

The *within-trial framework* might need to include new variables to be applied in real-world clinical practice guidelines

Impact of using the *within-trial framework* for comparing estimations in a British HIV guideline.

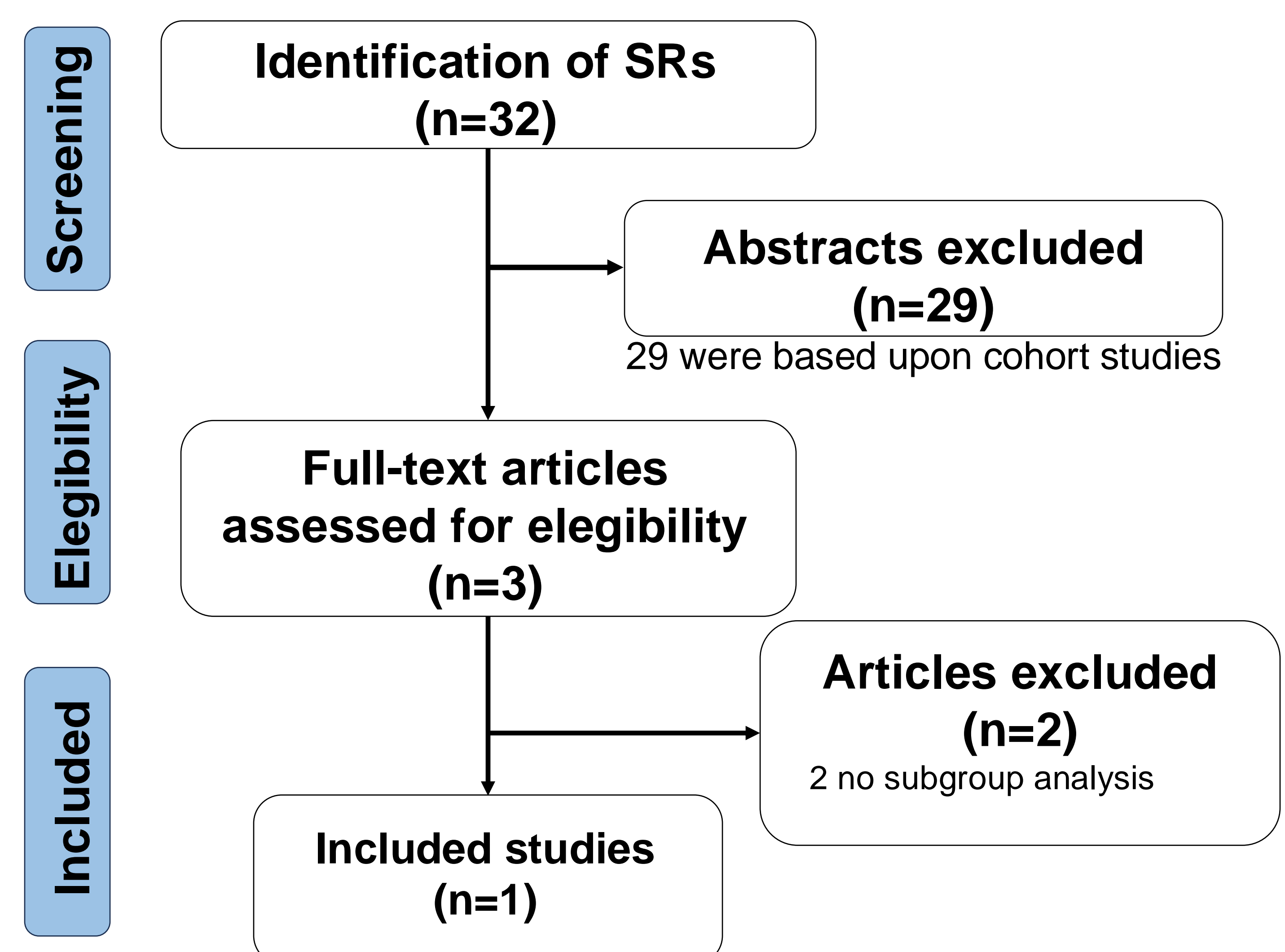
Background: Current methods to estimate the effects of an intervention in different subgroups in systematic reviews (SRs) of randomized clinical trials (RCTs) may produce aggregation bias, which is the overestimation or underestimation caused by the influence of a subgroup effect. This type of bias could skew both interpretation and applicability¹.

We aimed to assess whether estimating interactions and subgroups-specific treatment effects in meta-analyses of RCTs affect the recommendations for initiating antiretroviral therapy (ART) and selecting ART regimes in the 2022 British HIV Association (BHIVA) recommendations. We used the within-trial framework (WF) method presented by Godolphin et al. 2022¹.

Methods

- 1 We identified intervention SRs of RCTs included in the 2022 BHIVA recommendations.
- 2 Full text search for SRs with subgroup analysis.
- 3 We applied the *within-trial framework (WF)* using the STATA metafloat package.
- 4 We compared the new result with the original guideline recommendation and evaluated changes in the interpretation.

Results



The included SR had single-groups RCT subgroup meta-analysis, therefore we were unable to apply the within-trial framework. None of the recommendations of the 2022 British HIV Association guidelines on antiretroviral treatment for adults living with HIV-1 was modified based on this study.

Conclusions

- ✓ None of the recommendations of the BHIVA guideline would be modified after conducting WF.
- ✓ WF may be a valuable tool to identify and control aggregation bias.
- ✓ To include analysis of individual patient data of RCTs and estimating interactions between subgroups in cohort studies might be beneficial to apply this method.
- ✓ It became difficult to find enough subgroup analyses in this comprehensive clinical guideline to conduct WF. Therefore, this method may lack real-world applicability in other guidelines. In future investigations, the WF should be tested in other guidelines.

Limitation: Only one SR had subgroup analysis and it did not fully complete the requirements for the WF.

1. Original paper for the WF



Flores N, Briceño F, Weinborn S, Álvarez F, Loyola G, Grandi D, Leyton F, Bracchiglione J, Meza N, Garnham R, Madrid E.