Reviewer’s report

Title: Metabolic characterization of menopause: cross-sectional and longitudinal evidence

Version: 0 Date: 09 Nov 2017

Reviewer: Sybil Crawford

Reviewer's report:

Strengths of the study include the large number of metabolites included, large sample size, and cross-sectional plus longitudinal analyses.

Collapsing of reproductive stage categories - perhaps necessary for statistical power - may be obscuring patterns of stage-related differences. SWAN longitudinal analyses, for example, find an increase in lipids between the early and late perimenopause, suggesting that collapsing categories -2 and -1 may entail losing some information/needed detail. This collapsing, for example, may partially explain the lack of difference between premenopausal and transitioning women in cross-sectional analyses (bottom of p. 14), if category -2 is similar to premenopause. Conversely, the longitudinal analyses finding changes in metabolites for the group with an additional 2.5 years in the transition - which likely includes women transitioning from -2 to -1 - suggests possible differences between these two stages. Secondary or exploratory analyses keeping these stages as separate categories could be suggestive even if power is not high.

pp. 15-16: Please describe the analytic approach for fixed-effect meta analysis in the statistical analysis section. Also, please provide a more detailed rationale for this approach. It is unclear why a conventional fixed effect analysis - keeping subgroups separate - is insufficient or different from meta analysis.

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
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics.

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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