A Comparison of Frequentist and Bayesian Meta-analyses of Risk Factors for Respiratory Syncytial Virus Hospitalization in Premature Infants

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BACKGROUND

• Typically, direct meta-analyses (DMAs) are performed using frequentist methods; however, these methods are generally considered to be less robust than Bayesian techniques at accounting for trial heterogeneity.⁶
• The statistical heterogeneity that characterizes meta-analyses is driven by within-study and between-study variance.
• Fixed-effects models account only for within-study variation while, in principle, random-effects models recognize both types of heterogeneity.
• Bayesian-random-effects models are superior to frequentist-random-effects models with respect to estimating between-study variance, because they do not ignore the imprecision of the variance estimates.¹

METHODS

• A systematic literature review was conducted to identify clinical studies reporting risk factors for RSV hospitalizations in otherwise healthy premature infants (32-35 WGA) who had not received RSV prophylaxis.⁴
• A frequentist DMA of odds ratios for age and siblings was conducted using fixed- and random-effects models.

RESULTS

• Five observational studies included data suitable for meta-analysis for age or sibling risk factors for both; four were cohort studies,⁷ and one was a case-control study (Table 1).⁸
• Trial heterogeneity was low for all risk factors (QP value > 0.05 and I² < 20%) (Table 2).
• Age and sibling frequent fixed- and random-effects model estimates were significant at the 95% level of confidence (Figure 1, Table 2).
• Bayesian model estimates for these risk factors were also significant (Figure 1, Table 2).
• Although frequentist and Bayesian estimates were highly consistent for fixed effects, they were not consistent for random effects; the Bayesian 95% CIs were wider (Figure 1, Table 2).

REFERENCES

5. Blanken A, Van der Kolk M, Verheugen I, Beem K, Demacker PN, Kupper CS, et al. Respiratory syncytial virus disease in premature infants: The composite risk factor combining presence of school-age siblings with index infant attendance at day care reported in Blanken et al., 2013⁶ and Figueras-Aloy et al., 2009⁷ was assumed to be a proxy for the presence of school-age siblings.

CONCLUSIONS

• This study provides additional evidence that birth close to the start of the RSV season and the presence of school-age siblings are risk factors for RSV infection requiring hospitalization for otherwise healthy premature infants.
• Meta-analyses are typically characterized by considerable between-study variation; consequently, a Bayesian random-effects model is more likely to accurately reflect the true relative effect than a frequentist-random-effects model or any type of fixed-effects model.

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The value of conventional frequentist DMA that assessed age and siblings as risk factors for RSV infection requiring hospitalization in preterm infants.

The wider CIs of the Bayesian random-effects results indicate that the frequentist approach is likely to be underestimating the variance of the risk factor relative effects.

Comparison of frequentist and Bayesian random-effects model estimates should be undertaken in other DMA studies to further explore the underestimation of uncertainty by frequentist methods.

Frequentist DMA, particularly when based on small numbers of trials, should be validated by Bayesian DMA to ensure the robustness of the results.

LIMITATIONS

• The evidence base comprised only observational study data, rather than randomized controlled trial evidence.
• Observational data are more likely to be affected by bias due to underlying unknown confounders.
• Higgins J² and Cochrane Q which were used to assess trial heterogeneity, were not available.
• Covariate adjustments were not performed to account for clinical and methodological differences between studies. However, there was no evidence of substantial trial heterogeneity for any of the risk factors.

• The composite risk factor combining presence of school-age siblings with index infant attendance at day care reported in Blanken et al., 2013⁶ and Figueras-Aloy et al., 2009⁷ was assumed to be a proxy for the presence of school-age siblings.

• The hazard ratio reported in Ambrose et al., 2004⁵ was assumed to be a proxy for the odds ratio.

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