

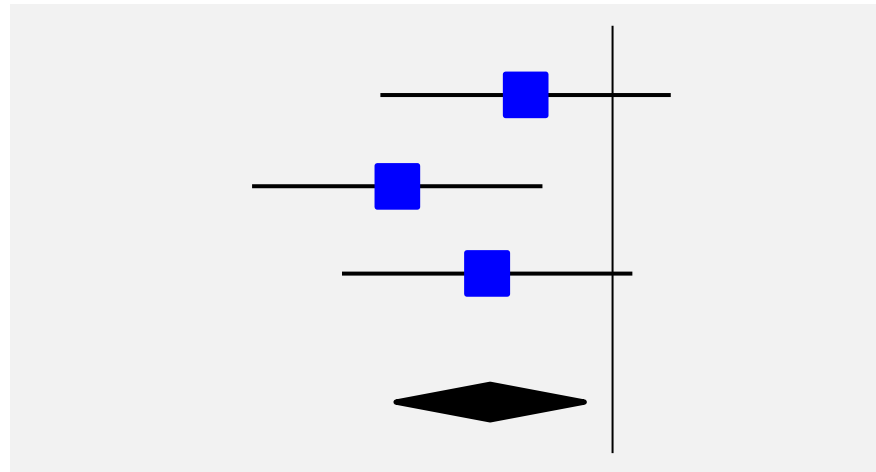
If pooling is not meaningful: Qualitative evidence synthesis

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SMG-Meeting, Cochrane Colloquium, London 2023

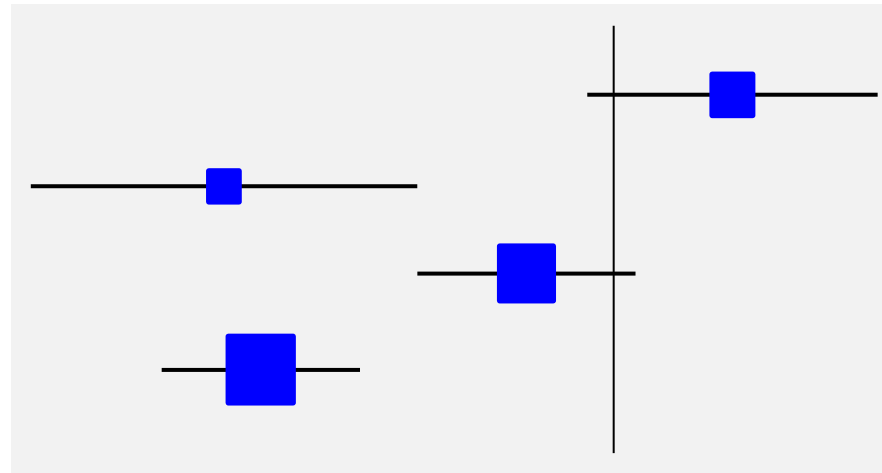
Ideal situation

- We have several studies for our PICO
- The results are homogeneous
- We perform a meta-analysis and calculate the pooled effect estimation
→ quantification of the effect
- We derive conclusions from this estimation



Common situation

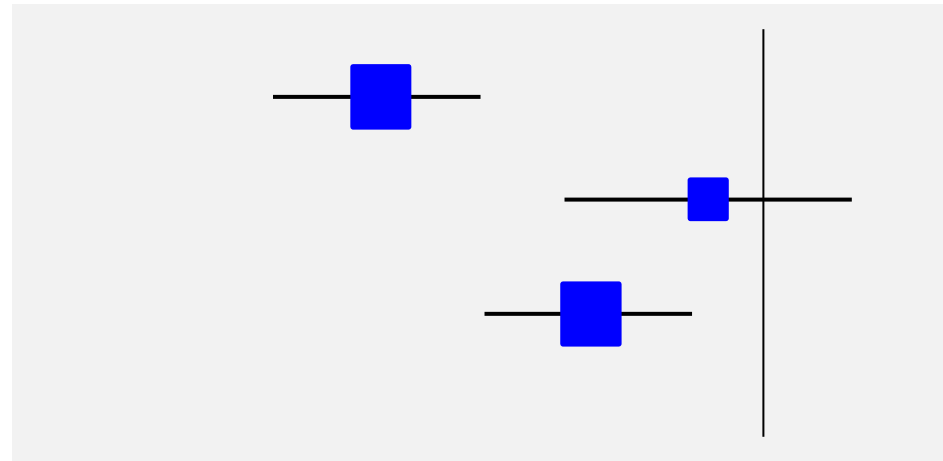
- The results are too heterogeneous to meaningfully interpret the pooled effect estimation.



- If the heterogeneity can be explained, separate meta-analyses can be performed within the homogenous subsets
- Often heterogeneity is not explainable. Should we stop here?

Common situation

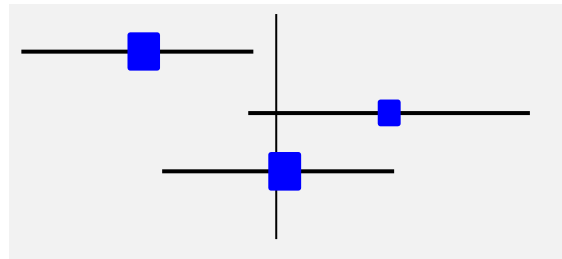
- If an effect direction is recognizable, clear statements can be made regarding benefit or harms



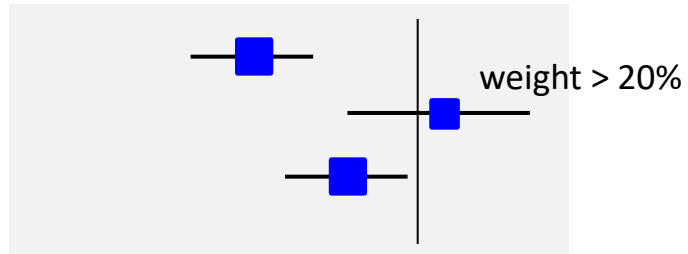
- → perform a qualitative evidence synthesis
- How to decide whether there is an effect direction or not?

Conclusive effects

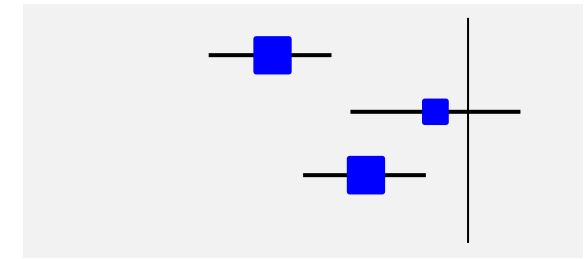
- Conclusive effect = a data situation in which it is possible to infer an effect, even though a common estimation of the effect is not meaningfully possible.



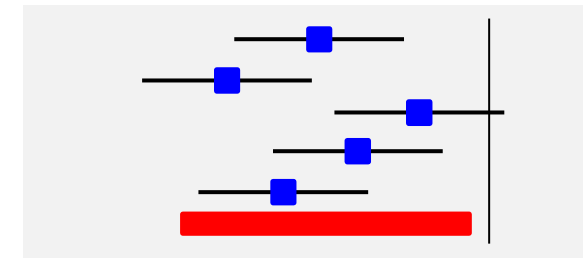
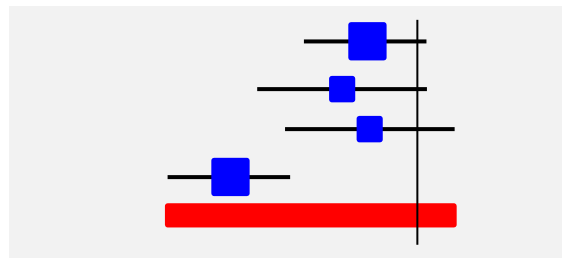
not conclusive



conclusive



weight < 20%

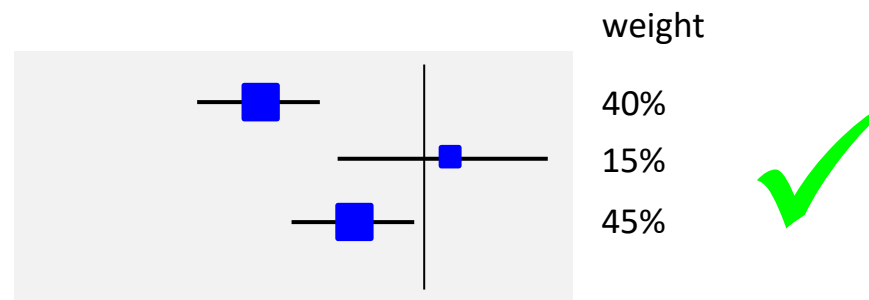
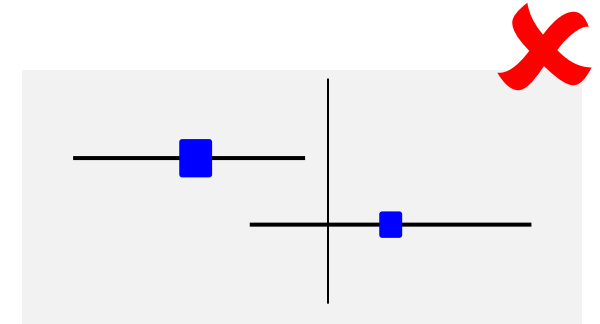


Determinants of conclusive effects

- Presentation of the prediction interval (if at least 4 studies are available)
 - Does it cover the zero effect?
- Direction of the individual study effects
- Weight of the studies in a (random effects) meta-analysis
- Statistical significance of the individual study effects

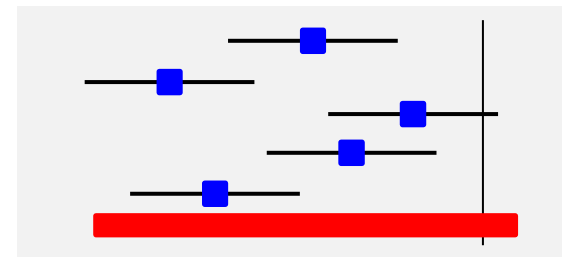
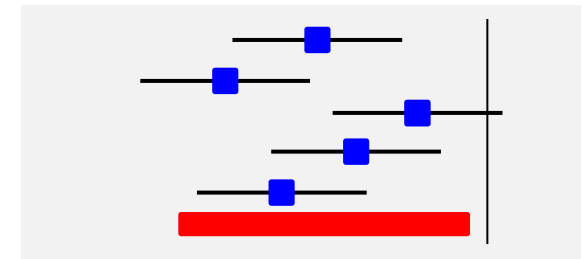
Less than 4 studies

- No presentation of the prediction interval
- Conclusive effects are present if:
 - the effect estimations of 2 or more studies are unidirectional, and
 - the overall weight of these studies is 80% or greater, and
 - at least 2 of these studies show statistically significant results, and
 - at least 50% of the weights of these studies is based on statistically significant results.



At least 4 studies

- The prediction interval is presented
- Conclusive effects are present if:
 - the prediction interval does not cover the zero effect, or
 - the prediction interval covers the zero effect, but the conditions for a conclusive effect in less than 4 studies are met.



Where do these specifications come from?

- Unfortunately, we did not find anything helpful in the literature.
- But we saw the need to develop something.
- Therefore, the methodologists in our institute examined many forest plots.
- Then we formulated these criteria by consensus.

Conclusive effects: Moderately or clearly conclusive?

- Further classification of conclusive effects: moderately vs. clearly conclusive
- It depends on the number of studies.

number of studies	clearly conclusive	moderately conclusive
2	conclusive effects	---
3	all studies show statistically significant results	<u>not</u> all studies show statistically significant results
4 or more	all studies show statistically significant results (in the same direction) or prediction interval does not cover the zero effect	prediction interval covers the zero effect

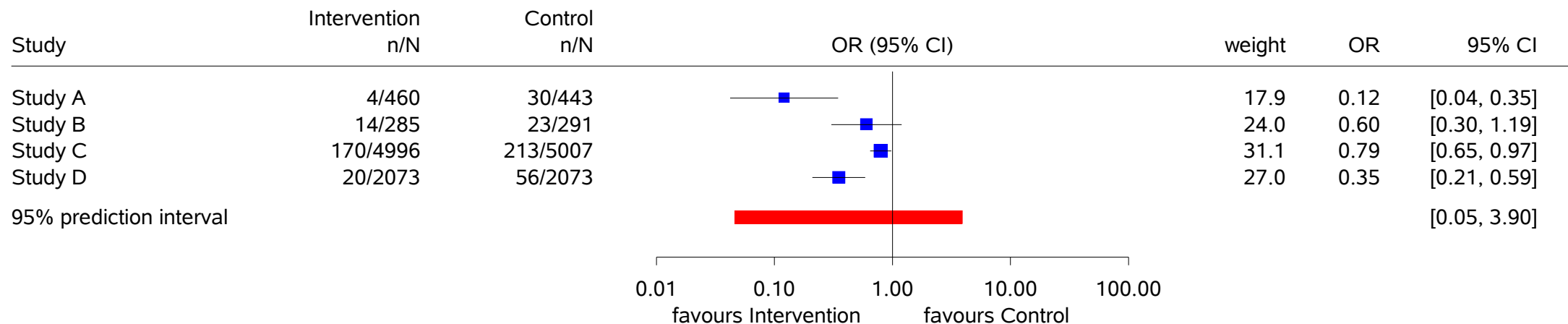
Why do we distinguish between clearly and moderately conclusive effects?

- Classification of the certainty of conclusions: proof, indication, and hint.
- In case of moderately conclusive effects: Reduction of the certainty of conclusions, e. g. from proof to indication.

Examples

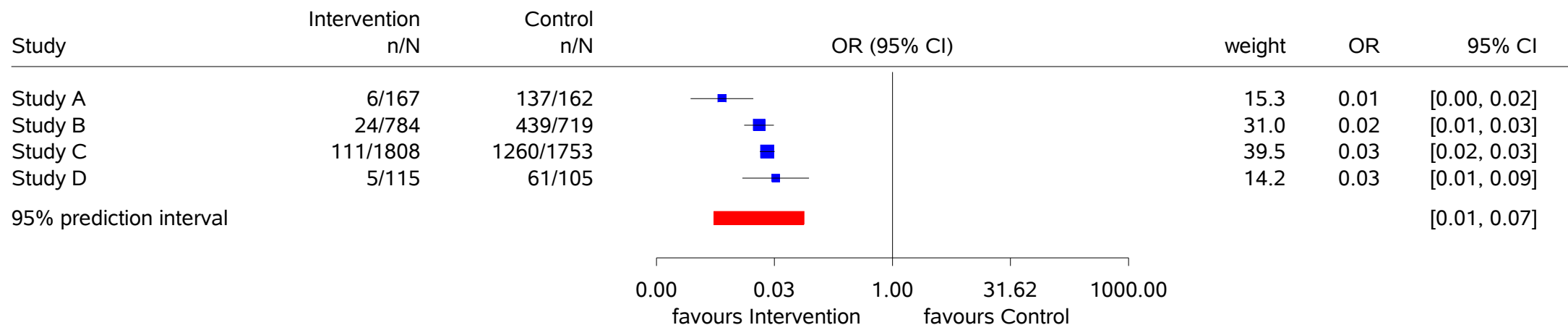
Example 1

moderately conclusive → indication of a benefit



Example 2

clearly conclusive → proof of a benefit



Summary

- Often the results are too heterogeneous to meaningfully interpret the pooled effect estimation.
- → A quantification of the effect size is not possible.
- However, if an effect direction is recognizable, clear statements can be made regarding benefit or harms.
- → concept of moderately and clearly conclusive effects
- The determinants of conclusive effects are: number of studies, prediction interval, direction of estimations, weight of the studies, statistical significance of the study results.
- Publication: General Methods, IQWiG, Chapter 3.1.4

https://www.iqwig.de/methoden/general-methods_version-6-1.pdf

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Thank you for your attention!

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