ARE SINGLE-ARM CLINICAL TRIALS SUFFICIENT TO ASSESS VALUE IN ONCOLOGY AND RARE DISEASES?

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Speakers

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Poll question

- There is an increase in regulatory approvals based on single arm trials, posing potential challenges for HTA. Should we wait for RCTs?
  - No, single arm trials are sufficient to assess value
  - Yes, without RCTs it is difficult to assess value

The challenge with single arm trials in the context of estimating relative treatment effects versus competing interventions

Jeroen Jansen

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Treatment effects and study effects

Network meta-analysis
Network meta-analysis

Key assumption network meta-analysis

\[
\delta_{AB(AB)} = \delta_{AB(AC)} = \delta_{AB}
\]

Relative treatment effect of B versus A in AB population assumed applicable to AC population (i.e., no differences in effect modifiers between AB and AC populations)

\[
\delta_{AC(AB)} = \delta_{AC(AC)} = \delta_{AC}
\]

Idem for the relative treatment of C versus A

\[
\Rightarrow \delta_{BC} = \delta_{AC} - \delta_{AB}
\]
Common situations

Two single-arm trials

Network of RCTs; one single-arm trial

One single-arm trial; one RCT

When you have only study level data:
“Aggregate level matching” – RCT and single-arm trial
Key assumptions indirect comparison—RCT and single-arm trial

\[ \mu_{A(AB)} = \mu_{A(C)} = \mu_A \]

Study effect from AB trial assumed applicable to C trial (i.e., no differences in prognostic factors between AB and C populations)

\[ \delta_{AB(AB)} = \delta_{AB(C)} = \delta_{AB} \]
\[ \delta_{AC(AB)} = \delta_{AC(C)} = \delta_{AC} \]
\[ \Rightarrow \delta_{BC} = \delta_{AC} - \delta_{AB} \]

When you have only study level data:
“Aggregate level matching” - network
When you have only study level data:
“Reference prediction”

Exchangeable effects regarding reference treatment
When you have individual patient data:
Population-Adjusted Indirect Comparison (2 Trials)

- Propensity score-based methods (matched adjusted indirect comparison)
- Outcome regression-based methods (simulated-treatment comparison)
Disconnected network with multiple RCTs and a single-arm IPD trial

1. Identify “best matching” trial or trials in network with the single-arm IPD trial
2. Adjust for differences between single-arm trial and “best matching” network trial regarding prognostic factors and effect modifiers
3. “Network” meta-analysis of all relevant studies in network including the “connected-trial”

Summary

- The desire to make novel treatments available to patients as soon as possible has led to a growing number of clinical trials that pose challenges to understand the comparative and cost-effectiveness of the intervention of interest
- Indirect comparisons involving single-arm trials rely on the assumption of no systematic differences in effect modifiers and prognostic factors between studies
- Access to patient-level data for one of the trials to adjust for between-trial differences may make this (strong) assumption easier to defend