Reviewer’s report

Title: The association between antibiotics in the first year of life and child growth trajectory

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Reviewer: Frank Scott

Reviewer's report:

In this original research, the authors utilize a novel dataset to assess the relationship between antibiotic exposure early in life and weight gain during the first year of life and at 5 years. They appreciate a significant association between this exposure and outcome after adjusting for multiple possible confounders, as well as a dose response with repeated exposures. These findings support a rapidly expanding body of both basic (murine-based) and human observational data suggesting this association. My enthusiasm for this research is tempered by the route of data collection and risk of recall bias; i.e. exposure misclassification. The authors address this, however, in their limitations. Beyond this significant limitation, their analysis is sound. I had the following additional minor comments and questions for the authors:

1) The authors note in the introduction the association between breastfeeding and weight gain when discussing possible confounders. They discuss this further in the discussion, but it may be worth expanding on this in introduction as well for the unfamiliar reader.

2) It may be useful for the reader to include a CONSORT diagram summarizing inclusions and exclusions from the universe of mother-child dyads in IFPSII.

3) Per the authors, the survey instrument inquired about antibiotic use within 2 weeks of administration/visit. If these instruments are completed every 2 months during the first 6 months, and then at 12 and 72 mo, this does not account for MOST of the potential exposure time. This is touched upon in the discussion, but likely deserves a bit more attention. Were any sensitivity analyses of exposure misclassification considered? How many prescriptions would need to be missed in those without the outcome to nullify the results, for example?

4) The authors introduce the acronym WLz on page 6, line 125. I do not think this was explicitly defined yet.

5) With regards to the "rate of acceleration" models, was any consideration given to timing of antibiotic exposure? Is it possible to incorporate this?

6) In the discussion, page 13 Line 276, the authors note "While this difference may be subtle at 6 years old, continued antibiotic exposure and the influence of other environmental factors
may continue to add to this effect". There are not really sound data regarding these later antibiotic exposures and risk of weight gain or obesity. Early onset obesity itself is associated with later obesity, however. I think this sentence requires clarification.

7) I am not sure I follow why the potential misclassification of outcome would bias the result towards the null. Outcome misclassification can bias point estimates in either direction, and this statement assumes that obesity misclassification is differential, without data to support it. Did the authors consider exploring the impact of outcome misclassification on their effect estimates?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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I am able to assess the statistics

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