Reviewer's report

Title: Vitamin C supplement use may protect against gallstones: an observational study on a randomly selected population

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Reviewer: Chung-Jyi Tsai

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This is a population-based study investigating the association between vitamin C supplementation and prevalence of gallstones using abdominal ultrasound examination as the tool of diagnosis. The report indicated that there was an inverse association between supplementation of vitamin C and gallstone prevalence. The strength of the report is the large sample size in a retrospective study.

1. In the Abstract: “To assess the possible influence………..” would be most appropriate as Aim or Purpose rather than Background.

2. In the Results of Abstract: “…….Female gender, hereditary predisposition…….were associated with risk of gallstone formation” This is a cross-sectional retrospective analysis rather than a prospective study, so it would be more appropriate to report as association with prevalence of gallstones instead of risk of gallstone formation. For same reason, it would not be appropriate to report a “protective effect” because this is not a clinical trial or prospective study.

3. In the Conclusions, for the same reason it would not be appropriate to conclude that “………a protective effect on the development of gallstones”

4. In the statistical model there is a covariate of inflammatory bowel disease, presumed as personal history, but it is was not reported in the tables.

5. In the results the authors reported regular vitamin C use and duration, but there was no dosage information and its analysis. For example, one tablet daily for one year vs. two tablets daily for six months may differ in the associations.

6. Because all the results were reported as odds rather than relative risk as this is a cross-sectional retrospective analysis, it would be better to use risk of gallstones in the manuscript.

7. What are the associations between vitamin C supplement and gallstone prevalence among participants with vs. without diabetes and others such as low vs high physical activity, obese vs. normal weight in BMI, males vs females, etc.

8. There is no validation study on the use of vitamin C for the data collected in the questionnaire.

9. It would be better to address the issue of misclassification in the assessment of exposures.