Commentary

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Commentary on 'Multivariate meta-analysis: potential and promise'

Roger M. Harbord[*†]

I thank Jackson, Riley, and White [1] for organising an enjoyable and stimulating meeting on multivariate meta-analysis and congratulate them for providing an excellent overview of the topic. My interest in multivariate meta-analysis is chiefly in its application to diagnostic test accuracy studies, illustrated by Example 1 in the paper. In these example data, which strictly concern *prognostic* accuracy rather than its *diagnostic* accuracy, the outcome is extremely rare, occurring in only 25 of the 567 patients across all the seven studies in the authors' Table 1 and with a mere six 'false negatives'. Although this is an extreme example, sparse binomial data occur frequently in diagnostic accuracy studies. I will discuss some of the issues that arise in its analysis.

1. Visual display

Although I like the 'bubble plot' for bivariate meta-analysis in general, it appears less than optimal for displaying proportions based on sparse data; four of the studies in Example 1 have sensitivity estimates of 1, which is not clear from the authors' Figure 1 as 0.5 has been added to the cell counts when estimating the logit of the proportions, giving differing estimates. The circles used to indicate the studies in the authors' Figure 2, produced by the STATA (StataCorp, College Station, Texas, USA) package `metandi` (authors' ref [30]), do not display the differences between the precision of estimated sensitivity and specificity. I have experimented with alternatives which give a reasonable visual indication that the specificities are much more precisely estimated than the sensitivities and that, while the specificities are clearly heterogeneous, there is little information on the sensitivities other than that they are reasonably high. It follows that estimates of the variance of sensitivity and its correlation with specificity will be highly imprecise: one might question whether a bivariate analysis is worthwhile in such circumstances.

2. Bayesian analysis

When there are few studies, and in particular when their data are sparse, fitting all five parameters of a bivariate model by maximum likelihood can present problems. A Bayesian approach that introduces prior information, particularly for the variance parameters, then becomes attractive. The authors briefly mention that Paul *et al.* (authors' ref [36]) recently presented a method for Bayesian meta-analysis of diagnostic test accuracy using integrated nested Laplace approximations (INLA), and I believe this method shows considerable promise for increasing the routine use of such analyses among those who are not comfortable with Markov chain Monte Carlo-based packages such as WINBUGS (Imperial College, London and Medical Research Council, Swindon, UK). I agree that suitable 'vague' priors are hard to specify; Paul *et al.* suggest as 'mildly informative' priors a normal prior for the Fisher z-transform of the correlation and inverse gamma priors on the variances, while others, e.g. [2], favour half-normal priors for the standard deviations, which are also available in the INLA software package [3], although this

University of Bristol, School of Social and Community Medicine, Canynge Hall, 39 Whatley Road, Bristol, BS8 2PS, United Kingdom

**Correspondence to: Roger M. Harbord, University of Bristol, School of Social and Community Medicine, Canynge Hall, 39 Whatley Road, Bristol, BS8 2PS, United Kingdom.*

†E-mail: roger.harbord@bristol.ac.uk

is currently incompletely documented. Other alternatives, such as the half-t or half-Cauchy favoured by Gelman [4], are conceptually possible with the INLA approach but are not currently implemented in the associated software package. In addition, as sensitivity and specificity are in general negatively correlated across studies but this parameter is particularly hard to estimate [5], it may be reasonable to give it a stronger prior and centre it away from zero. Whether suitable priors can be found for routine meta-analysis, such as those in systematic reviews recently begun by the Cochrane Collaboration [6], deserves further investigation. In addition, the INLA package might benefit from a purpose-built front end for diagnostic meta-analysis to make it easier to use and to interpret and present the output.

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