

Supplemental Data C: GRADE Criteria

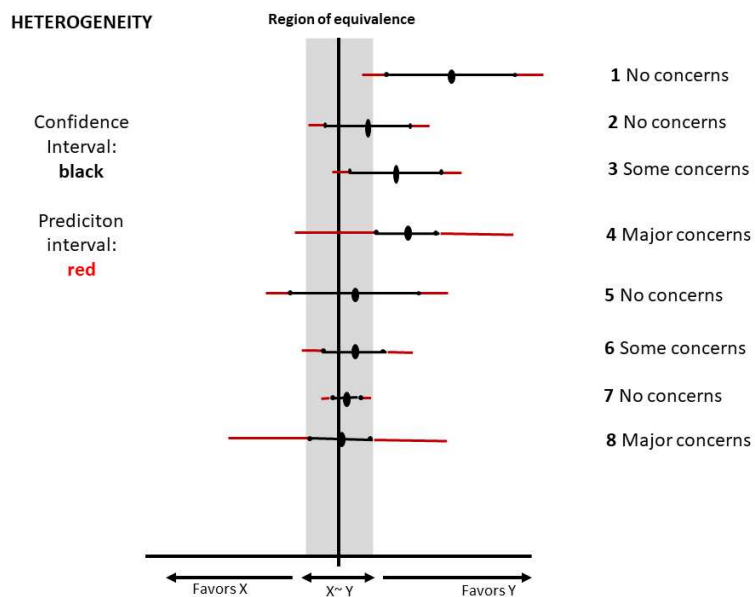
1. Limitations in study design – Cochrane Risk of Bias Tool 1.0

- Selection bias (random sequence generation, allocation concealment, group similarities at baseline);
- Performance bias (blinding of participants and/or healthcare providers);
- Attrition bias (drop outs and intention-to-treat analysis);
- Detection bias (blinding of the outcome assessors and timing of outcome assessment);
- Reporting bias (selective reporting).

We downgraded the quality of the evidence:

- By one level if >50% of participants were from studies with selection bias **and** performance bias.
- Inadequate randomization and lack of blinding may lead to an exaggeration of the intervention effect estimates [1–3].

Unexplained heterogeneity or inconsistency of results



- Pre-defined area/range of equivalence: We define a range of equivalence of SMD -0.5 to 0.5 [4].
- Downgrade two levels if there is a major concern and one level if there are some concerns.
- If there are very few trials, the amount of heterogeneity is poorly estimated and prediction intervals are unreliable, we will downgrade based on reference priors [5].

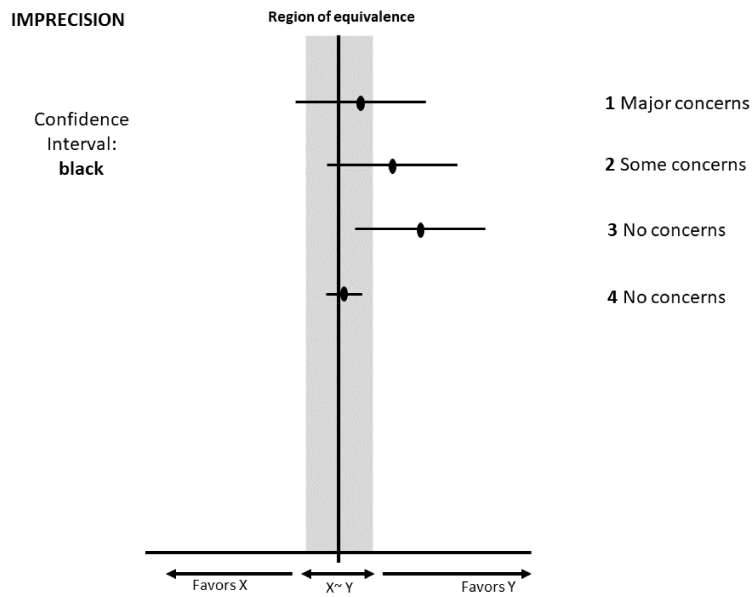
Indirectness

Domain (original question asked)	Description (evidence found and included, including evidence from other studies) – consider the domains of study design and study limitation, inconsistency, imprecision and publication bias	Judgment – is the evidence sufficiently direct?			
Population:		Yes	Probably yes	Probably no	No
Intervention:		Yes	Probably yes	Probably no	No
Comparator:		Yes	Probably yes	Probably no	No
Direct comparison:		Yes	Probably yes	Probably no	No
Outcome:		Yes	Probably yes	Probably no	No
Final judgement about indirectness across domains:	No indirectness ? => No downgrade. Serious indirectness ? => Downgrade one level. Very serious indirectness ? => Downgrade two levels.				

Two components for network meta-analysis:

- similarity of studies in the analysis to the target question (PICO)
- similarity of the studies in the analysis to each other (relates to transitivity assumption)

Imprecision



- Downgrade two levels if there is a major concern and one level if there are some concerns.

Publication bias [6]

Reporting bias may be suspected when the following occur:

- Prior documented evidence of reporting bias in trials in the field.
- meta-analysis is based on a small number of new studies, typically positive findings (e.g. new drugs may have positive findings early and later the true effect size becomes apparent).
- Industry-funded trials dominate
- Known unpublished data from grey literature not included.

Reporting bias is considered to not be present in the following situations:

- Analytical methods indicate the findings from small are similar to those in large/published studies
- Findings from unpublished studies agree with published studies.
- Prospective trial registration, protocol publication and/or clinical trial registries are used extensively in the field and do not indicate important discrepancies with published reports.

⇒ Downgrade one level if publication bias is suspected.

Criteria specific to NMA:

- Do **not consider imprecision** when rating the direct and indirect estimates to inform the rating of NMA estimates [7].
- **No need to rate the indirect evidence** when the certainty of the direct evidence is high and the contribution of the direct evidence to the network estimate is at least as great as that of the indirect evidence.

- 1 Savović J, Turner RM, Mawdsley D, *et al.* Association Between Risk-of-Bias Assessments and Results of Randomized Trials in Cochrane Reviews: The ROBES Meta-Epidemiologic Study. *Am J Epidemiol* 2018;**187**:1113–22. doi:10/gdgm64
- 2 Armijo-Olivo S, Fuentes J, da Costa BR, *et al.* Blinding in Physical Therapy Trials and Its Association with Treatment Effects: A Meta-epidemiological Study. *Am J Phys Med Rehabil* 2017;**96**:34–44. doi:10/gmhbgv
- 3 Armijo-Olivo S, Saltaji H, Costa BR da, *et al.* What is the influence of randomisation sequence generation and allocation concealment on treatment effects of physical therapy trials? A meta-epidemiological study. *BMJ Open* 2015;**5**:e008562. doi:10/gb5db8
- 4 Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. *Med Care* 2003;**41**:582–92. doi:10/dhstr
- 5 Rhodes KM, Turner RM, Higgins JPT. Predictive distributions were developed for the extent of heterogeneity in meta-analyses of continuous outcome data. *J Clin Epidemiol* 2015;**68**:52–60. doi:10/f6thkp
- 6 Nikolakopoulou A, Higgins JPT, Papakonstantinou T, *et al.* CINeMA: An approach for assessing confidence in the results of a network meta-analysis. *PLOS Med* 2020;**17**:e1003082. doi:10/ggthw8
- 7 Brignardello-Petersen R, Bonner A, Alexander PE, *et al.* Advances in the GRADE approach to rate the certainty in estimates from a network meta-analysis. *J Clin Epidemiol* 2018;**93**:36–44. doi:10/gcz4pg