Incorporating measures of study similarity in a meta-analysis

Tom M. Palmer, John R. Thompson, Martin D. Tobin

Centre for Biostatistics and Genetic Epidemiology,
Department of Health Sciences,
University of Leicester,
United Kingdom

email: tmp8@le.ac.uk

Hypothesis

In a meta-analysis studies that estimate different underlying effects are said to be heterogeneous. Heterogeneity can be due to differences in study design, outcome definitions or the characteristics of the study populations. Tests for heterogeneity are common but investigations of its causes are not; such investigations improve both the clinical relevance and the scientific understanding of a meta-analysis (Thompson 1994).

Methods

We constructed a distance measure that captures the similarity between studies in terms of quality, design and subjects. The studies were plotted using Multidimensional Scaling and then the effects were estimated using models that assume that studies that are close together should give similar estimates.

Multidimensional Scaling (MDS)

MDS is a dimension reduction technique in which dissimilarities between observations are represented in a lower dimensional space (Mardia et al. 1979).

Conditional Autoregressive (CAR) Modelling

In the proposed method the similarity measures are input into the variance structure of a CAR model (Besag 1974). As such the variance of the effect estimate was modelled as dependent upon the distance between the studies under MDS. The Multivariate Normal Distribution was used for the study effects (Kaiser et al. 2002).

Results

The methods were applied to a meta-analysis investigating the association between lung cancer and exposure to Environmental Tobacco Smoke (ETS) (Wolpert and Mengersen 2004).

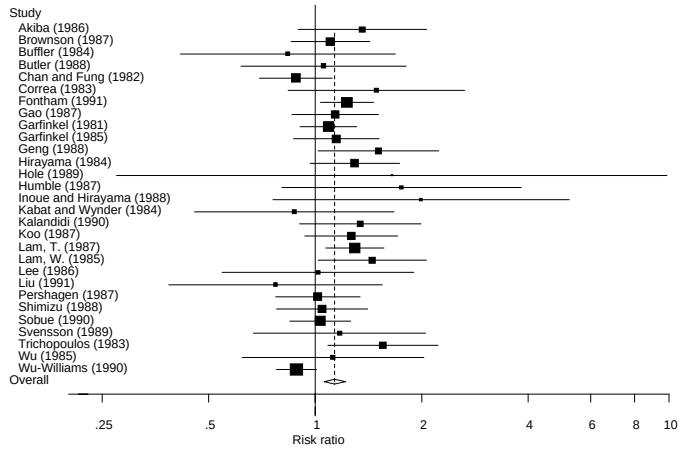

Figure 1. Forest plot of the ETS and lung cancer meta-analysis

	Relative Risk	Lower 95% C.I. limit	Upper 95% C.I. limit	
Fixed effects pooled RR	1.11	1.05	1.17	
Random effects pooled RR	1.14	1.06	1.22	
$Tau^{2\,\dagger}$	0.008	0	0.027	$Q(X^2)$ P=0.095
I^2 statistic	27	0	54	

† The 95% confidenc interval for tau-squared used the Q-Profile method (Viechtbauer 2006).

Table 1. Results of the ETS and lung cancer meta-analysis

Study design, year of publication, study location and study quality were summarised by the MDS dimension reduction technique. Categorising the MDS configuration plot by one of these variables showed its impact on the MDS.

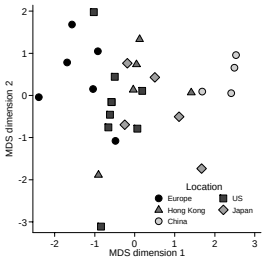

Figure 2. MDS configuration plot

There was some clustering by location.

The parameters in the CAR model were estimated using the Newton-Raphson algorithm.

Parameter	Estimate	Std. Err.	95% Confidence Interval	
Theta	-3.92	0.64	-5.16	-2.67
Lambda	1.10	0.09	0.92	1.28
Eta	0.06	0.01	0.04	0.09
Tau^2	0.02		0.01	0.07

Table 2. Maximum likelihood estimates for the CAR model

The CAR model results were most similar to the fixed effects analysis and showed that exposure to ETS gave a 10% (95%CI: -8%, 28%) increased risk of lung cancer.

The CAR model was used to produce a predicted surface of effect estimates.

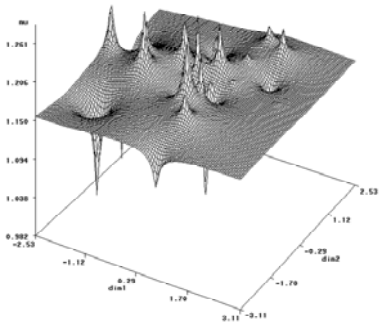

Figure 3. Predicted surface of effect estimates from the CAR model

Conclusions

The use of similarity measures such as MDS is a simple and effective way of modelling sources of heterogeneity in a meta-analysis. This work is most informative when two multidimensional scaling dimensions are plotted along with the study effect estimates to produce a three dimensional representation of the conditional autoregressive model.

References

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