SWAR 34: Assessing risk of bias (RoB) in randomised trials using Cochrane RoB tools and individual patient data

Objective of this SWAR
(1) To compare risk of bias (RoB) judgements arising from use of Cochrane RoB-1 and Cochrane RoB-2.
(2) To assess whether examination of individual participant data reduces uncertainty in RoB assessment or reveals any RoB that were missed when assessing reports of aggregate data using the Cochrane tools.

Study area: Risk of Bias
Sample type: Randomised trials
Estimated funding level needed: Low

Background
This Study Within a Review (SWAR) [1] will run in parallel with an individual participant data (IPD) meta-analysis of more than 20 randomised trials with more than 50,000 eligible participants investigating predictors of treatment response to inhaled corticosteroids (ICS) in chronic pulmonary obstructive disease (COPD) (PROSPERO: CRD42024508286).

The second Cochrane Risk of Bias tool (RoB-2) for randomised trials was developed to address limitations identified with the original RoB tool [2]. The revised tool uses signalling questions to address a broader range of RoB issues than the original Cochrane tool. It allows and encourages review authors to make a “best guess” about whether methodological requirements were likely to have been met or not (e.g. proper randomisation), thereby preventing the need to record many judgements as “unclear”. It is anticipated that a greater proportion of trials will be assessed as having low, instead of unclear RoB [2]. However, applying RoB-2 is believed to be more time consuming than applying RoB-1 and a study of 172 Cochrane Reviews that were published in 2023-24 found that most used RoB-1 (80.8%) rather than RoB-2 (18.6%) [3].

This SWAR will compare judgements made using RoB-1 and RoB-2. The trials included in the review will be randomly divided into two groups. Investigators will also be randomised to one of two sequences for assessing RoB. Two investigators will assess the first group of trials using RoB-1 and the second group using RoB-2. The other two investigators will assess the first group of trials using RoB-2 and the second group using RoB-1. Therefore, each tool will be completed in duplicate for each trial and disagreements will be resolved through discussion between the two investigators for each tool and trial. The investigators participating all have experience using RoB-1 and RoB-2. The use of the tools will be piloted using other COPD pharmaceutical studies and a calibration meeting will be held to ensure that all investigators apply standards consistently. We will track the time taken to complete each tool, disagreements, differences in RoB between RoB-1 and RoB-2, and whether data were found in trial publications, protocols, or supplementary documents.

In the second part of this SWAR, we will assess RoB using IPD, following guidance in the IPD handbook [4]. We will explore whether detailed assessment of IPD reduces RoB uncertainty or reveals any RoB that were missed when assessing the published report of aggregate data.

Outcomes considered will include exacerbations, mortality, quality of life, and pneumonia.

We anticipate that our findings might inform the future development of RoB tools for aggregate or IPD meta-analyses or the CONSORT statement, if, for example, the information to assess RoB is not adequately reported in a trial publication.

Interventions and Comparators
Intervention 1: Assessment of the risk of bias of the included trials using Cochrane RoB-1.
Intervention 2: Assessment of the risk of bias of the included trials using Cochrane RoB-2.
Intervention 3: Assessment of the risk of bias of the included trials at an IPD level, in accordance with guidance in the IPD handbook [4].

Index Type: Full Review; Methods evaluation within an IPD meta-analysis

Method for Allocating to Intervention or Comparator:
Randomisation

Outcome Measures
Primary: RoB judgements using Cochrane RoB-1, Cochrane RoB-2 and the IPD.
Secondary: Time to complete Cochrane RoB-1 and RoB-2; disagreement among assessors with Cochrane RoB-1 and RoB-2.

Analysis Plans
We will use comparative statistics to compare RoB judgements between RoB-1, RoB-2 and IPD; and to compare the time taken to complete each Cochrane tool and disagreement among assessors using RoB-1 and RoB-2.

Possible Problems in Implementing This SWAR
We have already gained access to the IPD of most relevant trials. Therefore, we do not anticipate any problems in completing these analyses.

References
1. Devane D, Burke NN, Treweek S, et al. Study within a review (SWAR). Journal of Evidence Based Medicine 2022;15(4):328-32.
2. Sterne JAC, Savovic J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019;366:l4898.
3. Sandoval-Lentisco A, López-López JA, Sánchez-Meca J. Frequency of use of the revised Cochrane Risk of Bias tool (RoB 2) in Cochrane and non-Cochrane systematic reviews published in 2023 and 2024. Research Synthesis Methods 2024 Sep 10. doi: 10.1002/jrsm.1755. [online ahead of print]
4. Riley RD, Tierney JF, Stewart LA. Individual Participant Data Meta-Analysis. A Handbook for Healthcare Research, Wiley. 2021.

Publications or presentations of this SWAR design

Examples of the implementation of this SWAR

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