Erasmus School of
Health Policy
& Management

From Trials to Target Populations: Extending Evidence for Decision-Making

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Health technology assessment

What is the effect* of the new technology [I] compared to the existing standard of care [C] on patient centered outcomes [O] among patients eligible for treatment [P] in local routine care [S]?

PICOs commonly used in HTA but need extending into estimands

*Typically interested in marginal treatment effects

P	Population: patients eligible for treatment (or subgroup)
I	Intervention: new intervention
C	Comparator: local standard of care in P
O	Outcome: Patient outcomes and QoL
S	Setting: Local routine care

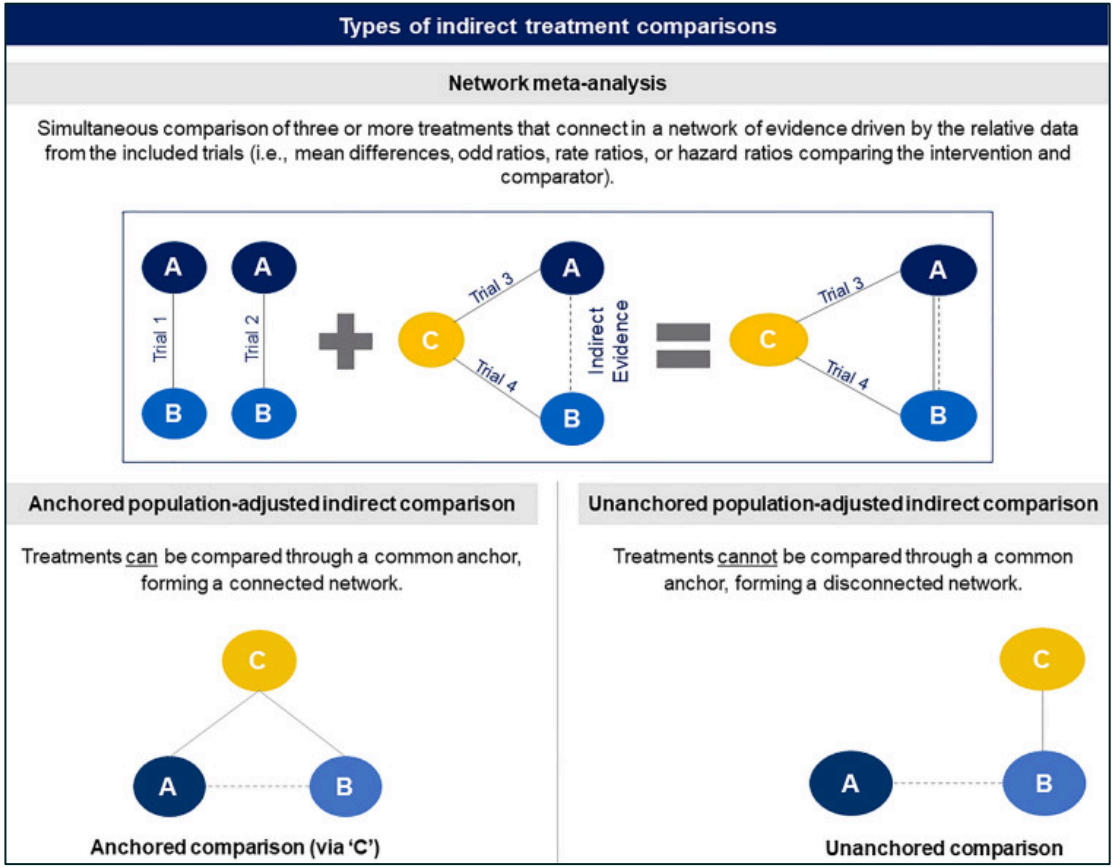
Treatment policy

Challenges in using registration trials

- HTA processes happen in parallel to regulatory approval
- HTA bodies rely on the trials (predominantly) conducted for regulatory approval
- Regulators ask different questions to HTA bodies: is the product safe and effective (risk-benefit)? May require different estimands.
- Even with high internal validity, external validity may be a concern

NICE assessment of AURA3 RCT comparing Osimertinib vs PDC EGFR T790M+ aNSCLC after 1L EGFR TKI treatment (TA653)	
P	Trial restricted to patients with an ECOG of 0 or 1; in UK 6-10% patients ECOG 2. In trial 65% of patients of East Asian family origin with possible treatment effect modification. **Median OS for Osimertinib was 13.9 months in UK cancer registry compared with 26.8 months in AURA3**
I	**Comparator**: FLAURA compared osimertinib with PDC. **Prior treatments**: Most patients received erlotinib or gefitnib. Afatinib is the most prescribed EGFR TKI in England for this population. **Subsequent treatments**: many subsequent treatments used in the trial are not routinely used in the NHS. In AURA3 the rate of treatment switching from PDC to osimertinib after disease progression was 71%. The committee thought that this was likely to bias overall survival results because using osimertinib in a third-line setting did not reflect NHS practice.
C	

Evidence synthesis and indirect treatment comparisons



De Santis et al. 2024, Adv Ther.

External validity & transportability

How do we extend from regulatory oriented clinical trials to answer questions for HTA bodies

Marginal effect of the new technology compared to the existing standard of care on patient centered outcomes among patients eligible for treatment in routine care?

Deliberative process

Transportability methods (population-adjustment)

Real-world evidence integration