Author's response to reviews

Title: Synbiotics, probiotics or prebiotics for full term infants: A Systematic Review

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Author's response to reviews: see over
Dear Mr Nehme Gabriel

Re: Submission of revised manuscript

Thank you for the opportunity to submit a revised manuscript to Nutrition Journal. My team and I have addressed all the comments from the reviewers. Below is a table which outlines each reviewer’s comments, the authors’ response and action taken or changes made in the manuscript. As requested, all changes / additions have been highlighted.

This systematic review explored the effects of Synbiotics, probiotics or prebiotics on **exclusively formula fed** full infants focusing on growth and clinical outcomes. Previous reviews (2007 to 2011) on term infants given probiotics or prebiotics focused on prevention of allergic disease and food hypersensitivity. Our results challenge previous reviews and practice guidelines making a case for more research on this population. This fits with the aims and scope of the Nutrition Journal. That is why we chose your journal to publish our review since Nutrition Journal publishes results that challenge current models, tenets and dogmas.

This systematic review is not under review in any other journal and none of the findings have been published before. The review used guidelines from the Cochrane Handbook for Systematic Review for Interventions, and conforms to the PRISMA reporting guidelines. The Human Research Ethics Committee at Stellenbosch University ruled that ethical approval to conduct this systematic review was not necessary as the data is already published and in the public domain.

It is our sincere hope that you publish this systematic review.

Best regards

Mary Mugambi
### Authors’ response to reviewers’ comments

<table>
<thead>
<tr>
<th>Reviewer’s comment</th>
<th>Authors’ response.</th>
<th>Action taken / changes made in the manuscript</th>
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<tr>
<td>1 Reviewer 1: Jose Manuel Moreno-Villares</td>
<td>The work is exclusively referred to syn, pro, and prebiotics in INFANT FORMULA or infant feeding but not as pharmacological treatment. I would add this is the title: IN INFANT FEEDING.</td>
<td>Page 1, Line 1 reads: Sybiotics, probiotics or prebiotics in infant formula for full term infants: A Systematic Review</td>
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<td>2</td>
<td>A mention should be done on breastfeeding as the ideal feeding for infants. As there are differences in the rate of growth between breastfed and bottle-fed infants, this should be noted in the paper.</td>
<td>Page 28, lines 9 – 15 reads: Breastfeeding statement</td>
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<td></td>
<td>A paragraph stating the authors’ support for breastfeeding was inserted in the discussion section of the manuscript.</td>
<td>By conducting this review on exclusively formula fed infants, the authors do not seek to diminish the importance of breastfeeding and promote formula feeding. The reviewers acknowledge the importance of breastfeeding for infants. They support exclusive breastfeeding for 6 months, thereafter safe complementary feeding from 6 months of age with continued breastfeeding up to 2 years and beyond as per the global recommendations for optimal infant feeding of WHO and United Nations Children's Fund (UNICEF). This is because breastfeeding is the ideal feeding method for infants. [99]</td>
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<td>3</td>
<td>Page 4, lines 4-10: it is unnecessary for the goal of the paper to include the explanation on the role of CRP and IL-6.</td>
<td>The description of CRP and IL-6 in the background section informs the reader why these 2 parameters were included in the systematic review, as reflected in the types of outcome measures, results and discussion sections. The authors agree that description of CRP and IL-6 is necessary.</td>
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<td>4</td>
<td>There is no need to make a specific comment on the status of the protocol (unpublished) Line 3, page 5.</td>
<td>Page 5 lines 1 – 3 reads: The Human Research Ethics Committee at the University of Stellenbosch, South Africa reviewed the protocol, ruled that all data to be collected for this review was from the public domain and was therefore exempt from ethical approval.</td>
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Reviewer 2: Julie Jones | Authors’ response. | Action taken / changes made in the manuscript
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1 | Page 26 line 16 - the use of less versus fewer | The word “less” was deleted and the word “fewer” inserted. | Page 26 lines 15 – 16 reads: In one study [52] there were fewer crying episodes in the control group than probiotic group. |
2 | My only question about the review is whether there should more be made of the types of probiotic strains, the viability of the strains under various conditions. Could these aspects have affected the outcomes? | No change was made on manuscript because of the following reason: There are several trials exploring the viability of different strains of probiotics under different conditions. [1, 2] In addition, there are trials exploring the different techniques of maintaining probiotic viability such as microencapsulation. [3] However, the studies that explore probiotic viability in vivo focus on rats. [1, 2, 3] There are no published human trials that used probiotics that are microencapsulated or have been subjected to viability trials. [3] Therefore the effect of probiotics (that have been subjected to viability trials) on the clinical outcomes addressed in this review could be focus of future research. | References: 