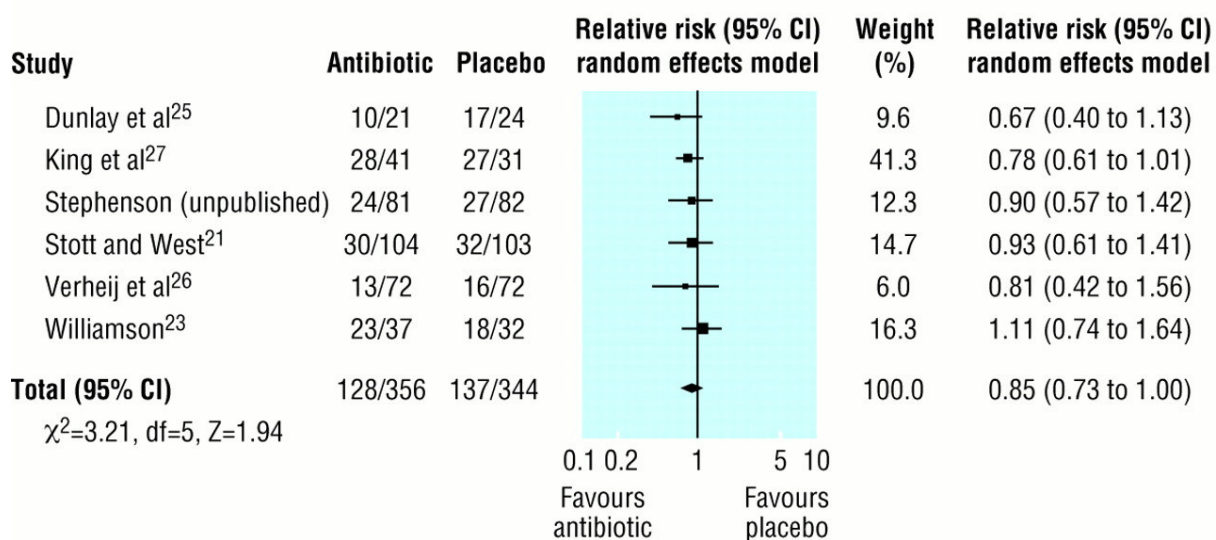


A meta-analysis puzzle solved?

In the exercise on “Meta-analysis”, we looked at some forest plots from Fahey, Stocks, and Thomas, (*BMJ* 1998; **316**: 906-910) “Quantitative systematic review of randomised controlled trials comparing antibiotic with placebo for acute cough in adults”.

Here is their Figure 2:

Proportion of subjects with productive cough at follow up

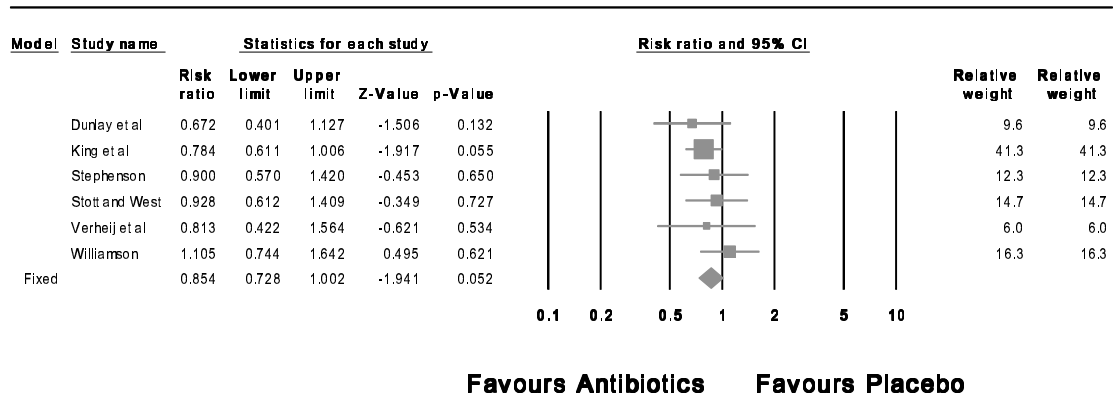


It is striking that the sizes of the square symbols for the point estimates bear no relation to the weights and that the diamond for the total does not correspond to the stated confidence interval, in that it crosses the vertical line through 1.0.

I extracted the data:

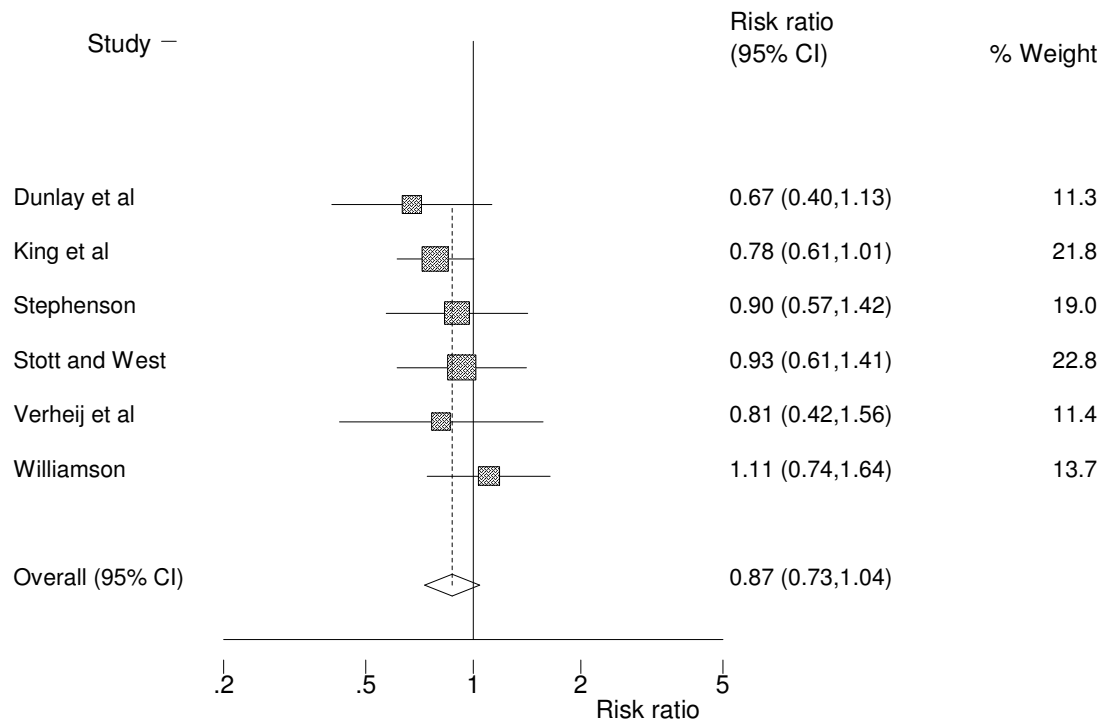
| Study | Antibiotic | | Placebo | |
|----------------|------------------|-----------------|------------------|-----------------|
| | Cough unresolved | Number in group | Cough unresolved | Number in group |
| Dunlay et al | 10 | 21 | 17 | 24 |
| King et al | 28 | 41 | 27 | 31 |
| Stephenson | 24 | 81 | 27 | 82 |
| Stott and West | 30 | 104 | 32 | 103 |
| Verheij et al | 13 | 72 | 16 | 72 |
| Williamson | 23 | 37 | 18 | 32 |

I put these into Comprehensive Meta-Analysis 2 (CMA-2) and got this forest plot:



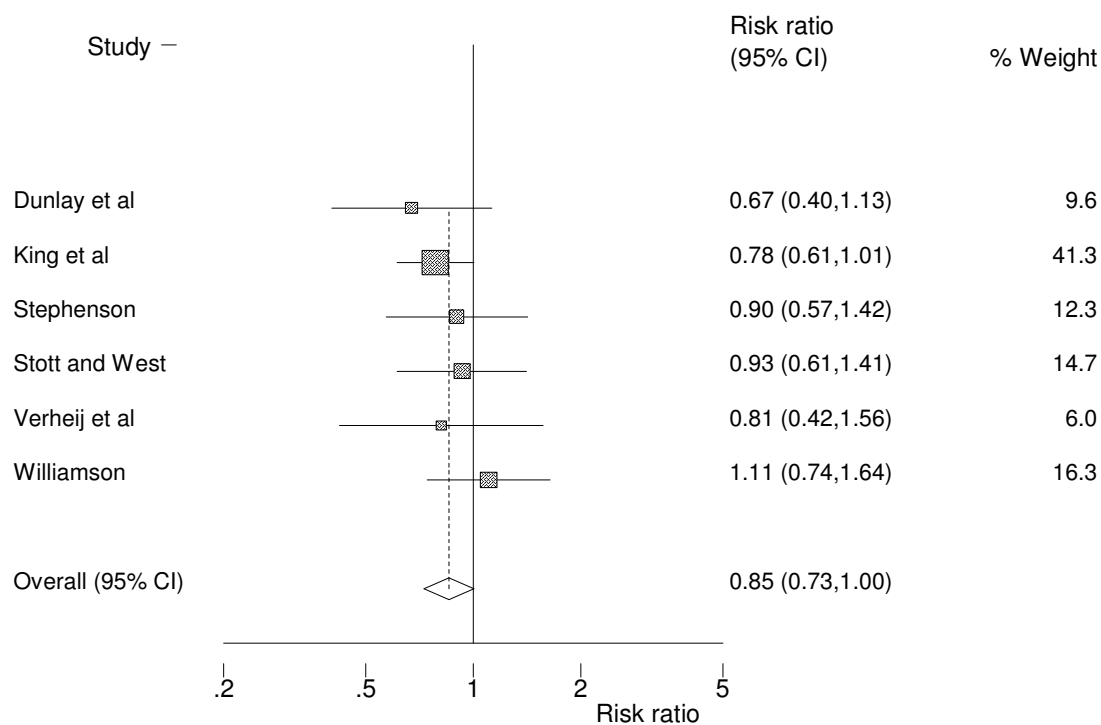
CMA-2 produced this graph using inverse variance weighting, the default method in CMA-2. I persuaded CMA-2 to put the weights on the forest plot. CMA-2 insists on putting relative weights for both fixed and random effects. This is why the numbers appear twice. For these data, the weights are the same using both fixed and random effects, because there is no evidence of heterogeneity. These weights are the same as those given in the original paper. They were obtained using the inverse variance method of weighting, which is the default method in CMA-2. The graph is quite different from the original paper, however.

I then analysed the same data using the command metan in Stata. To my great surprise, I got a different set of weights and a different picture:



The weights are completely different and appear to correspond much more closely to the forest plot of Fahey *et al.* Also the interval estimate for the combined risk ratio is 0.73 to 1.04, crossing the line through 1.0, as does the Fahey *et al.* graph. The metan command uses the Mantel-Haenszel method of weighting as the default.

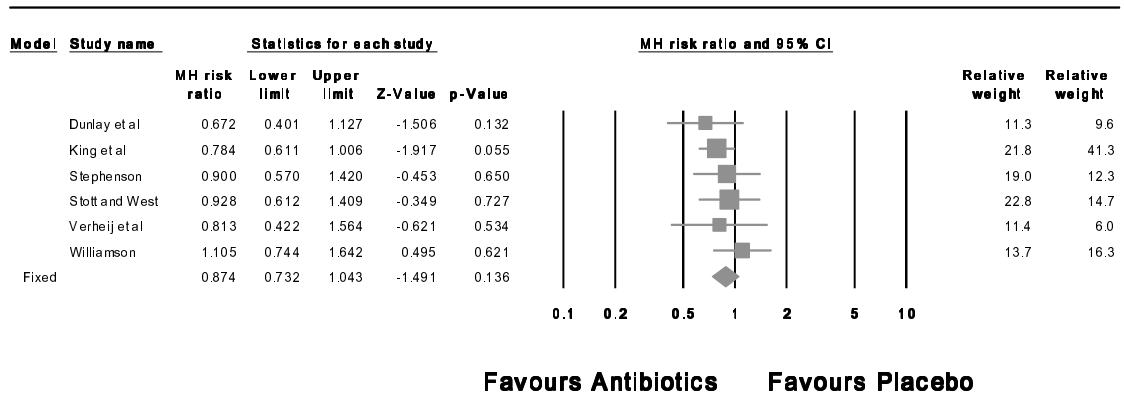
Inverse weighting is an option for metan. Here is the plot using inverse variance weighting:



These weights and the combined estimate correspond to those in Fahey *et al.* and to the default weights produced by CMA-2. The graph does not and the sizes of the squares and the diamond are different, and like those from CMA-2.

Stata offers two other methods of estimation using random effects, which for these data both produce weights and estimates identical to those by inverse variance weighting.

Finally, I tried the using the Mantel-Haenszel method, which is an option, in CMA-2:



Note that the second lot of weights, for the random effects model, are the same as those for the fixed and random effects models using minimum variance weighting.

My guess was that what had happened was that when the BMJ redrew the graph, they used the Mantel-Haenszel weights and then put the authors' data in as text separately, using what I guess to be their original inverse-variance weights.

I then emailed Prof. Fahey. He told me that the original draft paper which was submitted to *BMJ* did not have any forest plots, only tables of the meta-analyses. The forest plots were added somewhere in the review and editing process.

Martin Bland

23 February 2010