Joint EFSA / EBTC Colloquium

Briefing notes DG2: Bias-adjusted meta-analysis

1. Background

Evidence appraisal typically involves assessment of the validity or risk of bias (RoB) of each individual study. This is normally done using appraisal tools aimed at minimising subjectivity and increasing consistency and transparency in the process.

The available tools provide little or no guidance on how to assess the *impact* of threats to validity on the study results. For instance, most of them do not address the direction and magnitude of the internal biases identified within the tools. Studies are normally grouped according to different RoB categories (e.g. high, some concerns, low) and typically the result of study appraisal is addressed through sensitivity analyses or exploratory subgroup analyses.

It is also important to assess the relevance of studies to the research question at hand, for example in terms of populations studied and exposures measured. Differences in results that arise from these factors might be regarded as external biases. Again, subgroup analyses are often used to address these, but these tend to separate out the evidence rather than to integrate it.

Methods are available for synthesising evidence while accounting for internal and external biases and for the uncertainty about them. This is generally known as bias-adjusted meta-analysis, although it is rarely used in practice. Information about the biases may come from empirical evidence from an external collection of meta-analyses (Welton et al., 2009), expert knowledge elicitation (Turner et al., 2009) or a combination of the two (MRC Center Cambridge, 2017).

2. Objective

As a follow up of lecture 3, the objective of this group is to discuss the available quantitative approaches to combing evidence within a stream, accounting for all possible sources of bias and uncertainty.

The discussion will focus on:

- Comparing currently available methodologies for bias adjustment: advantages and limitations;
- Comparing these methodologies to the traditional meta-analytical approaches: benefits and issues;
- Identifying sources of evidence to inform bias adjustments, and how to account appropriately for all sources of uncertainty when making the adjustments;
- Possible solutions to the issues related to the use of currently available methodologies for bias adjustment;
- Recommendations for future developments in the field.

3. References

MRC Center Cambridge 2017. Development of a method for adjusting trial results for biases in meta-analysis: combining generic evidence on bias with detailed trial assessment. Available online: http://gtr.rcuk.ac.uk/projects?ref=MC_EX_MR%2FK014587%2F1

Turner RM, Spiegelhalter DJ, Smith GC and Thompson SG, 2009. Bias modelling in evidence synthesis. J R Stat Soc Ser A Stat Soc, 172, 21-47

Welton NJ, Ades AE, Carlin JB, Altman DG and Sterne JAC, 2009. Models for potentially biased evidence in meta-analysis using empirically based priors. Journal of the Royal Statistical Society: Series A (Statistics in Society), 172, 119-136

DG2	Bias-adjusted meta-analysis
Chair	Sofia Dias, University of Bristol, UK
Follow-up of lecture 3	Recent developments for combining evidence within evidence streams: bias-adjusted meta-analysis Julian Higgins, University of Bristol, UK
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