A comparison of one vs two stage dose-response meta-analysis

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Conclusions

One and two stage dose-response meta-analysis provide the same curves.

A one stage approach, however, allows:

- simultaneous estimation of both study-specific and pooled trend;
- inclusion of additional studies with only few data points;
- estimation of more flexible curves;
- interaction analysis with study level covariates;
- comparison of alternative models using information criteria.

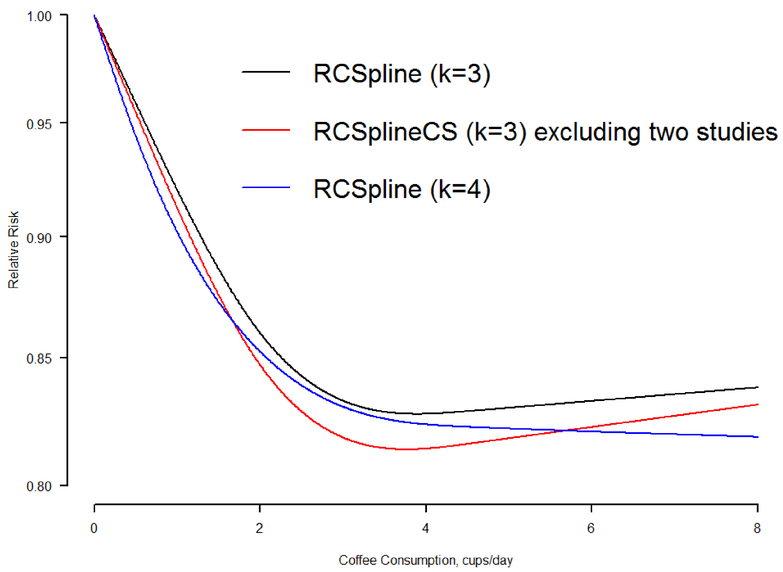

Figure 1. Predicted dose-response curves for a dose-response meta-analysis between coffee consumption and all-cause mortality. Models compared are restricted cubic splines with 3 knots, exclusion of studies with less than three exposure categories, and 4 knots.

Introduction

Dose-response meta-analyses are increasingly popular. A standard approach is a two-stage analysis: study-specific trend estimation and pooling of study-specific dose-response coefficients. An alternative one stage technique has never been fully described.

Aims

To investigate analogies and dissimilarities between the one- and two-stage dose-response meta-analysis using a real example.

One vs two stage approaches

We use restricted cubic splines (RCSpline) with k = 3 knots to examine the shape of the association between coffee consumption and mortality, based on *I* studies (*i = 1, …, I*)

Two-stage: $ln(RR_{ij}) = \beta_{1i}x_{1ij} + \beta_{2i}x_{2ij} + \varepsilon_{ij},\ j = 1, \dots, n_i$

$$(\hat{\beta}_{1i}, \hat{\beta}_{2i})^T \sim N\left((\bar{\beta}_1, \bar{\beta}_2)^T, \mathbf{\Psi}\right)$$

One-stage: $ln(RR_{ij}) = (\bar{\beta}_1 + u_{1i})x_{1ij} + (\bar{\beta}_2 + u_{2i})x_{2ij} + \varepsilon_{ij}$

$\varepsilon_{ij} \sim N(0, \mathbf{\Sigma}_i)$; $\quad (u_{1i}, u_{2i})^T \sim N(0, \mathbf{\Psi})$

In the two-stage approach, studies with less than three exposure categories are excluded (e.g. second study in Table 1).

id	author	cases	n	dose	RR	(95% CI)
1	LeGrady et al.	57	249	0.5	1.00	-
		136	655	2.5	0.75	(0.57, 0.99)
		144	619	4.5	0.84	(0.64-1.10)
		115	387	6.5	1.09	(0.83-1.43)
2	Nilsson et al.			0.0	1.00	-
				2.0	0.99	(0.86-1.14)

Table 1. Aggregated data for two studies included in a dose-response meta-analysis between coffee consumption and all-cause mortality.

Results

Excluding two studies with less than three exposure categories, both approaches provide the same coefficients estimates (Table 2).

The one-stage analysis avoids exclusion of such studies (Table 2) and may evaluate even more flexible curves, e.g. more knots in a spline model. The RCSpline with k=4 knots, however, has a higher AIC, suggesting that the simpler (k=3) properly fits the data (Figure 1). The same comparison can not be performed in a two-stage analysis.

analysis	excl.	$\hat{\beta}_1$	$\hat{\beta}_2$	$Var(\hat{\beta}_1)$	$Cov(\hat{\beta}_1\hat{\beta}_2)$	$Var(\hat{\beta}_2)$
two-stage	yes	-0.09216	0.08666	0.00019	-0.00018	0.00019
one-stage	yes	-0.09217	0.08665	0.00019	-0.00018	0.00019
one-stage	no	-0.08357	0.07714	0.00020	-0.00018	0.00017

Table 2. Dose-response coefficients estimates for one- and two-stage dose-response meta-analysis between coffee consumption and all-cause mortality.

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