

January 20th, 2012

The BMJ Open Editorial Office

Dear Editor,

RE: BMJ Open - Decision on Manuscript ID bmjopen-2011-000679.R1

Thank you very much for your editorial work on our manuscript entitled “A systematic review with meta-analysis of comprehensive interventions for preschool children with autism spectrum disorder: study protocol”. We also very much appreciate Dr. Iliana Magiati’s helpful suggestions. We took her comments into account in our revised manuscript.

Responses to Dr. Iliana Magiati’s comments:

[- Consider replacing the term “preschool autism spectrum disorder” with “preschool children with ASD” throughout the document in order to meet APA guidelines regarding best use of language to describe participants](#)

The term “preschool autism spectrum disorder” has now been replaced with “preschool children with ASD” throughout the document.

[- Despite the good standard of English language, I would still advice the authors to review their manuscript one more time for grammar and syntax.](#)

Our manuscript has now been reviewed for grammar and syntax.

[- Change “most” individuals in final line of first paragraph to “many” individuals – in fact, many outcome studies in adulthood show that many individuals remain very vulnerable and in need of services.](#)

This has now been changed.

[- Please consider including one or two references as examples of behavioral, social-communication and multimodal developmental interventions in the second paragraph of the introduction.](#)

One reference for each model has now been included.

In more detail,

[These programmes tend to fall into three models; i\) those based on behaviour change which use applied behavioural analysis \(ABA\) \(e.g. ⁵\); ii\) those focused on therapies targeted at improving the social communication impairment, the core symptom of](#)

autism (e.g. ⁶); iii) multimodal interventions targeted across areas of autistic children's development (e.g. ⁷).

References:

5. Smith T, Groen AD, Wynn JW. Randomized trial of intensive early intervention for children with pervasive developmental disorder. American Journal on Mental Retardation 2000;105(4):269-85.

6. Green J, Charman T, McConachie H, Aldred C, Slonims V, Howlin P, et al. Parent-mediated communication-focused treatment in children with autism (PACT): a randomised controlled trial. The Lancet 2010;375(9732):2152-60.

7. Dawson G, Rogers S, Munson J, Smith M, Winter J, Greenson J, et al. Randomized, controlled trial of an intervention for toddlers with autism: the Early Start Denver Model. Pediatrics 2010;125(1):e17.

- Can you clarify what you mean by “intermediate developmental endpoints” and “surrogate endpoints” (p.4, last line, p.5 first line)?

‘Surrogate endpoint’ is a well characterized term in the trials and intervention literature – essential an intermediate outcome that is a proximal equivalent to the endpoint change desired (for in change in immune status after vaccine) and can in some way ‘stand for it’. The text now clarifies our meaning here in relation to the intermediate developmental endpoints reported in studies.

In more detail,

Specifically, there has been variation in whether endpoints have been framed in terms of specific autism symptom outcomes, non autism-specific outcomes that are not specific to autism (such as for instance IQ), or ‘intermediate’ endpoints relating to aspects of development that may have some relationship to later autism symptoms – examples would be changes in joint attention or parent-child interaction. These latter two kinds of outcome are often reported, without necessarily strong justification, as if they were the equivalent of change in autism symptoms (i.e. as ‘surrogate’ endpoints); and this can cause real confusion.

- Clarify the “quality criteria” ratings mentioned in Methods, Type of Studies section.

This part has now been corrected as below.

We will include randomized controlled trials and subject these to a rating on the Cochrane Collaboration tool for assessing risk of bias.

- I am not sure that “adaptive behavior functioning” as measured by the Vineland Adaptive Behaviour Scales constitutes an intermediate outcome – social and communication skills are primary areas of difficulty in ASD and I would think they are primary or secondary outcome.

We agree with the reviewer and “Adaptive behaviour functioning” has now been put into the secondary outcomes.

- Please consider including “trial” and “outcome” too in your search terms.

These have now been included in the search terms.

- The exclusion criteria need to be more clearly written with more attention to language/grammar.

The exclusion criteria have now been corrected.

- With exclusion criterion 7 do you mean that you will exclude all studies who do not have a TAU comparison group? What if a study compares a behavioral with a developmental approach? Wouldn't the findings of such a study be directly relevant to the aims of your systematic review and meta-analysis?

We need to limit the studies to those using a TAU comparison group because of our statistical analyses. Following Cochrane Handbook for Systematic Reviews of Intervention, we are using an inverse variance method within a random effects model. This requires treatment of TAU arms in a standard way – excluding comparisons of two test treatments in which the baselines are not TAU.

- Please delete the age groups of adolescents and adults from your list in p. 13, point 3, as your study is only on pre-school children.

These have now been deleted.

- The first paragraph of the discussion needs to be written in a more “moderate” tone – i.e. “this study will provide the most reliable basis for decisions on early intervention”. Clearly this depends on the quality of the study eventually so best to rephrase to “can provide a more reliable basis”.

The first paragraph of the discussion has now been corrected according to these comments.

In more detail,

Meta-analysis of RCTs across types of intervention for preschool children with ASD is an important step in providing a reliable basis for implementation decisions. Since previous analyses have been essentially restricted to specific intervention types, and often with different outcome criteria, a study across three representative models: behavioural, multimodal developmental or communication-focused models will guide future clinical practice and research trials for children with ASD.

All correspondence should be sent to

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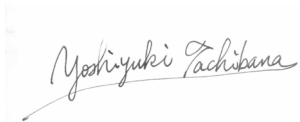
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We are looking forward to your replies.

Sincerely yours,

Yoshiyuki Tachibana

A handwritten signature in black ink that reads "Yoshiyuki Tachibana". The signature is written in a cursive style and is positioned below the typed name.