Reviewer’s report

Title: Effects of cow's milk beta-casein variants on symptoms of milk intolerance in Chinese adults: a multicentre, randomised controlled study

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Reviewer: Karen Dwyer

Reviewer's report:

This paper by Mei et al is a large study of 600 Chinese subjects who recorded GIT symptoms following a single dose of 300ml milk containing either A1/A2 or A2 protein. They show that the consumption of A2 milk consistently reduced symptoms across age groups including those that were galactose absorbers. An interesting article.

My questions and comments:

The authors state that lactose intolerance was self reported. More clarity about what the subjects self reported and their definition of lactose intolerance would be helpful.

The authors have used recall over the previous 24 hours to assess food intake. A food diary would have been a preferred method over the course of 8 days especially when sources of lactose can be "hidden" or "unexpected". I am not confident that all the subjects were totally off lactose when required.

The sample size needs more explanation rather than based on previous studies (which were very small), what was the power required to detect a difference.

This study was performed with a single 300ml drink. The data may have been more striking with longer exposure.

More clarity re the stats is required. The table of absorbers v non absorbers have what appear to be very minor differences being statistical. would be good to present this in a way where the absolute difference can be ascertained. ie: the difference between 0 and 0. I appreciate the ranges vary and expressing this as a plot may make the difference more apparent.

The authors hint in the discussion that A1 induced inflammation may be linked to the symptoms yet there is no data regarding GIT inflammation presented. this is a major flaw.

The authors state that the symptoms may be a consequence of the A1 beta casein - what is the amount of A1 protein in the milk used. Is there any literature to support that this dietary quantity
will induced GIT inflammation. Ie: does it correlate with the concentrations used in the in vitro studies referenced.

I think the title needs to reflect the implication of the role of A1. At present the focus is on lactose - there is no measure of lactase and the conclusion is the A1 protein is impacting GIT health.

**Level of interest**

Please indicate how interesting you found the manuscript:

An article of importance in its field

**Quality of written English**

Please indicate the quality of language in the manuscript:

Acceptable

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I have received funding from A2 milk to examine type 1 diabetes in a mouse model. I have a paper under consideration looking at the lactase expression in these mice (off shoot paper).

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