

Workshop: Developing Summary of Findings (SoF) tables for Cochrane Reviews

Exercise

- Complete exercise using a Cochrane Review
- Work in small groups
- Select someone to report any comments to the whole group
- Watch the time
- Read the following instructions

1. Familiarize yourself with the review (if you are not yet familiar with it): read the abstract
2. Identify **1 main comparison** to work on (fill in top of blank SoF on page 6)
3. Select up to **7 important outcomes** for this comparison (10 MINUTES)
 - a) Generate a list of relevant outcomes (see **worksheet 1** on page 2)
Consider:
 - **PRIMARY OUTCOMES:** List outcomes that the authors of the systematic review identified as primary outcomes (see CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW)
 - **REPORTED OUTCOMES:** Add other outcomes for which data are reported (see RESULTS and ABSTRACT)
 - **IMPORTANT OUTCOMES:** Add any other outcomes that were not reported in the review, but you think might be important to someone making a decision to use or not to use the interventions being the subject of the review (make sure to include both benefits and adverse effects and to include costs, if relevant)
 - b) Rank importance of the outcomes and find consensus within your small group about which outcomes are important enough to be included in the SoF table (worksheet 1)
 - c) Choose up to 7 outcomes that you think are most important to patients and should be included in the SoF table; transfer them to a blank SoF table (see **worksheet 3** on page 6).
4. Choose one outcome to work on (choose another if time permits)
5. **Assess the quality of evidence** for this outcome according to the GRADE approach
 - a) Use **worksheet 2** (page 3) to mark the quality of the evidence for the outcome
 - b) Consult the criteria for assessing the quality of evidence on page 4 and 5
 - c) Find the relevant information in the following sections of the review: DESCRIPTION OF STUDIES, METHODOLOGICAL QUALITY, DISCUSSION and RESULTS, RISK OF BIAS TABLE.
 - d) Fill in the Quality of the Evidence column in the SoF with the GRADE.
6. **Summarise the findings** for the outcome. Calculate numbers and fill in the SoF
 - a) Find the results for the outcome in the RESULTS section or META-ANALYSIS GRAPHS.
 - b) Consult “How to calculate numbers for SoF” on page 7 and 8.

Materials from Summary of Findings Workshop at 16th Cochrane Colloquium 2008. Developed by Holger Schünemann, Elie Akl, Jan Brozek, Signe Flottorp, Gordon Guyatt, Regina Kunz, Andy Oxman, Nancy Santesso, Gunn Vist
If you are interested in using these materials, contact Holger Schunemann at support@gradepr.org

Worksheet 1: List of outcomes from the systematic review

Title of the systematic review: _____

Comparison: _____

Choose **up to 7** most important outcomes to be included in the SoF table. Transfer the selected outcomes into the blank SoF sheet (see **worksheet 3**).

Rate the relative importance for each outcome on a 9 point scale ranging from 1 (not important) to 9 (critical).

1 – 3 **not important** and not included in the SoF table

4 – 6 **important** but not critical for making a decision (inclusion in the SoF table may depend on how many other important outcomes there are)

7 – 9 **critical** for making a decision and should definitely be included in the SoF table

Outcome	Importance	Include in SoF table?	
		Yes	No
1.		Yes	No
2.		Yes	No
3.		Yes	No
4.		Yes	No
5.		Yes	No
6.		Yes	No
7.		Yes	No
8.		Yes	No
9.		Yes	No
10.		Yes	No
11.		Yes	No
12.		Yes	No
13.		Yes	No
14.		Yes	No

Worksheet 2: Assessing the quality of evidence across studies for an outcome

(See criteria and definitions on page 5 of this handout.)

Quality criteria	Rating (circle one for each criterion)	Footnotes (explain reasons for downgrading)	Quality of the evidence (Circle one per outcome)
1st Outcome:			
Limitations in design	No serious (-1) very serious (-2)		⊕⊕⊕⊕ High
Inconsistency	No serious (-1) very serious (-2)		⊕⊕⊕○ Moderate
Indirectness	No serious (-1) very serious (-2)		⊕⊕○○ Low
Imprecision	No serious (-1) very serious (-2)		⊕○○○ Very Low
Reporting Bias	Unlikely likely (-1) very likely (-2)		⊕○○○ Very Low
2nd Outcome:			
Limitations in design	No serious (-1) very serious (-2)		⊕⊕⊕⊕ High
Inconsistency	No serious (-1) very serious (-2)		⊕⊕⊕○ Moderate
Indirectness	No serious (-1) very serious (-2)		⊕⊕○○ Low
Imprecision	No serious (-1) very serious (-2)		⊕○○○ Very Low
Reporting Bias	Unlikely likely (-1) very likely (-2)		⊕○○○ Very Low
3rd Outcome:			
Limitations in design	No serious (-1) very serious (-2)		⊕⊕⊕⊕ High
Inconsistency	No serious (-1) very serious (-2)		⊕⊕⊕○ Moderate
Indirectness	No serious (-1) very serious (-2)		⊕⊕○○ Low
Imprecision	No serious (-1) very serious (-2)		⊕○○○ Very Low
Reporting Bias	Unlikely likely (-1) very likely (-2)		⊕○○○ Very Low

GRADE quality assessment criteria

Downgrading is cumulative, but the lowest level of quality is: very low ⊕○○○

Limitations of design:

- lack of allocation concealment
- lack of blinding (particularly if outcomes are subjective and their assessment highly susceptible to bias)
- large loss to follow-up
- failure to adhere to an analysis according to intention-to-treat principle
- stopping a trial early for benefit
- Selective reporting of events: investigators neglect to report outcomes that they have measured (typically those for which they observed no effect).

Inconsistency:

Widely differing estimates of the treatment effect (i.e. heterogeneity or variability in results) across studies suggest true differences in underlying treatment effect. When heterogeneity exists, but investigators fail to identify a plausible explanation, the quality of evidence should be downgraded by one or two levels, depending on the magnitude of the inconsistency in the results.

Inconsistency may arise from differences in:

- populations (e.g. drugs may have larger relative effects in sicker populations)
- interventions (e.g. larger effects with higher drug doses)
- outcomes (e.g. diminishing treatment effect with time).

Indirectness:

There are two types of indirectness.

1. Indirect comparison – occurs when a comparison of intervention A versus B is not available, but A was compared with C and B was compared with C. Such trials allow indirect comparisons of the magnitude of effect of A versus B. Such evidence is of lower quality than head-to-head comparisons of A and B would provide.

2. Indirect population, intervention, comparator, or outcome – the question being addressed by the authors of a systematic review is different from the available evidence regarding the population, intervention, comparator, or an outcome.

Imprecision:

Results are imprecise when studies include relatively few patients and few events and thus have wide confidence intervals around the estimate of the effect.

1. For dichotomous outcomes

- total (cumulative) sample size is lower than the calculated optimal information size (OIS)
- total number of events is less than 300
- 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both negligible effect and appreciable benefit or appreciable harm. GRADE suggests that threshold for "appreciable benefit" or "appreciable harm" that warrants downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

Exception

When event rates are very low, 95% confidence intervals around relative effects can be very wide, but 95% confidence intervals around absolute effects may be narrow. Under such circumstances one may not downgrade the quality of evidence for imprecision.

2. For continuous outcomes

- 95% confidence interval includes no effect and the upper or lower confidence limit crosses the minimal important difference (MID), either for benefit or harm
- if the MID is not known or use of different outcomes measures required calculation of an effect size (ES), we suggest downgrading if the upper or lower confidence limit crosses an effect size of 0.5 in either direction.

Publication Bias

Publication bias is a systematic underestimate or an overestimate of the underlying beneficial or harmful effect due to the selective publication of studies (publication bias). That is, investigators fail to report studies they have undertaken (typically those that show no effect)

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Quality of evidence across studies for the outcome

- ⊕⊕⊕⊕ **High** Further research is very unlikely to change our confidence in the estimate of effect or accuracy.
- ⊕⊕⊕○ **Moderate** Further research is likely to have an important impact on our confidence in the estimate of effect or accuracy and may change the estimate.
- ⊕⊕○○ **Low** Further research is very likely to have an important impact on our confidence in the estimate of effect or accuracy and is likely to change the estimate.
- ⊕○○○ **Very low** Any estimate of effect or accuracy is very uncertain.

Worksheet 3: Summary of Findings table

[Title:]						
Patient or population:						
Settings:						
Intervention:						
Comparison:						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
				()		
				()		
				()		
				()		
				()		
				()		
				()		

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

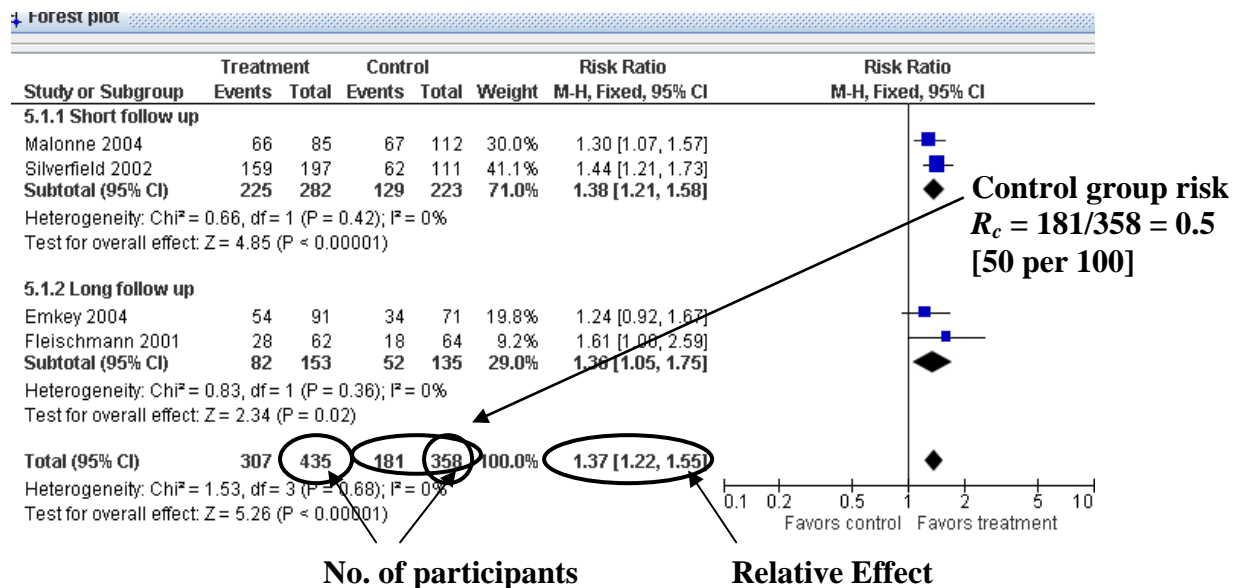
CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[Footnotes:]

How to calculate numbers for SoF

Meta-analysis graph for a DICHOTOMOUS OUTCOME



Assumed risk

Calculate the control group risks (ideally this would be the median control group risk or any other plausible estimate of risk in the population of interest) of the included studies to determine the low risk population risk or high risk population risk to include in the SoF.

Alternatively the mean control group risk (R_c) can be included in the SoF

$$R_c = \frac{\sum n_c}{\sum N_c}$$

where n_c is the number of events in control groups and N_c is the total number of participants in the control groups

Relative effect

Pull relative effect directly from the meta-analysis and include in the SoF table.

Corresponding risk

When using a Risk Ratio, multiply the Assumed Risk by the Risk Ratio.

Do the same with the confidence interval limits.

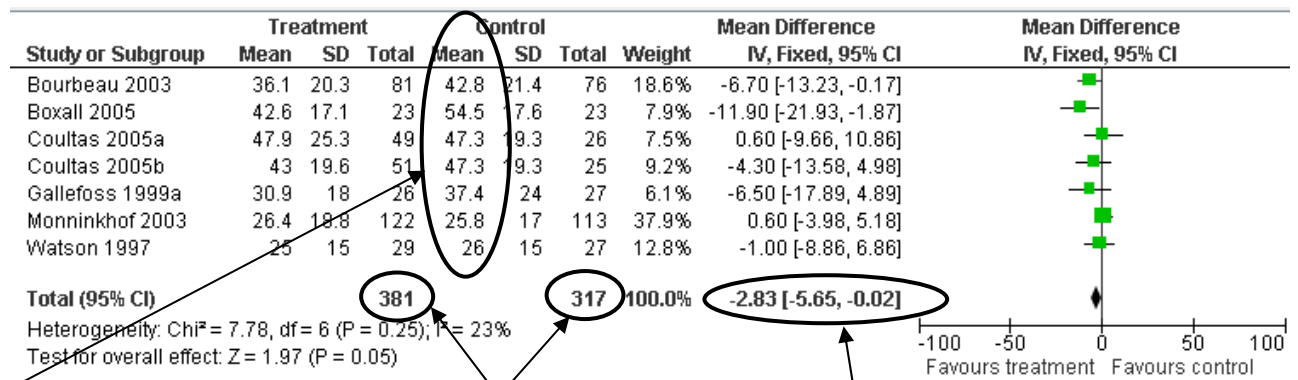
When using a Odds Ratio, convert OR to RR and then multiply the Assumed Risk by the Risk Ratio.

$$RR = \frac{OR}{1 - (R_A \times (1 - OR))} \quad \text{where } R_A \text{ is the assumed risk.}$$

Confidence intervals

To calculate the confidence intervals of the corresponding risk use the confidence limits of the relative effect.

Meta-analysis graph for a CONTINUOUS OUTCOME using Mean Difference



Range of control group scores

No. of participants

Mean difference

Assumed Risk

Determine the range of scores at end of study in the control group. In example, 26 to 55.

Corresponding Risk

Use value for Mean Difference. In example, 2.8 lower (5.7 to 0.2 lower).