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Letter: Efficacy and safety of hydrolyzed formulas for cow's milk allergy management: A systematic review of randomized controlled trials - Authors' reply

We thank Dr Berni Canani et al for their constructive comments on our systematic review.

1. The Cochrane Handbook for Systematic Reviews of Intervention states that among effect measures for dichotomous data, which include risk ratio (RR), odds ratio, risk difference and number needed to treat, 'no single measure is uniformly best, so the choice inevitably involves a compromise'.¹ Thus, while we respect the authors' preference of risk difference, we have chosen a RR, well in line with current recommendations for a systematic review.
2. We are aware that a cumulative incidence was an outcome of interest in the trial by Berni Canani et al (2017).² It is, however, not unusual that compared with individual trials systematic reviews focus on different outcomes. Our systematic review, based on the registered protocol, focused on pre-defined outcomes. We appreciate the authors' decision to report individual components. We agree with the authors that it helps the readers to judge whether the components are reasonable combined. It also helped us when performing a systematic review.
3. We appreciate the authors' comment that the analysis of tolerance acquisition was performed correctly. We respect the authors' opinion that the data could have been presented differently. However, it is our opinion that the presentation of the data was achieving the goal of our systematic review, and the approach suggested by the authors would not have changed the overall conclusion.
4. & 5. *Errare human est*. We apologize for the errors. All of them were due to the errors made when transferring data to the manuscript. We thank the authors for table with corrected values. Of note, the correction did not change the overall conclusions of our review.
5. In our systematic review, eczema and urticaria were calculated at 12, 24 and 36 months (not from 12 to 24 months).
6. Once again, we thank Dr Berni Canani for providing additional data from 2 trials for our systematic review. However, at that time, as stated in our manuscript, only the data sets of tolerance acquisition to cow's milk proteins were obtained from the authors. We did not receive a full data set.
7. As stated in our response to comment #1, the Cochrane Handbook states that no single measure is consistently the best.¹ Concerning

pooling data from two studies, the Cochrane Handbook states that a meta-analysis may be performed, if PICO is similar enough to combine the data from minimum two studies.³ It does not matter whether the data come from the same research group, as long as the data were not duplicated.

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2. Berni Canani R, Di Costanzo M, Bedogni G, et al. Extensively hydrolyzed casein formula containing *Lactobacillus rhamnosus* GG reduces the occurrence of other allergic manifestations in children with cow's milk allergy: a 3-year randomized controlled trial. *J Allergy Clin Immunol*. 2017;139(6):1906-1913.e4. <https://doi.org/10.1016/j.jaci.2016.10.050>. Epub 2016 Dec 30 PMID: 28043872
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