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Aims
- Review the properties and assumptions of methods for population-adjusted treatment comparisons, including Matching-Adjusted Indirect Comparisons (MAIC) and Simulated Treatment Comparisons (STC).
- Provide guidance on their use in health technology appraisal (HTA).

Background
In HTA submissions, a company wishes to compare their treatment B with that of a competitor C. Standard indirect comparison methods cannot be used, but meta-analysis assumes that there are no differences in effect modifiers between the populations, and require a common comparator or network effect model—which is often not the case. Effect modification is present on a given scale, relative effects \( \exp(t AB_{i}) = \frac{Y_{A}g_{YCA} - Y_{B}g_{YCA}}{Y_{A}g_{YAB} - Y_{B}g_{YAB}} \) between treatments that are specific to a given population. P, where \( w_{i} = \frac{1}{N_{i}} \), are the mean of the relative effect estimates.

In an ideal scenario, individual patient data (IPD) would be available on trials, and an IPD Network Meta-Analysis could be performed. However, it is more likely that only one company has access to the IPD and neither company has access to the other company’s IPD. Population-adjustment methods seek to use available IPD to adjust for between-trial differences, or even use unmatched network methods, under certain assumptions (assumptions 1a and 1b).

In a network model with an ADM, any treatment model can be used to underpin the choice of a common comparator in Figure 4b. Figure 4b. The network model when there is no in-study adjustment or there are single-study ADMs, an unanchored comparison is the only option (Figure 4d).

Methods for population adjustment
Population adjustment methods are broadly of two types:
1. Propensity score matching, such as Matching-Adjusted Indirect Comparisons (MAIC), Simulated Treatment Comparisons (STC) and turns, where individual patient data (IPD) were available on trials, and an IPD Network Meta-Analysis could be performed. Network Meta-Analysis was preferred, including a common comparator or network effect model—which is often not the case. Effect modification is present on a given scale, relative effects \( \exp(t AB_{i}) = \frac{Y_{A}g_{YCA} - Y_{B}g_{YCA}}{Y_{A}g_{YAB} - Y_{B}g_{YAB}} \) between treatments that are specific to a given population. P, where \( w_{i} = \frac{1}{N_{i}} \), are the mean of the relative effect estimates.

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Recommendations
The focus of the following recommendations is statistical and clinical validity, transparency, and consistency in the use of population-adjustment methods for health technology appraisal. The results of population-adjusted analyses are incomplete if they cannot be obtained for the correct target population. The shared effect modifier assumption holds for active treatments A and C if:
- Assumption 2b. If effect modification is present on a given scale, relative effects \( \exp(t AB_{i}) = \frac{Y_{A}g_{YCA} - Y_{B}g_{YCA}}{Y_{A}g_{YAB} - Y_{B}g_{YAB}} \) between treatments that are specific to a given population. P, where \( w_{i} = \frac{1}{N_{i}} \), are the mean of the relative effect estimates.

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