Outcome Reporting Bias in Randomised Controlled Trials: An assessment using Multivariate Meta-Analysis

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Abstract

- ***Selective outcome reporting*** **occurs when a subset of the originally recorded outcomes in a trial are selectively reported in a publication based on their results.**
- **We assessed 21 systematic reviews that considered treatments for rheumatoid arthritis. We analysed the impact of Outcome Reporting Bias (ORB).**
- **For the example of Auranofin, *high risk of ORB* were awarded to at least one trial for *tender joints count, pain, physician global* and *acute phase reactant.***
- **Findings of our analysis show that *multivariate meta-analysis* offers one such sensitivity analysis to *adjust for ORB* when there is missing trial data for many review outcomes.**

Materials and Methods

- **Systematic reviews published by the Cochrane Musculoskeletal Group that considered treatment of rheumatoid arthritis were identified.**
- **Reviews were assessed for Outcome Reporting Bias (ORB) in relation to an established core set of eight outcomes for rheumatoid arthritis (Table.1).**
- **A nine-point classification system previously developed was used to assess the potential risk of ORB[2] (Table.2).**
- **The impact of ORB was assessed by comparing estimates from a *univariate* and *multivariate meta-analysis* for both *fixed* and *random* effects models[3].**
- **To calculate covariances[4] to be used in the Multivariate random effects model we considered within-study correlations between the core outcomes which were obtained from analysis of individual patient data conducted by a previous study.**

Table.1 Core outcomes set for assessment of rheumatoid arthritis[1]

Tender Joints Count (TJC)
Swollen Joints Count (SJC)
Patient's assessment of pain (Pain)
Physician global assessment (Phy. global)
Patient global assessment (Pat. global)
Patient assessment of functional ability (Function)
Acute Phase Reactants (Erythrocyte sedimentation rate ESR) or (C-reactive Protein CRP) (APR)
Radiological Damage (RD)

Table.2 ORBIT Classification System

Clear that the outcome was measured and analysed
A) Analysed p>0.05 (High Risk)
B) Analysed p<0.05 (Low Risk)
C) Analysed but insufficient for MA (Low Risk)
D) Analysed but no results reported (High Risk)
Clear that the outcome was measured but not necessarily analysed
E) Measured but not necessarily analysed (High Risk)
F)Measured but not necessarily analysed (Low Risk)
Unclear whether the outcome was measured
G) Not mentioned – LIKELY measured (High Risk)
H) Not mentioned – UNLIKELY measured (Low Risk)
Clear that the outcome was not measured
I: Outcome NOT measured (No Risk)

Flow Chart of the Systematic Reviews assessed

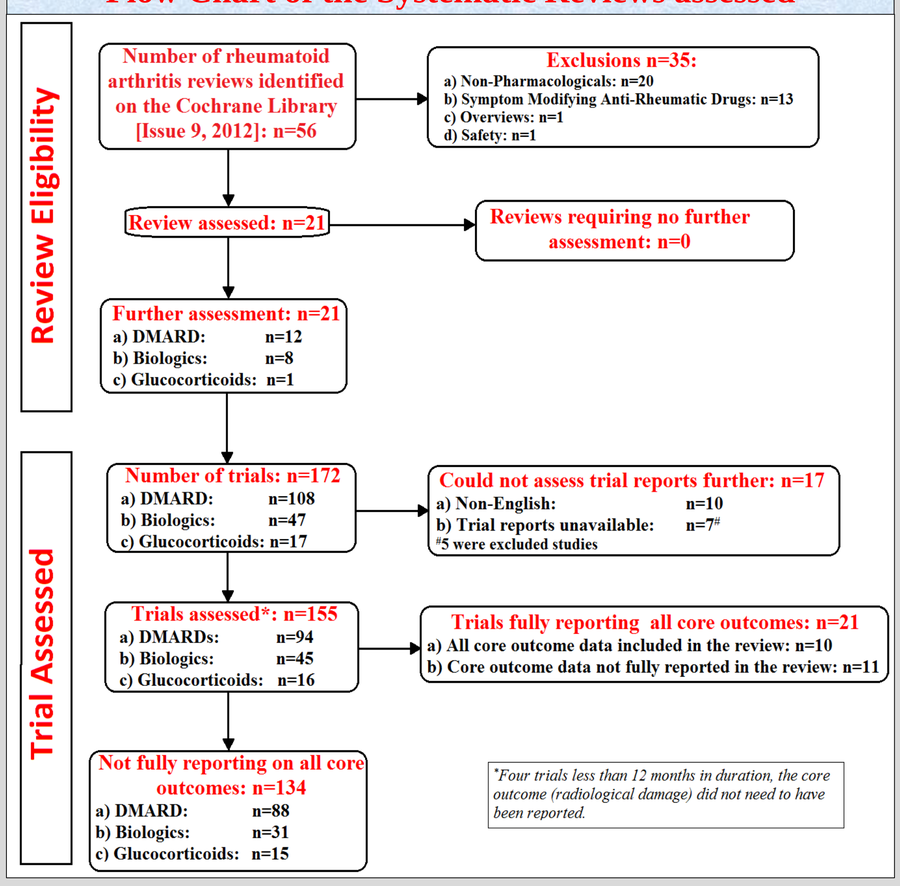


Figure.1 Overall missing data and missing data as result of high ORB classification (%)

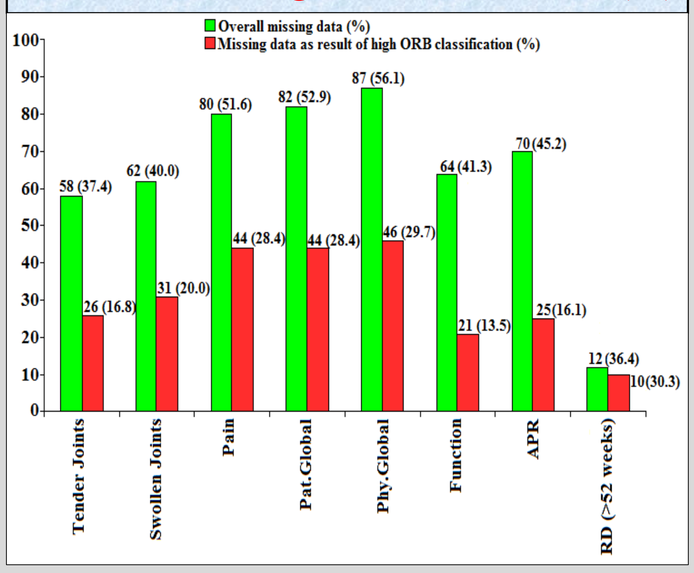
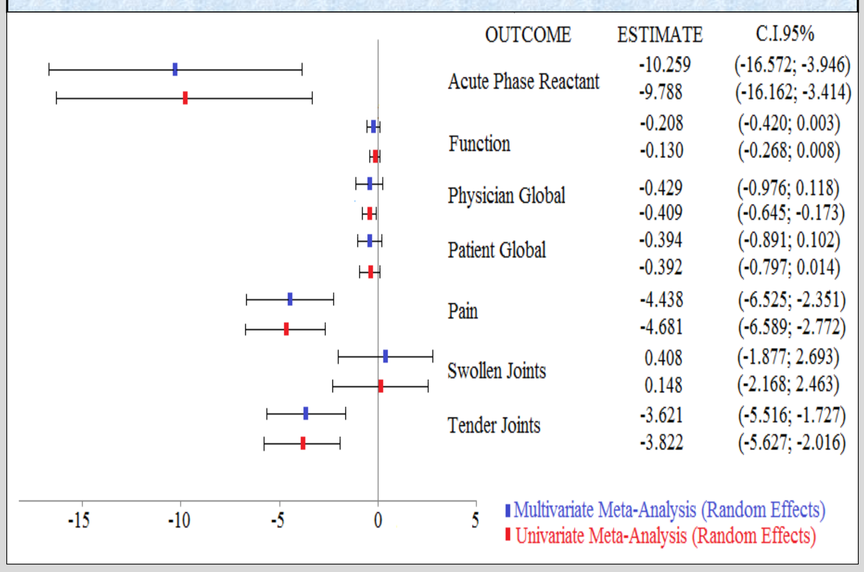


Figure.2 Multivariate Random effects Meta-analysis (REML) (Auranofin vs. placebo)



Results

- **We assessed 21 SRs. In particular we assessed 155 clinical trials (94 disease modifying anti-rheumatic drugs DMARDs, 45 biologics and 16 glucocorticoids) (Flow Chart).**
- **The current analysis of the 21 SRs assessed (Figure.1) has demonstrated a high percentage of missing data for some outcomes (Pain, Patient global and Physician Global).**
- **Some outcomes considered are highly correlated (Pain and Pat.Global, 91%) other outcomes are low correlated (APR and SJC 17%).**
- **When we applied the multivariate random effects meta-analysis for a systematic review of Auranofin versus placebo[5] (Figure.2), we found that some outcomes (TJC, Pain) the shift towards the null suggests that ORB could be a problem because the univariate result overestimates the treatment effect.**

Conclusion

- ***Multivariate meta-analysis*** **offers a solution to adjust for the impact of missing data and ORB.**
- **In the review showed in this poster, the summary treatment effect estimates and their statistical significance changed importantly when multivariate meta-analysis was used to reduce ORB through additional information from correlated outcomes.**

References

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