**Author’s response to reviews**

**Title:** Exosomal microRNAs as potential circulating biomarkers in gastrointestinal tract cancers: A systematic review protocol

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**Author’s response to reviews:**

Re: Manuscript no # SYSR-D-17-00172 entitled "Exosomal microRNAs as potential circulating biomarkers in gastrointestinal tract cancers: A systematic review protocol"

Dear Editor in Chief, Systematic Reviews

On behalf of the authors, we are very pleased to receive the valuable comments of reviewers. We have amended the manuscript in line with the reviewers’ suggestions and therefore a revised manuscript is now being submitted. In order to accelerate the re-review process, all changed and modified parts of revised manuscript have been highlighted with yellow background. We hope it warrants the readership and is acceptable for publication in “Systematic Reviews”.

We are looking forward to hearing from you in due course.

Yours sincerely,

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Reviewers comments:

There are a few issues I’d like the authors to clarify:

1. On line 39-40 the authors state "This systematic review will be reported in line with the Preferred Reporting Items for Systematic Reviews (PRISMA-P) guidance ". This is incorrect. The completed review is likely to be reported using PRISMA. This issue is again mentioned on lines 145-146 "In addition this systematic review will be reported in line with the Preferred Reporting Items for Systematic Reviews (PRISMA-P) guidance ". The completed review will likely use PRISMA whereas the write-up of the protocol might use PRISMA-P.

Reply:

- According to reviewer's comments, the completed review will be reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidance which is mentioned on page 1, line 40-41 and page 4, line 147-148
2. On line 151 the authors state "Observational studies investigating circulating exosomal miRNAs in diagnosis and prognosis of GI malignancies, including upper and lower GI, and hepatopancreato-biliary will be included." Can the authors clarify for the reader what types of observational studies? Without this detail interested readers will not be able to replicate their review.

Reply:
- For more clarification, the Observational studies such as Cross-sectional; Case-control and Cohort studies have been added to the inclusion criteria of the manuscript based on the reviewer's comments (page 4; line 152).

3. On line 201 the authors indicate quality assessment of the primary studies will be contacted. However, the authors do not provide any information about the dimensions of quality that will be assessed. I', requesting the authors provide this information in the paper.

Reply:
- To reply the above comment, due to the methodological complexities of observational studies, the final risk of bias will be performed by the Newcastle-Ottawa Scale (NOS) for coverage of different types of studies (cross-sectional; case-control and cohort studies). Moreover the NOS tool has been endorsed by Cochrane Collaboration to assess the quality of observational studies. This tool is composed of 8 items which is developed as a collaboration between the University of Newcastle, Australia, and the University of Ottawa, Canada (47,48) The complementary information about the tool and its adaptations for observational studies (cross-sectional; case-control and cohort studies) are illustrated in the manuscript text and three appendix files. (Page 1, line 46) and (Page 5, line 203-205) and (Page 6, line 260-262).


The complementary information about the tool and these ten eight items are illustrated in three appendix files (Page 6, line 260-262).