Methods to be used in reviews – CCG standards

Data analysis

The number of outcomes should be kept to a minimum, as increasing the number of outcomes increases the chance of finding spurious results. Both potential harms and benefits of the intervention should be taken into consideration.

Analyses may be narrative, such as a structured summary and discussion of the studies' characteristics and findings, or quantitative, i.e. involving a meta-analysis. Authors of reviews are encouraged to include someone with statistical knowledge of meta-analyses / systematic reviews, or search for this expertise locally. For more information we refer to the Cochrane Handbook for Systematic Reviews of Interventions, but please note the following:

- Survival data are time-to-event data. Time-to-event data can never be analyzed as a continuous outcome, i.e. using mean or median time-to-event.

- Sometimes studies present for example the n-year survival in both intervention groups, i.e. a dichotomous outcome. However, time-to-event data can only be analyzed as a dichotomous outcome if the status of all patients in a study is known at a fixed time point, i.e. none of the patients is lost-to-follow-up. This is rarely the case. The Cochrane Childhood Cancer Group only allows analyzing time-to-event data as a dichotomous outcome if it is absolutely certain that the status of all patients in a study is known at the fixed time point. In all other cases time-to-event data should be expressed as a hazard ratio, if necessary using Parmar’s method to obtain all data needed.

- Reviewers are free to discuss time-to-event data as a dichotomous outcome in the discussion section of their review, but only when they state the problems associated with such an analysis. For more information on time-to-event data see: Van Dalen EC, Tierney JF, Kremer LC. Tips and Tricks for understanding and using SR results. No. 7: time-to-event data. Evid-Based Child Health 2007; 2: 1089-90.

- When for a particular outcome only one study is available and there are no events in one of the treatment groups, it is impossible to calculate a relative risk/risk ratio or odds ratio. The Review Manager software gets round this by adding half a case to the treatment group with no events. If you are doing a meta-analysis with many studies and most of these studies have events in both treatment groups, adding an extra half event in one treatment group doesn’t make much difference to the overall estimate of the relative risk/risk ratio or odds ratio. However, if you have only one study and you add half an event to one treatment group, the relative risk/risk ratio or odds ratio, its 95% CI and the p-value are misleading. For these outcomes you should calculate the Fischer’s exact p instead (it is not possible to perform this calculation within the Review Manager software).

- Cochrane Childhood Cancer uses $I^2>50\%$ as the cut-off value for considerable heterogeneity. If possible intention-to-treat analyses should be performed; if this is not possible an explanation should be provided.