Author's response to reviews

Title: A retrospective study showing Maintenance treatment options for paediatric CD in the first year following diagnosis after induction of remission with EEN: supplemental enteral nutrition is better than nothing!

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Author's response to reviews: see over
Dear Dr Norman,

Re: MINOR REVISE DECISION: BMC Gastroenterology MS: 1326132745109222

Many thanks for reviewing our manuscript and giving us the opportunity to revise it further based on the comments of the reviewers and editors. We have adapted the manuscript to include the many helpful suggestions given by yourself and the other reviewers. Please find attached our revised manuscript and below our responses to the reviewers points. For ease of reference we have included our responses in red font.

EDITOR'S COMMENTS TO AUTHOR:
While all the reviewers felt this was worthy of publication, the discussion in particular was felt to need quite a bit of editing as listed below.

Many thanks for your comments and on your constructive criticism. We have adapted our manuscript to include your suggestions and changes including shortening and revision of the discussion.

REVIEWERS' COMMENTS TO AUTHOR:

Reviewer: 1
Comments for Transmission to the Authors

Reviewer: Dr Andrew Day

Reviewer's report:

COMMENT FOR THE AUTHORS
The manuscript authored by Duncan and colleagues considers the impact of ongoing supplementary enteral nutrition after a course of EEN in children with Crohn disease

Overall Comment
This work provides further data supporting the practice of recommending
supplementary enteral nutrition as an ongoing intervention in children with CD. The work is, however, limited by the numbers (n=15) that were taking these ongoing supplements and the report’s retrospective nature

Specific Comments:

1. The Abstract and parts of the Manuscript contain several sentences that commence with numbers (e.g. 15) rather than words (e.g. fifteen).

Thank you very much for your comments. Numbers have been used in the abstract for conciseness, we have however changed the layout in the main text where numbers at the start of sentences have been changed to words.

2. The Abstract reports that all of the 48 children were in remission at the end of the 8 weeks course of EEN. Subsequently in the Results section, it is stated that all of the 48 had either clinical response or in remission. This feature should be consistent.

Many thanks for your comment. We have changed to abstract to reflect that patients had either shown significant clinical response or were in remission.

3. Further, did those who were in remission at 8 weeks have better outcomes than those who just had improvements?

Many thanks for your comments. There was no clear benefit for patients in remission compared to those who responded but the analysis is limited by several factors including overall patient numbers and the retrospective nature of the study.

4. In providing the details of those who were in remission at 12 months, it is not clear if these children had entered remission with initial therapy and then remained in remission for the whole of the subsequent period, or if they had achieved remission at some time point (e.g. 12 weeks) and then remained in remission at 12 months or if they were simply in remission at 12 months (regardless of initial response and any intervening relapses)

Many thanks for your comments. All patients that were in remission at 12 months had entered remission with initial therapy and remained in remission for the whole of the subsequent period.

5. The Introduction comments about a lack of Classic Symptoms (which are accepted as pain, diarrhoea and weight loss), and then goes on to describe these being present. This should be revised to be more clear.

Many thanks for your comments. We have changed to introduction as detailed below.

‘Presentation in the paediatric population is often with a variety of symptoms, abdominal pain is usually a prominent feature alongside persistent or recurrent diarrhoea with or without blood.’
6. The Introduction comments about diagnostic delay: the final part of this section implies that diagnostic delay is only important in adolescents. This could be revised also

Many thanks for your comments. We have changed the introduction to reflect this comment.

‘Due to the diverse range of symptoms diagnosis can often be delayed, with associated issues of poor growth and undernutrition for all patients as well as delayed puberty in the adolescent patient group.’

7. The Methods comments about “physicians global assessment” (the overall assessment of an experienced paediatric gastroenterologist). This should be referenced appropriately to an earlier description of PGA. This is not the method utilised, then an alternative term should be used with appropriate reference also applied.

Many Thanks for your comment. We have referenced Buchanan E, Gaunt W, Cardigan T et al. The use of exclusive enteral nutrition (EEN) for induction of remission in children with Crohn's disease (CD) demonstrates that disease phenotype does not influence clinical remission. *Alimentary Pharmacology and Therapeutics* 2009;**30**(5):501-7 which also used a PGA.

8. The children who received ongoing supplements had these feeds for a variable length of time (from 4 to 12 months). It would seem feasible that the length of continuing feeds is important in longer term outcomes. Were the authors able to define this?

Many thanks for your comments. Unfortunately we were unable to define this clearly but would hope that future studies would be able to assess this by collecting information at predefined more regular intervals than used in this study.

9. Also, it appears that the assessment of outcome at 12 months is considered regardless of the duration of supplementation. It may be helpful to consider a formal review of this analysis by a statistician.

Many thanks for your comments. In this current study our numbers were felt to be too small to make a significant assessment of these differences.

10. How were the authors able to confirm that the children were compliant with the supplementary feeds? And that the volume reported was accurate?

Many thanks for your comment. We assessed the compliance and volume of feeds taken from dietetic and nursing notes as well as medical records. Patients were offered telephone and email support throughout this treatment and therefore we hope to have optimised compliance. Unfortunately to assess this fully we are relying on patients being honest with ourselves and in reporting their intake which is subject to error.
11. NG and n-g are both used: one abbreviation should be used consistently

Many thanks for your comment. We have changed to n-g to ensure consistency throughout the paper.

12. The Discussion would benefit from revision and attention to detail. Presently it is a little disjointed. For example, the detail about adult studies of supplementary feeds are separated by a paragraph discussing a different topic.

Many Thanks for your comment. We have revised the discussion to ensure it flows better and decreased the word count from 1637 words to 1408 words.

13. Also, the adult studies included patients who entered remission by different routes (not all of them were treated with EEN first). This may of relevance to the impact of this intervention

Many thanks for your comment. We agree that the route of entering remission may be of relevance to the impact of the intervention. No change has been made to the manuscript based on this comment.

14. In addition to the outcome presented (remission), did the groups differ otherwise? (such as growth outcomes, surgical outcomes etc

Many thanks for your comment. We were unable to assess if the groups differed otherwise but would hope that future studies would be useful in assessing these patient groups in more detail.

Reviewer 2

Reviewer: Kristina Norman

Reviewer's report:
This is an interesting retrospective report on the 'real-life' situation in children with CD after EEN.

I only have some minor remarks (Minor Essential Revisions):

1) are the groups (MEN+azathioprine; MEN only, azathioprine only, nothing) comparable in age, sex or disease location or nutritional status? in order to evaluate the findings this would be important to know. Do the authors have any data on why parents/children chose to continue with the respective treatment?

Many thanks for your comments. We do not currently have further information on the disease location or nutritional status of the patients within the groups. All groups were comparable for age and sex of patients. Our experience of EEN as a centre allowed us to be able to offer and support patients and families with MEN as a treatment option. As we state in the text the clearest reason for patients going onto supplements was whether they were able to take EEN orally or by n-g.
2) how was intake evaluated retrospectively? did parents/children keep diaries, or was it merely estimated at follow up visits?

Many thanks for your comment. We assessed the compliance and volume of feeds taken from dietetic and nursing notes. Patients were offered telephone and email support throughout this treatment and therefore we hope to have optimised compliance.

3) the discussion is somewhat lengthy and appears slightly repetitive.

Many thanks for your comment. We have revised the discussion to ensure it flows better and decreased the word count from 1637 words to 1408 words.