

**Title: Conducting one-stage IPD meta-analysis: which approach should I choose?**

*Alternative methods for dealing with within trial clustering have been proposed for conducting IPD 'one-stage' meta-analysis. Does it matter which one is used? Will it affect the estimates and their precision?*

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*EB Methods Verdict on: Individual participant data meta-analysis of continuous outcomes: A comparison of approaches for specifying and estimating one-stage models. Statistics in Medicine. 2018;1–17.*

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Meta-analysis of studies using individual participant data (IPD) is increasingly common, and is likely to grow in popularity as a result of increased data sharing with repositories for collaborative data sharing become more established. IPD meta-analysis allows systematic reviews to pool data, beyond what is possible based only on the summary statistics, e.g. intervention effects, reported in published papers and also provides the opportunity of fitting appropriate statistical methods to obtain summary estimates.

Two-stage and one-stage meta-analyses are the commonly used statistical approaches in IPD. In the 'two-stage' meta-analysis, the analyst derives summary estimates from the IPD for each study, and then pools them together along similar lines as in a standard non-IPD meta-analysis. In a 'one-stage' meta-analysis, a single model is fitted directly using the results from each study. In this one-stage approach, it is important to make allowance for differences between studies (heterogeneity), which can be achieved by allowing study-specific effects into the statistical model. If done successfully, 'one-stage' meta-analysis appears the more attractive of the two options, as it takes full advantage of the available data from individual participants without needing to perform additional intermediate steps.

As the field has developed, various methodological approaches have been suggested for performing 'one-stage' IPD meta-analysis. The paper by Legha *et al.*, recently published in *Statistics in Medicine*, provides a comparison of these available methods, and the extent to which they affect the final estimate of effect size and its confidence interval. A particular focus of the paper is the way to allow for 'within-trial clustering'. This is a type of study-specific effect that is related to the need to account for clustering in the analysis of cluster-randomised controlled trials – participants taking part in the same study are typically drawn from a common patient group, which makes them 'more similar' than those from different studies.

For those considering conducting a one-stage IPD meta-analysis, the results of Legha's paper are reassuring. The main conclusion is that two competing approaches – named the 'stratified intercept' and the 'random intercept' – give similar results across a range of plausible scenarios, much of which

is demonstrated using simulation. Likewise, methods for estimating confidence intervals for pooled effect sizes give broadly similar levels of coverage. The decision as to which of these models to use therefore does not appear to critically influence the estimate of effect size or the precision to which it is estimated.

These findings are based on simulations of trial results with equal numbers of participants allocated to intervention and control groups, and a continuous outcome measure. As for most simulation studies, interpretations are necessarily restricted to the scenarios for which the authors have generated data. Further reassurance might be provided by a greater comparison of these methodological approaches – and indeed, a comparison with two-stage models – using real trial data.

### **EB Methods Verdict:**

The choice of methods for dealing with within trial heterogeneity as part of a one-stage IPD analysis – the ‘stratified intercept’ or the ‘random intercept’ – does not affect the findings. Either method is adequate and provide similar results on both the estimates and the confidence intervals around these estimates. This is specifically so in situations when the outcomes are continuous and the trials included balanced.

### **Declaration of interests**

### ***Acknowledgements:***

### ***References***

Legha A, Riley RD, Ensor J, Snell KIE, Morris TP, Burke DL. Individual participant data meta-analysis of continuous outcomes: A comparison of approaches for specifying and estimating one-stage models. *Stat Med*. 2018 Aug 13. doi: 10.1002/sim.7930.