation:

Comments:

The work is a follow on piece to a seminal meta-analysis by these authors of studies on the effects of diet and /or PA interventions on gestational weight gain and maternal and offspring outcomes. The current meta-analysis uses individual level data to determine if differences in outcomes examined existed for subgroups of women in particular.

This is an important contribution to the literature with potential to be incorporated into WHO guidelines. There are important in ante-natal intervention to prevent gestational diabetes. The findings around reductions in caesarian section are also important. The work has broad applicability and is suitable for publication in BMJ. The authors make a number of recommendations around future research particularly around need for longer term outcome assessment.

The design is appropriate and the overall sample size sufficient to answer the research question posed. Combining IDP and non-IDP enhances this particularly with regard to the findings around gestational diabetes. The composite outcomes were determined by a two-round Delphi survey previously published.

Participants are adequately described. The inclusion and exclusion criteria for the interventions need to be more detailed. Do "lifestyle" interventions include stress management interventions if these are part of a multi-component intervention addressing diet+/PA/Sedentary Behaviour?

There needs to be consistency in intervention definition which is variously described for example as
"diet and PA based interventions" – p 12 Line 20
"lifestyle interventions" p 12 Line 42
"interventions based on diet and/ PA – p, 13 Line 42 –which presumably is the correct version
"diet and lifestyle based interventions" p29, L 12
"lifestyle interventions" p29, L 23.

Methods These are mainly adequately described. The study is reported in line with recommended guidelines. Main outcome measures: difference in gestational weight gain and differences in composite maternal and composite infant outcomes. Secondary outcomes are individual maternal and offspring complications.

The composite outcomes were determined by a two-round Delphi survey previously published. Is pre-term birth more likely an infant outcome? A definition of pre-term delivery needs to be given as all other variables are defined.

Results are presented principally in tables. In general these are clear and easy to follow. Table 1: 95% CI would be best

presented using brackets.

Discussion. This seems rushed and could be elaborated more fully especially in the light of previous literature. The conclusion needs to be rewritten to be more specific in terms of its importance and implications for ante-natal care. What this study adds needs to be revised (see below)

P24 L10. Suggest replacing "with a much stronger evidence for....." by "with a statistically significant reduction in gestational diabetes".

P26 Lines 7-12. " The impact of.....is not known.

P26 Lines 16-18. This sentence needs to be reworded as the authors did not examine the effects of the individual intervention components.

P27 Line 27. The word diabetes needs to be added after gestational

P27 Line 36: Whether magnitude of benefit.....varies.....needs.....

P27 Line 41: insert "in those countries" after particularly

P27 Line 50: "needs assessment" suggest replacing with "needs to be assessed"

Referencing- content is up to date and relevant but needs to be fully revised to be consistent in style and formatting e.g References 1,2,12, 16, 21, 38 etc

Abstract: Primary and secondary outcomes need to be stated.

Other

There are a number of additional grammatical and / typographical errors:

P14 L 57

P15 L47 Delete the word "the"

Use comma for thousands e.g p22 Lines 48 and 50,: 3,719; 11,666 and in tables to improve readability.

Recommendation: the paper is an important piece of collaborative work which would benefit from careful proof reading and with attention to the above.

Catherine Hayes. MD, MPH, FFPHMI, MRCP, D. Obst, DCh, Dip. Med. Mgt.

Additional Questions:

Please enter your name: Catherine Hayes

Job Title: Associate Professor in Public Health

Institution: Trinity College Dublin

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No

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If you have any competing interests (please see BMJ policy) please declare them here:

Reviewer: 2

Recommendation:

Comments:

Effects of lifestyle interventions in pregnancy on maternal and offspring outcomes: Individual participant data (IPD) meta-analysis of randomised trials

The primary outcomes were gestational weight gain, composite maternal and composite offspring outcomes. The secondary outcomes were individual maternal and offspring complications. It is a well written paper and the statistics

seem to be adequate

The maternal composite outcome included gestational diabetes mellitus (GDM), hypertensive diseases in pregnancy, preterm delivery and caesarean section.

The offspring composite outcome included stillbirth, small-for-gestational age (SGA), large-for-gestational age (LGA) fetus, and admission of the offspring to the neonatal intensive care unit (NICU).

I believe that the use of composite outcomes is a necessity to gain knowledge of rare adverse events. The strength of using a composite outcome is that real outcomes might be included and not only proxies. Unfortunately, I do not gain access to the Delphi analysis done to identify the composite outcomes. The outcome of this is, however, also the major shortcoming of this study.

1/ As a clinician, an advisor for the patient, most important maternal outcomes to avoid by lifestyle advice should include shoulder dystocia, venous thromboembolic events, anal sphincter tears, hypertension and GDM.

2/ In the newborn composite outcome the authors included both SGA and LGA. When doing a lifestyle intervention with diet and exercise the major effect will be to lower fetal/newborn weight. We know that with lower maternal weight gain, there will be lower newborn weight. By including both SGA and LGA in their composite outcome, the authors restrict the possibility to show this important effect.

3/ A more relevant and more powerful analysis to show this difference would be to compare difference in expected weight/ birthweight either in grams (as the maternal analysis) or by newborn weight deviation (birthweight minus expected weight/birth weight

4/ SGA is usually used as a proxy for fetal growth restriction. In this paper lifestyle intervention aim to lower the maternal and fetal increase in weight to lower adverse outcome. In a study like this, SGA should not be an adverse outcome.

5/ Further, for me it seem adequate to correct SGA and LGA for gestational age at delivery against a standard/reference. However, to adjust for maternal BMI and parity is partly taking away the differences you aim for.

6/ In Lifestyle advice involving exercise, maternal weight/BMI is not a good outcome variable due to redistribution of fat and muscle tissue. I would expect the

newborn weight differences to be more pronounced and to be the main single newborn outcome variable.

The authors state this in the end. "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."

Minor

After defining Individual Participant Data by IPD this should be used in the paper

It is not easy to understand the reason for non-IPD studies. This should be written more transparent

The authors had not been clear with why they used 20 years as age-categorization.

The is used without explanation and it seem to be a post-hoc definition

The paper may have a more informative headline
Statistics seem adequate, but I would recommend that someone used to IPD analysis to review it

Conclusion: It is a good paper that adds to our knowledge and will be a reference. However, I believe that the study will underestimate the true differences. An analysis of differences in newborn weight /gestational weight by a growth standard would add even more.

Additional Questions:

Please enter your name: Pelle G Lindqvist

Job Title: Associate professor/Senior consultant

Institution: Clintec, Karolinska Institutet

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

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