Recommendations

The focus of the following recommendations is statistical and clinical validity, transparency, and consistency in the reporting of indirect treatment comparisons (ITCs) using individual participant data (IPD). These recommendations are intended to ensure comparable results between studies, and aid in the meta-analysis of indirect evidence where there is an absence of consistent evidence, or where there are single-arm studies involved.

Recommendations 4. Submissions using population-adjusted analyses in a connected network need to provide evidence that the target outcomes can be predicted with sufficient accuracy in relation to the relative treatment effects, and present an estimate of the likely range of residual systematic error in the ‘adjusted’ unanchored comparison.

If this evidence is not provided, the amount of bias in the unanchored comparison is unlikely to be substantial.

Methods for population adjustment

Population adjustment methods are broadly of two types:

• Propensity score matching, such as Matching Adjusted Indirect Comparisons (MAIC), Signorovitch et al. (2011), when individuals in the All-Trials are weighted so that the observed covariate distributions match those of the target population.

• Outcome regression, such as Simulated Treatment Comparison (STC), Carr and Shakir (2010), when a model is fitted in the All-Trials and used to predict outcomes in the target population.

Recommendations

- Propensity score matching methods should adjust for all effect modifiers and prognostic variables. This is equivalent to a logistic propensity score model, which includes all effect modifiers in imbalance.

- Outcome regression methods should include all effect modifiers and prognostic variables. This is equivalent to a linear predictor scale, with the same link functions that are usually employed for those outcomes.

Recommendations

- Propensity score matching methods should adjust for all effect modifiers (in imbalance or not), but have prognostic variables. Outcome regression methods should adjust for all effect modifiers in imbalance, but any prognostic variables and effect modifiers that improve model fit.

- For unanchored comparisons, both propensity score weighting and outcome regression methods should adjust for all effect modifiers and prognostic variables, in order to reliably predict outcomes in the target population.

- For anchored comparisons, only adjusting for effect modifiers minimizes bias unnecessarily without reducing precision. Unanchored comparisons require all covariates to be adjusted for, in predictions of absolute outcomes.

- Adjusted indirect comparisons applied to IPD trials may be the most appropriate target population analysis.

- The use of population-adjustment methods for health technology appraisal.

If this is the case, then the relative effect $\alpha$ is not for any population. The stand-off effect modification assumption is evaluated on a clinical basis, and is more likely to be satisfied by treatments in the same class.