Reviewer's report

Title: Maternal caffeine intake during pregnancy is associated with birth weight but not with gestational length: results from a large prospective observational cohort study

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Reviewer: Alastair Hay

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This is one of the largest studies to assess the effect of caffeine on pregnancy outcomes. Although the question of what effect caffeine has in pregnancy is not new many of the studies which investigated the relationship in the past were poorly conducted. Invariably, the assessment of caffeine intake in earlier investigations was inadequate and sometimes attributed solely to coffee drinking, and even where beverage type was noted no account was taken of the strength of the brew or the exact quantity consumed.

This current study on some 60,000 pregnant women finds an increase in gestational length with coffee consumption but a decrease with caffeine suggesting that other components of coffee may play a role. The authors also find a reduction in birthweight with increased caffeine intake, an increase in babies born small for date and increased risk of pre term delivery. There findings are well analysed according to their reported methodology with appropriate confounding factors controlled for in their analyses,

Major compulsory revision

1) The above findings are important and confirm those of a study published in 2008 ( the CARE study, ref 62 in this manuscript ). Like the CARE study the authors of this manuscript validated their tool for assessing caffeine intake. However, unlike the CARE study group which had published detailed comparisons of caffeine intake from different sources, including use of biomarkers to confirm consumption, the paper the current authors refer to as validation for caffeine intake merely refers to whether intake was correctly classified. It is thus not possible to make a detailed assessment of their measure of caffeine intake and this is something which needs addressing, perhaps by inclusion of an additional table or figure showing how well the questionnaire (used in this study ) performed in relation to weighed food intakes. In fairness the authors do claim that there is a good agreement between their food frequency questionnaire and coffee intake. This being the case they should show the data as the measure of intake is crucial as referred to earlier.

Minor essential revision

As I interpret the data the authors found no threshold of effect for total caffeine intake for their SGA group ( small for date ) with assessments using all three
variations on defining SGA. Their data on birth weight is less easy to interpret but it would be helpful if the authors were to say whether they observed any threshold effect for this outcome.

As the findings of this study and the earlier CARE study are similar it has implications for regulators. Advice to mothers to be in the UK changed following publication of the CARE study with pregnant women advised to limit caffeine intake and to stay below 200mg per day. The CARE study did not identify a threshold for reduction in fetal growth restriction either. Taken together with this study even more cautious advice for pregnant women may be necessary.

Discretionary revisions

This is a valuable addition to the literature on the effect of caffeine in pregnancy. The major findings in this manuscript of an effect of caffeine on birthweight were identified in the earlier CARE study which used a well validated measure of caffeine intake. It would help to stress this in the paper if only to indicate to others contemplating similar investigations that intake must be measured carefully.

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I have no competing financial conflicts of interest but am one of the authors of the CARE study referred to above and which was published in 2008.