MOSS Guidance for 'Split Body Trial' Reviews

A 'Split Body Trial' refers to when randomization of interventions takes place within individuals, with different interventions being applied to different body parts (e.g. to the two eyes or to teeth in the two sides of the mouth).

Please note that this document is not intended to act as detailed statistical guidance for 'how' authors should incorporate data from Split Body studies.

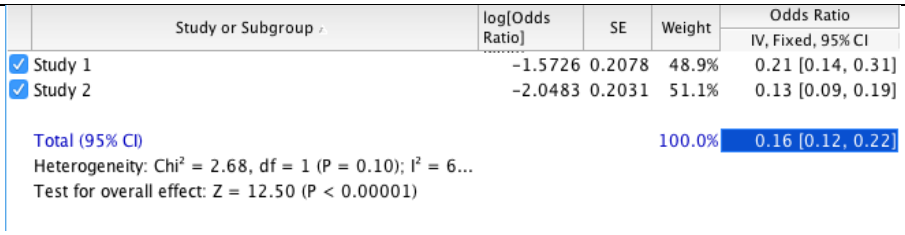
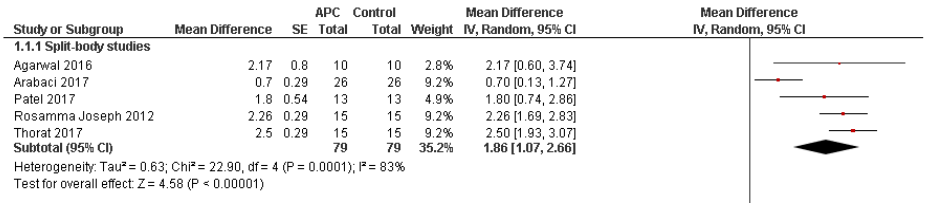
This is a list of high level 'Guiding Questions' to help **MOSS editors** assess how likely it is that data from these studies were appropriately incorporated in the review and assess whether the relevant information has been presented in the review in a clear and appropriate manner.

Answering 'no' to any of these questions does not automatically mean the authors have made an error. It is simply a red flag that indicates (a) authors need to provide more detail or further clarification, or (b) a deeper investigation by an experienced statistician may be needed.

More detailed guidance on these methods can be found in the list of additional resources at the end of this document.

Review Section	Guiding Question
Author Team	1. Does the systematic review author team include an experienced statistician who was responsible for these analyses? • *If not clear from the authors' names or affiliations, this could be found in the section 'Contribution of Authors'.* • *If not, look for an explicit statement elsewhere that they worked with an experienced statistician when necessary.*
Methods	2. If data from 'Split Body Trials' is eligible for inclusion, is this clearly stated in the section 'Criteria for considering studies for this review'?
	3. Was the decision to include these types of studies appropriate? • *For example, can we be confident that there was no risk of any potential 'carry across effect' with this intervention/outcome (e.g 'could the receipt of the intervention at one site contaminate any other sites being investigated?')*
	4. Is there a clear plan for how the data would be incorporated in the section 'Methods > Unit of Analysis issues' • *Note that the plan cannot just be to incorporate data as it normally would, as this can overestimate or underestimate the precision of the study.*

	5. Is there a clear plan for what steps will be taken if the study does not correctly report data? • *Trials of these type are often poorly reported. Plans should be made in advance, for example, "we will use correlation coefficient/estimate from other correctly reported study/explore to enable inclusion and analysis of data from split-body trials that have been reported as parallel group comparisons. Where no estimate is available and where possible, the impact of choice of values will be explored via sensitivity analyses", etc*
	6. Is there a clear plan for studies that use a mixture of split body and parallel group assignment (e.g., some participants received two interventions, but others only received one, etc)? • *For example, depending on how data was presented, authors could plan to extract data separately, could contact study authors where data has been analysed incorrectly, subgroup according to study design / reporting, could acknowledge that including incorrectly analysed and poorly reported split-body studies could contribute more noise than truth and choose to omit from analyses and pool narratively, etc.*
	7. In the section 'Assessment of risk of bias in included studies', is there a clear plan to use the variant of the Cochrane Risk-of-Bias 2 tool for randomized trials specifically for 'crossover trials'? • *Additional considerations that should be included in the risk of bias assessment for these studies include potential carry over effects and selective reporting issues?*
Results / Data and Analysis	8. Are the studies which include data from 'Split Body Trials', clearly listed in the section 'Results > Description of Included Studies'?
	9. If the study presented dichotomous data, is it analysed using either 'Mantel Haenszel Odds Ratio' or 'Becker Balagtas marginal method'?
	10. If the study presented dichotomous data, does the forest plot show data being pooled using Log Odds Ratio and Standard Error and using the Generic Inverse Variance method? • *E.g.*

	
	11. If the study presented continuous data, does the Forest plot show data being pooled using mean difference and standard error, and using the Generic Inverse Variance method? 
	12. Can the different study designs be clearly distinguished in the forest plot? • *e.g., through use of 'footnotes' attached to relevant study labels in the forest plot, or different 'subgroups' for each type of design, etc*
	13. Have the decisions made while incorporating this data been acknowledged and explored via sensitivity analyses?
Discussion	14. Have the decisions made while incorporating this data been acknowledged and explored in the section 'Potential biases in the review process'? • *e.g., If the split-body data have been incorrectly reported then a value may be imputed to account for the clustering. There may be situations where the unadjusted data is used, ignoring any clustering, or you are unable to use the data from these trials.*
Characteristics of included Studies	15. If the included study made use of a 'Split Body' design, is it clearly acknowledged in the corresponding 'Characteristics of Included Studies' tables?
Risk of Bias Tables	16. Does the Risk of Bias assessment use the variant of the Cochrane risk-of-bias 2 tool for randomized trials specifically for 'crossover trials'? • *Additional considerations include potential carry over effects and selective reporting issues?*

Additional tables	17. If the study presented dichotomous data as log odds ratio, is there an 'Additional Table' included that presents the original raw data?

For more detailed guidance, please see;

1. **Cochrane Handbook** – section 23.2 (https://training.cochrane.org/handbook/current)

2. **Cochrane Training** – Module 6 'Analysing the Data' (https://training.cochrane.org/interactivelearning/module-6-analysing-data)

3. **Methods Papers**

   - Diana R Elbourne, Douglas G Altman, Julian PT Higgins, Francois Curtin, Helen V Worthington, Andy Vail, Meta-analyses involving cross-over trials: methodological issues, International Journal of Epidemiology, Volume 31, Issue 1, February 2002, Pages 140–149, https://doi.org/10.1093/ije/31.1.140

   - Margaret R Stedman, François Curtin, Diana R Elbourne, Aaron S Kesselheim, M Alan Brookhart, Meta-analyses involving cross-over trials: methodological issues, International Journal of Epidemiology, Volume 40, Issue 6, December 2011, Pages 1732–1734, https://doi.org/10.1093/ije/dyp345

   - Curtin F, Altman DG, Elbourne D. Meta-analysis combining parallel and cross-over clinical trials. I: Continuous outcomes. Stat Med. 2002 Aug 15;21(15):2131-44. PubMed PMID: 12210629.

4. **Example review**

   - Ahovuo-Saloranta A, Forss H, Walsh T, Nordblad A, Mäkelä M, Worthington HV. Pit and fissure sealants for preventing dental decay in permanent teeth. Cochrane Database of Systematic Reviews 2017, Issue 7. Art. No.: CD001830. DOI: 10.1002/14651858.CD001830.pub5.