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Letters to the Editor

## Response to the Letter to the Editor regarding “Methods for microbial needleless connector decontamination: A systematic review and meta-analysis”

To the Editor:

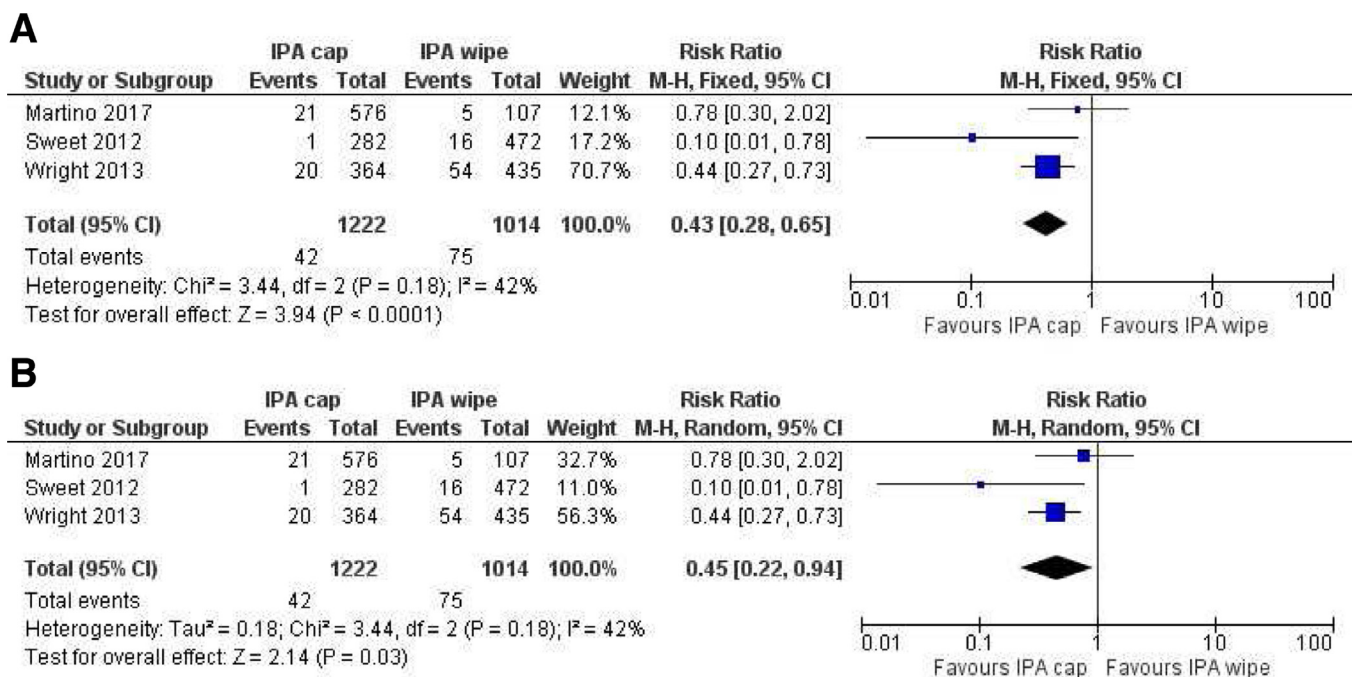
We wish to thank Glélé et al for their interest in our article, “Methods for microbial needleless connector decontamination: A systematic review and meta-analysis” by Flynn et al.<sup>1</sup> We hope that this is a demonstration of a growing interest in needleless connector decontamination and will help increase the quality and quantity of research on the topic.

Glélé et al are correct, we stated that a random effects model was used, but included the fixed effect model instead. We performed

both random and fixed effects approaches, for which the findings hardly differed (Fig 1), however we were remiss in not clarifying this in the published manuscript.

We used the Cochrane methodology (Higgins and Green<sup>2</sup> and Review Manager [RevMan version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014]) software to conduct the meta-analyses. As Glélé et al suggested, there are multiple acceptable approaches to analyze these data, nevertheless, the Cochrane Collaboration uses robust, open-source, replicable methodology.<sup>2</sup> Figure 1A shows the original meta-analysis of the alcohol impregnated cap versus the isopropyl alcohol wipe using the fixed methods approach, and Figure 1B shows the same comparison, using the random effects model. This demonstrates similar risk ratio and confidence intervals, and so in this case the decision to use a fixed or random effects model had no impact on results.

We used the Mantel-Haenszel model for meta-analysis of dichotomous variables in RevMan, as the Mantel-Haenszel model has been shown to perform well for fixed effects analysis and in the case of sparse data.<sup>3</sup> Glélé et al suggest that this is not appropriate because of the (possible) statistical heterogeneity due to low number of studies in the review (our analyses demonstrated moderate  $I^2$  values.) The decision for which meta-analysis model to use in a review is much more nuanced<sup>3</sup> than a consideration of statistical heterogeneity alone, and



**Fig. 1.** Forest plots of alcohol impregnated caps versus isopropyl alcohol wipes to prevent catheter-associated bloodstream infection (A, fixed effects approach; B, random effects approach). CI, confidence interval; IPA, isopropyl alcohol; M-H, Mantel-Haenszel model.

should incorporate elements of clinical setting or patient characteristics. The alternative models suggested by Glélé et al including the Bayesian binomial model certainly offer an alternative statistical approach to be considered for future reviews, in which randomized controlled trials are to be included.<sup>4</sup>

We concluded in our original publication, in-line with Glélé et al, the results should be interpreted cautiously. We believe this is primarily because of the lack of randomized studies, overall low sample sizes, and data quality. Decontamination products are used across the world every day to prevent severe complications such as bloodstream infection. However, our study has demonstrated that this practice is based on low quality evidence. We believe this is a clinical practice that can be causing significant harm, and innovations need to be evaluated using high quality studies, including randomized controlled trials as soon as possible.

## References

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**Conflicts of interest:** None to report.

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