University of York Department of Health Sciences
M.Sc. Module: Systematic Reviews
Suggested answers: Meta-analysis

(a) *What kind of study is this?* This is a systematic review and meta-analysis.

(b) *In the summary we read 'Resolution of cough was not affected by antibiotic treatment (relative risk 0.85 (95% confidence interval 0.73 to 1.00)),' What is a relative risk? What does the 95% confidence interval tell us?* This is actually the relative risk of cough ***not*** resolving (Figure 2). The relative risk of non-resolution of cough is the proportion of those treated with antibiotics whose coughs did not resolve divided by the proportion on placebo whose coughs did not resolve. The confidence interval tells us that we estimate that in the population of patients with cough, the relative risk of non-resolution is between 0.73 and 1.00.

(c) *Why do the authors say that resolution of cough was not affected? Do you agree with this interpretation?* They say this because the confidence interval just includes 1, the null hypothesis value for the relative risk. I disagree with the interpretation. There could be a relative risk as small as 0.73, indicating a modest advantage to antibiotics, and the null value only just gets into the confidence interval. They are interpreting 'not significant' as meaning 'no difference', a classic mistake.

(d) *What kind of graphs are shown in the figures?* These are forest plots.

(e) *In the figures, what kind of scale is used for the relative risks? Why are these scales used here?* The relative risk is on a logarithmic scale. The log scale is used because the confidence intervals are calculated for the log relative risks. Also, a relative risk of 0.5 in one direction (halving) corresponds to a relative risk of 2 in the other direction (doubling). On the log scale these become equal and opposite differences.

(e) *In the figures, what do the squares and the horizontal lines represent?* The square represent the point estimates, the relative risks observed in the studies. The lines represent the confidence intervals. The authors do not say to what the squares are proportional. They are not proportional to the sample sizes or to the weights. (The weights are proportional to the inverse of the variances of the log relative risks.) I think these figures are badly drawn.

(f) *In the figures, what do the diamond or lozenge shapes represent?* The diamonds represent the combined estimates of the relative risks and their confidence intervals. The thickest point of the diamond marks the position of the point estimate of the relative risk and the width of the diamond represents the confidence interval.

(g) *Do you think the diamonds are drawn correctly?* They are not drawn correctly. The confidence interval in figure 2 should just touch 1.0, not overlap it, and in figure 3 the interval should overlap 1.0. not just touch it!

(h) *In the analysis of side effects of treatment, the authors say: 'When the one trial which reported an increase in side effects from placebo was excluded, the heterogeneity between trials was reduced and side effects were significantly associated with antibiotic use'. What does 'heterogeneity' mean here? Do you think the author's approach is reasonable?* 'Heterogeneity' means that it was not plausible that there was a common difference for all trials. The approach is to exclude the trial they don't like and repeat the analysis. I think this is very dubious. No other reason is given. To then conclude that there is a difference seems unjustified to me.

(i) *What are the main conclusions as whether antibiotics should be used in the treatment of acute cough? Are they justified by the data?* The authors conclude that treatment with antibiotics is unlikely to alter the course of illness in most adult patients presenting with acute cough and that a minority may have side effects from treatment. The first conclusion seems too strong to me, though I would accept that the benefits of antibiotics are modest. The second conclusion could have been drawn without any data at all! Perhaps they could say that the risk of side effects with antibiotics may be slightly less than on placebo (which is plausible as the antibiotics may prevent some things which might be called side effects but which are in fact consequences of the disease) or may be more than doubled.