Abstract No.
MSR54

A Comparison of MAIC and STC Methods to Support the Decision at Feasibility Assessment Stage

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BACKGROUND

- **Evaluating comparative effectiveness** of interventions vs all relevant comparators (selected based on the requirements of the local health technology assessment [HTA] agency as treatment recommended, indicated and/or used) is the cornerstone of HTAs.
- Often, evidence is not available from head-to-head clinical trials for all comparators of interest and an **Indirect Treatment Comparison (ITC)** is required.
- Standard ITC methods assume **no between-trial differences** in the distribution of **treatment effect modifiers**. When this assumption does not hold, population-adjusted ITCs such as **Matching-Adjusted Indirect Comparison (MAIC)** and **Simulated Treatment Comparison (STC)** can be considered.[1]

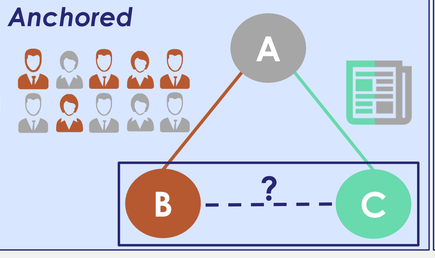
OBJECTIVES & SETTING

- To offer a **descriptive comparison** of the two methods based on conceptual and statistical criteria.
- To provide **guidance** on the selection of each method depending on the context of the analysis.

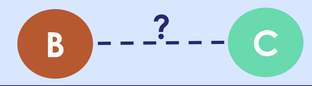
RESULTS - MAIC vs STC Conceptual and statistical differences

- Pivotal trial: **Individual patient data** (IPD) available for **A vs B**
- Comparator trial: **Aggregate data** only for **A vs C**
  - ➢ Interested in the **relative treatment effect of B vs C** (indirect estimate)

Anchored
Use of relative treatment effect based on randomization per trial
Need to adjust for **effect-modifiers**

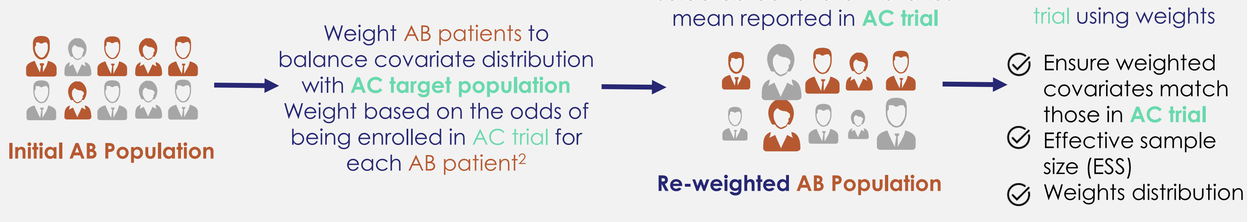


Unanchored
Requires the assumptions that absolute outcomes can be predicted by the covariates; need to adjust for **effect-modifiers** and **prognostic variables**



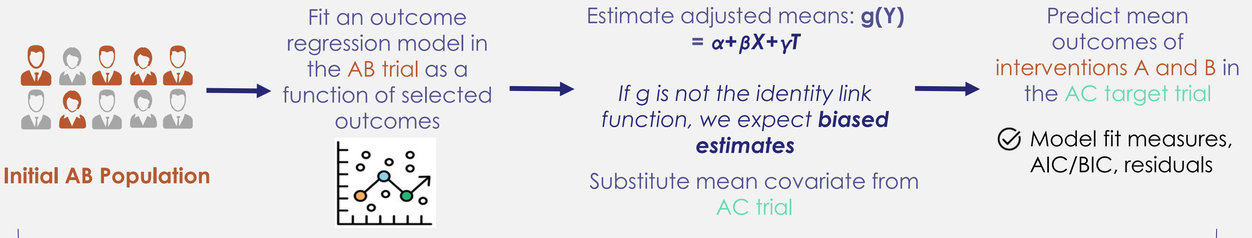
MAIC

Propensity score weighting-based approach



STC

Outcome regression-based approach; an outcome model is fitted to IPD, to which the mean relevant characteristics of comparator trial arm are applied



Conduct the **anchored ITC in the AC population** based on the **Bucher approach**: $\hat{\Delta}_{BC(AC)} = g(\bar{Y}_{C(AC)}) - g(\bar{Y}_{A(AC)}) - (g(\hat{Y}_{B(AC)}) - g(\hat{Y}_{A(AC)}))$

Unanchored
Similar first steps as anchored comparison for both methods
Estimation of absolute outcomes for B as in the C population
Relative treatment effect based on individual absolute outcomes

MAIC

Assumption: All effect modifiers are known and observed in both trials so that they can be adjusted for
How to assess? ❑ Identification of all potential factors through literature review, subgroup results of trials, clinical expertise, etc.

- ➢ Inclusion of all potential effect modifiers in weighting model
- **AC** population entirely included in **AB**
- ❑ Comparison of eligibility criteria between trials (restrict AB trial if needed) and population characteristics at baseline

STC

Unanchored
All **effect modifiers and prognostic factors** need to be known and observed

- ➢ Inclusion of all potential effect modifiers in regression model, as well as potential prognostic factors should they improve model fit
- **AC** population has sufficient overlap with **AB** (less strict than MAIC)
- ❑ Comparison of eligibility criteria between trials (restrict AB trial if needed) and population characteristics at baseline
- Should be conducted using the identity link function, potential bias if conducted on another scale
- Time-to-event outcomes: require use of parametric distribution
- ❑ Fit distributions to identify the best one
- ❑ Assess relevance of using same distribution across treatment arms
- Regression parameters estimated based on **AB** data are applicable to **AC** population

Results only valid in the population described by the **AC** trial

CONCLUSIONS

MAIC more used than STC

As presented by Pooley et al., 2019[3], between 2014 and 2019:

- 21 NICE submissions including a MAIC
- 4 NICE submissions including a STC

➢ Mixed responses by the ERG with criticism concerning prognostic and effect modifying variables

MAIC

- Interested in multiple outcomes, single or few comparator(s)
- Working with non-linear outcomes, e.g., time-to-event outcomes

STC

- Interested in multiple comparators, small set of outcomes
- Reweighted population is reduced, few reweighted participants influence the results
- Pivotal trial more restricted than comparator's trial regarding effect modifiers

DISCUSSION

- Recent paper from NICE (CHTE 2020[4]) invites to revise guidelines and reassess the use of MAIC vs STC based on results from simulations studies favoring STC on the grounds of greater precision.
- New population-adjusted approach could be considered; **Multi-level Network meta-analysis** (ML-NMR) which accommodates broader target population, even generated from external sources and is generalizable to larger networks.

References:
1. Philippo et al. 2016, NICE DSU Technical Support Document 18: Methods for population-adjusted indirect comparisons in submissions to NICE.
2. Signorovitch et al. 2010, Comparative effectiveness without head-to-head trials.
3. Pooley et al. 2019, PNS299 THE INCREASING USE AND ACCEPTANCE OF ALTERNATIVE STATISTICAL APPROACHES TO INDIRECT COMPARISON IN THE NATIONAL INSTITUTE OF HEALTH AND CARE EXCELLENCE (NICE) HEALTH TECHNOLOGY ASSESSMENT (HTA) SUBMISSION PROCESS.
4. Abrams et al. 2020, CHTE2020 SOURCES AND SYNTHESIS OF EVIDENCE; UPDATE TO EVIDENCE SYNTHESIS METHODS

Abbreviations:
AIC: Akaike information criterion, BIC: Bayesian information criterion, ERG: Evidence review group, ESS: Effective sample size, HTA: Health technology assessment, IPD: Individual patient data, ITC: Indirect treatment comparison, MAIC: Matching-adjusted indirect comparison, ML-NMR: Multi-level network meta-regression, NICE: National Institute for Health and Care Excellence, STC: Simulated treatment comparison, TSD: Technical Support Document

ISPOR Europe, Vienna, AT; November 6 – 9, 2022