

Dear Editor,

Please find enclosed the edited manuscript in Word format (16822-review.docx).

Title: Effects of cereal fiber on bowel function: intervention trials systematically reviewed

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Thank you for the critical comments on our manuscript. We have taken care editing the manuscript according to your indications.

Please find below our answers to the comments raised by the reviewer.

Comments To Authors

This is a useful review on bowel functions as a result of adding specific cereal fibers to the diet. Several suggestions are offered for improving the clarity of the manuscript. In the abstract and elsewhere, please specify if the confidence intervals are 95% CI.

- *Thank you for your positive support on our manuscript. All confidence intervals are 95%. We have clarified in the Material and Method section (page 9, line 159) that CI stands for the 95% confidence interval of the regression analyses.*

The reported change in stool frequency of 4/1,000ths of a day implies a level of precision not possible to determine from data that are usually recorded as stools/day. Converting this fraction into minutes is <6 minutes difference.

- *We agree that in individual experiments with a limited number of individuals it would not be possible to determine changes in stool frequency to the same level of precision estimated in our systematic review. The increase in stool frequency with 0.34 bowel movements per day is sufficiently informative for the reader. Therefore we deleted Frequency index results (Results section page 12, line 246).*

Can the authors make any qualitative conclusions about the cereals other than wheat? If not, perhaps the title should be changed to reflect that absence of information from other grains.

- *Thank you for your suggestion to change the title to reflect the absence of information from other grains. The systematic review was designed to conduct a comprehensive analysis on effects of all intact cereal dietary fibers on bowel function. Given the limited numbers of observations on other cereals, and the differences in types of fiber between*

cereals, we felt we did not have sufficient information to draw even qualitative conclusions for other cereals. Because the review was designed to cover the effects of intact cereal dietary fiber on bowel function for all grains we think the title should reflect that.

The authors excluded studies on people with constipation or diarrhea. It would seem advisable to include these groups if those conditions were not the result of pathology since those groups would benefit more than healthy subjects and more than ? of studies were excluded.

- Thank you for this suggestion. Ultimately, we excluded studies conducted in people with constipation or diarrhea for two main reasons. First, our study did not intend to address treatment of existing constipation or diarrhea. We focused on how fiber may affect bowel function in generally healthy populations. While fiber may be helpful in alleviating symptoms associated with functional constipation or constipation associated with insufficient fiber and fluid intake, increasing fiber may not be helpful, and could be contraindicated in cases of severe constipation, or from opioid- or other drug-induced constipation. It may also be contraindicated in severe diarrhea. Second, reviewing the literature on ICDF in relation to bowel function, most observations are based on experiments in healthy individuals. Too few observations are available to conduct a proper analysis on the observations from experiments in individuals suffering either from constipation or diarrhea. Future studies focusing on the potential effects of fiber among individuals with existing constipation or diarrhea would be greatly appreciated. We identified only 1 publication (Eherer 1993) that examined individuals with pre-existing diarrhea. Also, the data on individuals suffering from constipation provide too little and scattered information for a solid analysis (see table below).*

		intervention	total bulk	dry bulk	water	frequency	Transit time
Smith	1980	wheat bran	X	X			
Badialdi	1995	wheat bran	X			X	X
Graham	1982	wheat bran	X		X	X	
		corn bran	X		X	X	
Holma	2010	rye bran	X			X	X
Kanauchi	1998	barley	X		X	X	
Salvioli	1984	wheat bran				X	
Shariati	2008	wheat bran				X	
Andersson	1979	wheat bran				X	X
Marcus	1986	wheat bran					X

For the comparisons of transit time, the methods used for each study should be listed and it is likely not possible to combine them all because different methods (e.g., dye passage versus radio-opaque pellets) measure rates of first passage and passage of 90% of markers, as an example.

- *We agree that our assumption of comparability between the methods used to measure transit time may have influenced the categorization in initial transit time < 48 hrs and ≥48 hrs, and therewith may have influenced reported effects. However for the final outcome we have used the Δ transit time in the analysis based on the assumption that the Δ transit time may be independent of the methodology used. If we had grouped the data according to the methodology for transit time, we would have had insufficient data to make an estimate of the effect of intervention with cereal dietary fiber on transit time.*

There is a lot of duplication of text throughout with some wording and information repeated multiple times; a thorough editing is required to eliminate these. There is also duplication of information in the tables and appendices. The point that such studies have been conducted over 90 years is made 3 or 4 times – once is sufficient.

- *Thank you for this suggestion to help make the paper more concise. We have reduced duplication throughout the text to eliminate redundancy as recommended.*

There is a lot of duplicate text throughout.

- *We have edited the text or deleted text at different places in the manuscript:*
 - *pg 6/line73 (deleted: almost a century of)*
 - *pg 7/line 84 (deleted: The most studied ICDF is wheat dietary fiber, and primarily wheat bran fiber, with experimental studies examining the role of wheat bran on bowel function dating back nearly 90 years)*
 - *pg 7, line 85 (deleted: predominantly wheat fiber)*
 - *pg 10/line 1 (deleted: Changes in the following outcomes were examined: total stool weight, dry stool weight, percentage water in stool, number of bowel movements, and transit time.*
 - *Pg 11/line 215 (deleted: Given the limited number of studies examining these other sources of ICDFs, results on bowel function outcomes of the ICDF's from the non-wheat sources were evaluated on the basis of the means of observations or on individual observations.*
 - *Pg 14/line 268 (deleted: Quantitative estimates of the effects on parameters for healthy bowel function from other sources of ICDF, such as oat, barley, rice, corn, rye, and sorghum, were not feasible given the small number of studies.*
 - *Pg 14/line 284 (paragraph edited)*

- *Pg 15/line 319 (deleted: in which studies through 1991 were included)*
- *Pg 17/line 396 (deleted: An amount as low as 5.7 g of wheat fiber may have beneficial and substantial effects on bowel function)*

There is also duplicate information in the tables and the appendices.

- *We agree that there is duplicate information in table 2 and appendix 4. For readability of the information we propose to keep the duplication of the information on wheat, barley and corn in appendix 4.*

On line 236, the authors calculate that the lowest effective dose of wheat bran was 5.7 g/d. Then they should not show data for changes per gram. Changes per 5.7 g or 10 g would be better. Why is reference 54 cited for this number if it is based on your regression analysis?

- *We understand that the inclusion of “lowest effective dose” may raise confusion. This lowest effective dose is indeed not based on our regression analysis but is from one of the included individual studies that observed a significant effect on total stool weight with an amount of wheat dietary fiber as 5.7 g/d.. We have called out this reference to indicate that with a low amount of wheat dietary fiber (5.7 g/d) a measurable effect on total stool bulking is possible. We have clarified in the text to ensure it is clear that this finding is from another study that we thought important to mention (pg 13, line 259-260)*

In the discussion of why intestinal function changes (lines 289+), there is no mention of changing the colonic microbiota, their activity, or the amount and type of mucin produced in the colon.

- *The effects of dietary fiber on colonic microbiota have gained scientific attention in the last two decades. We are aware that changes in dietary fiber intake may influence colonic microbiota, thereby influencing bowel function. However, our systematic review was not intended to identify changes in microflora. We focused on outcome parameters that are directly indicative of bowel function. Any comment on the effects of changes in colonic microflora composition on bowel function would have been speculative.*

Appendix 5 is not called out in the text.

- *Thank you for noting this oversight. We have now called out Appendix 5 in the text (page 15, line 367).*

The claim on lines 321-2 on no effect of percent water in stools contradicts your proposal in lines 290+ that water holding was increased.

- *Thank you for this comment. We have explained the effect of the water binding capacity of ICDF: “The effects of wheat bran fiber on stool weight are largely attributable to its high*

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resistance to fermentation by colonic bacteria, combined with its water binding capacity (1 g of fiber binds about 3 g of water), therefore contributing to a stronger effect on increasing stool bulking compared to more easily fermented ICDF, such as those from oats and barley". (pg 15, line 289-294).

- *On pg 16, line 319-322 we included the following explanation with respect to the observation that the percentage of water in stools did not increase: Adding dietary fiber that is resistant to fermentation does not increase the overall percentage of water as the amount of water bound by the fiber is similar to the average water content of fecal samples (about 75%).*

We hope we have sufficiently addressed your comments in our answers to the reviewer's comments and revisions to the manuscript.

Best regards,

On behalf of Kristin Verbeke, Paige Miller,

Jan de Vries

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