

Format for ANSWERING REVIEWERS



April 3, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name:CMS probiotic revised manuscript UEN.doc).

Title: Early probiotics to prevent childhood metabolic syndrome - a systematic review

Author: Haribalakrishna Balasubramanian, Sanjay Patole

Name of Journal: *World Journal of Methodology*

ESPS Manuscript NO: 16715

The manuscript has been improved according to the suggestions of reviewers and editors:

Reviewer 1

[1] There are many spaces missing between words, please check. **Response:** We have corrected this in the manuscript [2] Organism names should be written in italics: **Response:** We have incorporated this change in the manuscript.

Reviewer 2

[1] How did the authors start to study microbial on children metabolic syndrome? This issue is related to the rationality of this study, and the reason why no RCT was found. The evidence seemed weak. **Response:** We agree that prospective studies show only an association between altered gut microbiota and childhood obesity, type 1 diabetes. The causal pathways are still unclear. Considering the global health burden of childhood metabolic syndrome (CMS), studies to assess the rationality of probiotic use in its prevention are essential. This has been clarified in the conclusion (Page 9, line 5-8, text in red)

[2] Prevalence of MS differed in regions. The authors speculated that it was due to difference of MS definition. How did the definition differ? Were there any reasons for the difference of prevalence of MS other than definition? For example, diet and ethnical factors.

Response: Yes, there are many potential reasons for the difference in the prevalence estimates of CMS besides definition. These include the age and gender, ethnicity, and nutritional status of the population. (Ref: Silveira et al. Endocrinol Metab Synd 2013). This is now clarified in the introduction. (Page 3, text in red)

[3] Are there any difference between adult metabolic syndrome and child one? Diet and exercise affect MS in

adult. How do diet and exercise affect MS in child?

Response: We agree that the pathogenesis of CMS is complex. The risk factors for adult MS and CMS are different. Diet and lifestyle are risk factors for adult MS, whereas prematurity, low and high birth weight, rapid catch up growth, maternal undernutrition, maternal obesity and diabetes are potential risk factors for the components of CMS. This highlights the importance of early interventions (perinatal, early postnatal) to prevent CMS. This has now been elaborated in the discussion.(Page 8, line 36-37, text in red)

[4] The authors stated that WHO defined MS as insulin resistance in the presence of any two of obesity, hypertension, etc. This definition has been accepted world-wide. Were there any direct relation between MS and gut microbiota?

Response: There are no studies to show direct relation between MS and gut microbiota (Page 8, line 35, text in red). Effect of gut flora have been studied predominantly on obesity, adiposity, weight gain, glucose tolerance have been predominantly studied.

Reviewer 3: The manuscript is interesting and well written. I accept it in the current form.

Reviewer 4: [1] The abbreviations does not appear in the abstract. **Response:** All abbreviations (except RCTs) in the abstract have been expanded. [2] Conclusion paragraph should write more impressive and give a clear message to the readers. **Response:** We have modified the conclusion paragraph as suggested.

Editors suggestions

- 1 Format has been updated as per the requirements of systematic review
- 2 PMID and doi has been included for the references.
3. Comments section has been included.
4. Conflict of interest statement has been included.
5. Biostatistics and data sharing statement are not applicable for our paper

Thank you again for publishing our manuscript in the *World Journal of Methodology*.

Sincerely yours,

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