Variations in long-term outcome reporting among offspring followed up after lifestyle interventions in pregnancy: a systematic review.

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Abstract

Background: Mother and their offspring may benefit from lifestyle interventions during pregnancy. We systematically reviewed the literature to map and evaluate the quality of long-term offspring outcomes in follow-up cohorts of randomised controlled trials (RCTs).

Methods: We searched MEDLINE, EMBASE, CINAHL, Database of Abstracts of Reviews of Effects, and Cochrane Central (until March 2019) for all RCTs evaluating any lifestyle (diet or exercise) intervention during pregnancy and their follow-up cohorts. Two reviews evaluated the extracted outcomes using two standardised assessment tools, one for quality of reporting (score range 0-6) and another for the variation in outcome selection. We extracted data in duplicate and reported using natural frequencies, medians, ranges, means and standard deviation (SD).

Results: We captured 30 long-term offspring outcomes reported in six articles (four studies). Offspring anthropometric measurements were the most commonly reported outcomes. There was a large variation in the measurement tools used. The mean overall quality score for outcome reporting was 3.33 (SD 1.24), with poor reporting of secondary outcomes and limited justification for the choice of the reported outcomes. Most studies showed selective reporting for both their primary and secondary outcomes.

Conclusion: The quality of reporting for long-term offspring outcomes following lifestyle interventions in pregnancy is varied with evidence of selective outcome reporting. Developing a core outcome set will help to reduce the variations in outcome reporting to optimise future research.

Keywords: lifestyle, follow-up cohorts, offspring, outcomes, core, variation, reporting bias**.**

Introduction

Mothers entering pregnancy as obese or overweight are at increased risk of adverse maternal and offspring health outcomes[1]. Progressive maternal obesity is a recognised public health issue and many health regulators are promoting healthy lifestyle (dietary and exercise interventions) in pregnancy as primary prevention to optimise maternal and offspring health[2,3]. Lifestyle interventions appear to improve short-term maternal and offspring outcomes[4], but their effect on long-term outcomes remains imprecise[5,6].

Variations in outcomes reporting is a well-recognised problem that hinders evidence synthesis and increases research wastage[7]. Producing standardised core outcome sets involving all relevant stakeholders is proposed as a solution[8]. We aimed to map up the reported long-term offspring outcomes in follow-up studies of randomised controlled trials (RCT) of lifestyle interventions in pregnancy and evaluated their quality.

Methods

We performed a systematic review using a prospective protocol (PROSPERO CRD42018112791) and reported with findings as per PRISMA guidelines[9].

Literature search and study identification

We updated the search of major electronic databases (MEDLINE, EMBASE, CINAHL, Database of Abstracts of Reviews of Effects, and Cochrane Central) from our previously published systematic review on randomised trials evaluating lifestyle interventions in pregnancy[4] till March 2019 and amended it to capture their follow-up studies reporting on offspring outcomes following exposure to a lifestyle dietary intervention in utero alone or in combination with physical activity compared to routine care or minimal intervention. We performed complementary searches in Google Scholar

and Scopus, and contacted researchers in this discipline to identify relevant ongoing trials. We did not apply any search filters or language restrictions. Appendix 1 provides details of the search strategy. We excluded studies that included only women with gestational diabetes at baseline, involved animals, or reported on non-clinical outcomes.

Study inclusion and data extraction

Two researchers (ROR and CAP) selected studies independently in a two-stage process. First, we screened titles and abstracts to identify potentially relevant citations, we then screened the full articles of relevant citations against our inclusion criteria. Any discrepancies were resolved by discussion with two other reviewers (ER and BHA).

We extracted data in duplicate on the following variables: names of authors, year of publication, acronym of RCTs, journal of publication, country of study conduct, type of interventions evaluated, sample size in the randomised trial and in the follow-up study, population characteristics, duration of offpsring follow-up, outcomes reported, rational for outcome selection, employed measurement tools and reporting units.

Quality of outcomes reporting and risk of selective reporting

We used a standardised tool to assess the quality of outcomes reporting in the included studies in six items[10]. We awarded one point for each of the following: if the primary outcome was stated; if it was clearly defined; if the authors planned to report on any secondary outcomes prospectively; if the secondary outcomes were clearly defined; if the choice of the reported outcomes was justified; and if any methods were used to enhance the quality of outcomes measurement such as the repeating measures or training in the use of measurement tools. A maximum score of 6 could be awarded for a study. We considered a score above 4 to be of high quality, 2–4 as moderate quality, and less than 2 as low quality.

We constructed a matrix of reported outcome using the Outcome Reporting Bias in Trials tool (ORBIT) matrix generator (http://ctrc.liv.ac.uk/ORBIT/) listing the reported outcome domains per each study[11,12]. The ORBIT tool helps to identify missing outcomes data and assess the variation in outcome selection. For each outcome domain, full, partial, and no reporting were distinguished from the information provided in the included studies.

Statistical methods

We reported using natural frequencies, medians, ranges, means, and standard deviation (SD) where appropriate. We captured the rates of reporting among included studies for each individual outcome and its respective domain. We did not assess publication bias, due to the small number of studies included. Statistical analysis was conducted using Stata v.14 (Stata Corp, 2015).

Results

Characteristics of included studies

The search strategy identified 58 randomised trials of lifestyle interventions in pregnancy, of which 41 studies (70.7%) reported on neonatal outcomes. Of these, only six randomised trials (6/41, 14.6%) planned to follow-up their cohorts prospectively[13-18] and four (4/41, 9.7%) published their findings in six articles[19-28] (Figure 1).

The median sample size of included randomised trials was 540 participants (range 250−1555) and for the follow-up offspring cohorts was 218.5 participants (range 157−1512). The intervention was diet-based in one trial[20] and a mixed intervention (diet and physical activity) approach in three[19,21,22]. Clinical trials were conducted in Denmark,

Ireland, Germany and UK with a follow-up period ranging from 6 to 32 months after delivery (Table 1).

Reported outcomes in follow-up cohorts

In total, 30 offspring outcomes were reported in three outcome domains: anthropometric, biochemical and developmental with a median of 10 per study (range 1-19) (Table 2). The most commonly reported primary outcome were birth weight and infant BMI each reported in three out of four studies (75%). All included studies reported on anthropometric outcomes but there were large variations in reporting individual outcomes (Tables 2,3). Infant height, triceps skinfold thickness, subscapular skinfold thickness and abdominal circumference were the most reported secondary outcomes in this domain (3/4, 75%). Only one study reported on biochemical[25] and developmental outcomes[23]. There was a large variation in the measurement tools used to report on various outcomes specifically using plain units (Kg and Cm) and Z-scores (Table 2).

Quality of outcomes reporting

The primary outcome was clearly stated and defined in all included articles reporting on 4 studies (6/6, 100%). Only two articles stated secondary outcomes prospectively (33%) and one provided clear definition for those outcomes (17%). Justification for the use of reported outcome were also provided in one article (17%) and four articles reported on methods used to enhance the quality of outcomes measurement (67%). The mean overall quality score for outcomes reporting in included studies was 3.33 (SD 1.24) (Figure 2).

Our outcome reporting matrix depicts variation in outcome selection with potential reporting bias for both primary and secondary outcomes (Table 3). Only two

studies reported on both birth weight and BMI at follow-up as primary outcomes[26, 28]. Articles on the findings of the Lipo study reported various outcomes of interest across three publications[23-25].

Discussion

In this review we mapped up the reported long-term offspring outcomes in following randomised trials on lifestyle intervention in pregnancy. The quality of outcomes reporting was varied, with a high risk of selective outcome reporting. We notice a trend of reporting various offspring outcomes across different articles of the same planned study with inconsistent use of outcome measurement tools such as reporting anthropometric measurements using metric units or z-scores. This variation increases uncertainty and hinders meaningful evidence synthesis.

Strengths and limitations

We conducted our review using a prospectively registered protocol and updated our previously published systematic search strategy[4]. We captured all the reported outcomes and assessed their quality using established tools[10, 29,30] in duplicate. We reviewed each trial prospectively registered protocol to capture any omitted outcomes suggestive of selective reporting and constructed an outcome reporting matrix following on current recommendation[11-12]. The main weakness of our review is the limited number of included studies all having a limited follow up period (ranging from 6 to 32 months postnatal), still, we captured a relatively high number of reported offspring outcomes. Future studies with longer follow up time might focus its reporting on additional outcomes of interest[13-18].

Implications for future research

Effective and feasible public health interventions are needed to optimise maternal and offspring health outcomes facing the current obesity epidemic. Lifestyle interventions seem to offer some benefits on the short-term[4,17,31,32] but the long-term benefits remain imprecise. There is an apparent need for more follow-up studies of randomised cohorts to aid meaningful evidence synthesis. In such process, inaccurate and selective outcomes reporting is undesirable.

The choice of primary and secondary outcomes should be clearly defined and justified prospectively, a practice we seldom observed in our review. Evaluating the clinical significance and feasibility of the employed outcome measurement tools in this field is also warranted. Future research efforts should be planned in consensus among all stakeholders in this field (obstetricians, paediatricians, public health specialists, dieticians and patient representative groups) to draw up a clear roadmap for efficient evidence synthesis and impactful research.

We advocate the production of a specific core outcome set[6,33,34] for lifestyle interventions in pregnancy taking into consideration all relevant short and long-term maternal and offspring outcomes. Furthermore, there is a need to optimise and standardise the applied measurement tools to avoid meaningless reporting on important outcomes[35]. Developing such set in consensus among all relevant stakeholders (e.g. obstetricians, neonatologists, paediatricians, dieticians, mothers and lay consumers) will help to highlight the key outcomes of focus for future studies and the recommended measurement tools to aid future evidence synthesis.

Conclusion

The quality of reporting for long-term offspring outcomes following lifestyle interventions in pregnancy is varied with evidence of selective outcome reporting. Developing a core outcome set will help to reduce the variations in outcome reporting to optimise future research.

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