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

November 14, 2018

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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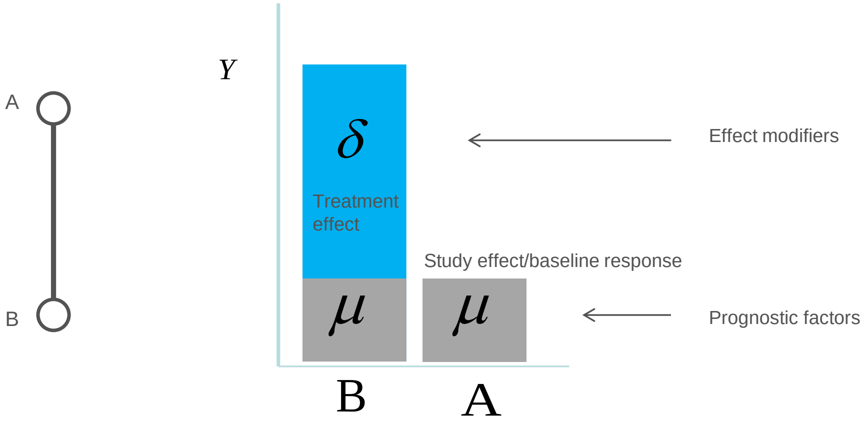
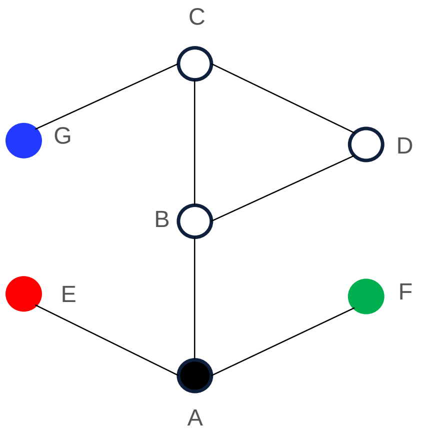
PRECISION XTRACT

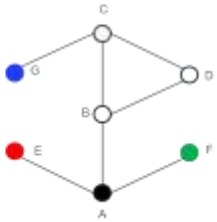
Treatment effects and study effects

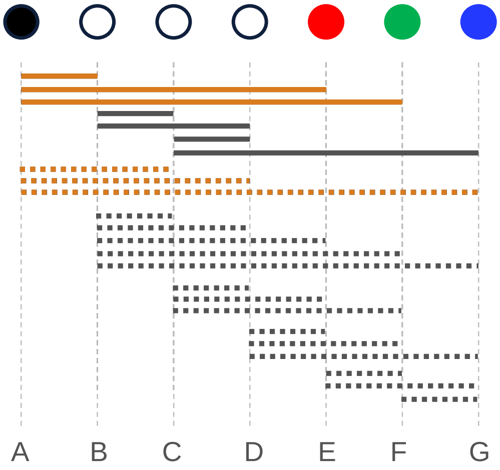


Network meta-analysis



Network meta-analysis

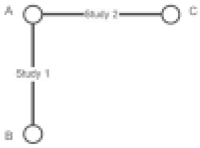


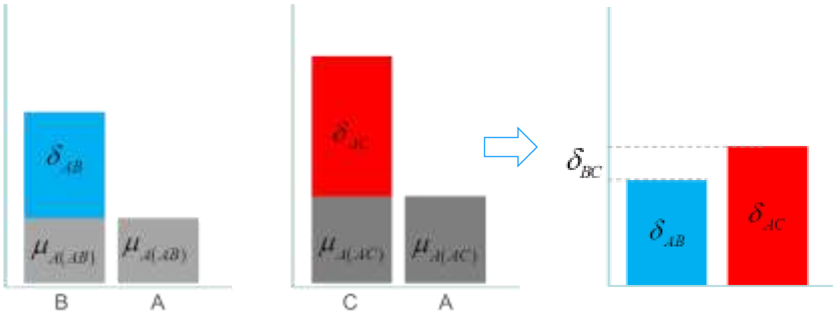


—— Direct comparison

······ Indirect comparison

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 (ie, no differences in effect modifiers between AB and AC populations)

$$\delta_{AC(AB)} = \delta_{AC(AC)} = \delta_{AC}$$

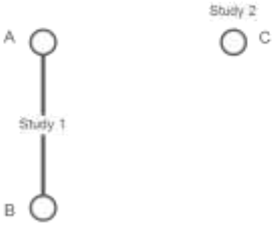
Idem for the relative treatment of C versus A

$$\Rightarrow \delta_{BC} = \delta_{AC} - \delta_{AB}$$

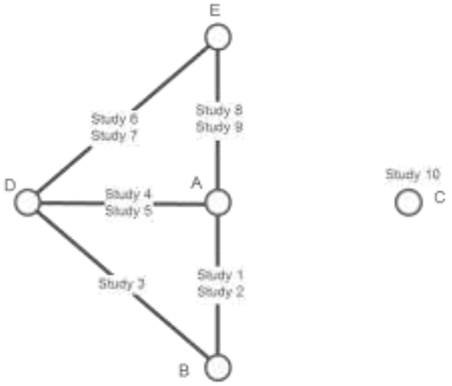
Common situations

Two single-arm trials

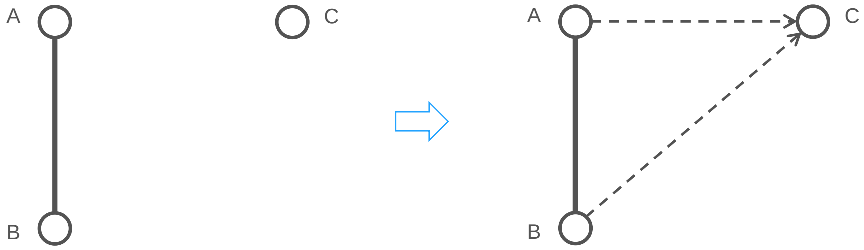
One single-arm trial; one RCT



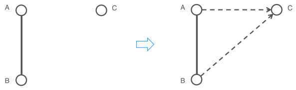
Network of RCTs; one single-arm trial

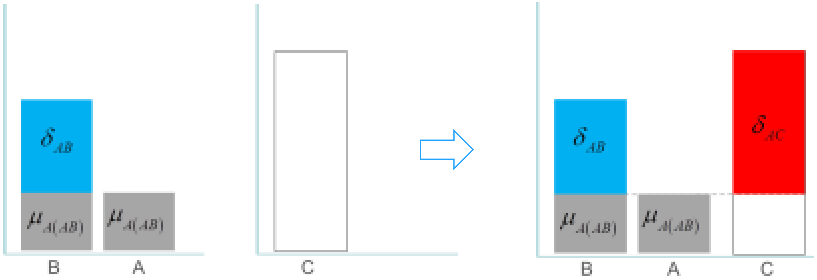


When you have only study level data: “Aggregate level matching” – RCT and single-arm trial



Key assumptions indirect comparison—RCT and single-arm trial





$$\mu_{A(AB)} = \mu_{A(C)} = \mu_A$$

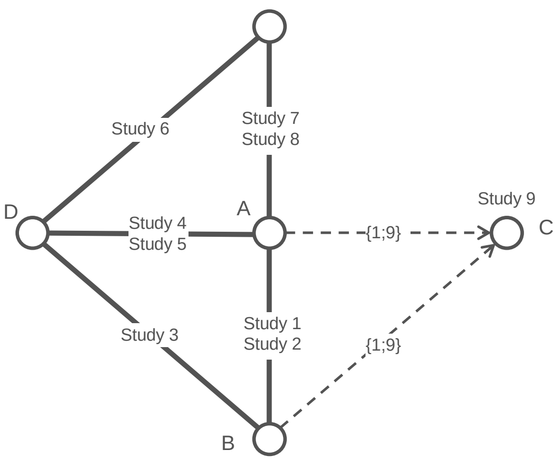
Study effect from AB trial assumed applicable to C trial (ie, no differences in prognostic factors between AB and C populations)

$$\delta_{AB(AB)} = \delta_{AB(C)} = \delta_{AB}$$

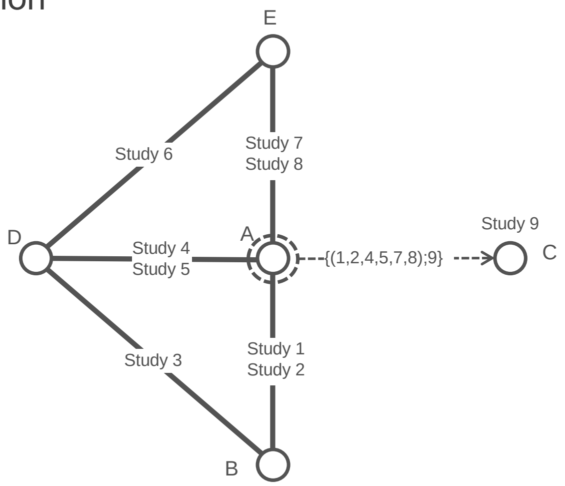
$$\delta_{AC(AB)} = \delta_{AC(C)} = \delta_{AC}$$

$$\Rightarrow \delta_{BC} = \delta_{AC} - \delta_{AB}$$

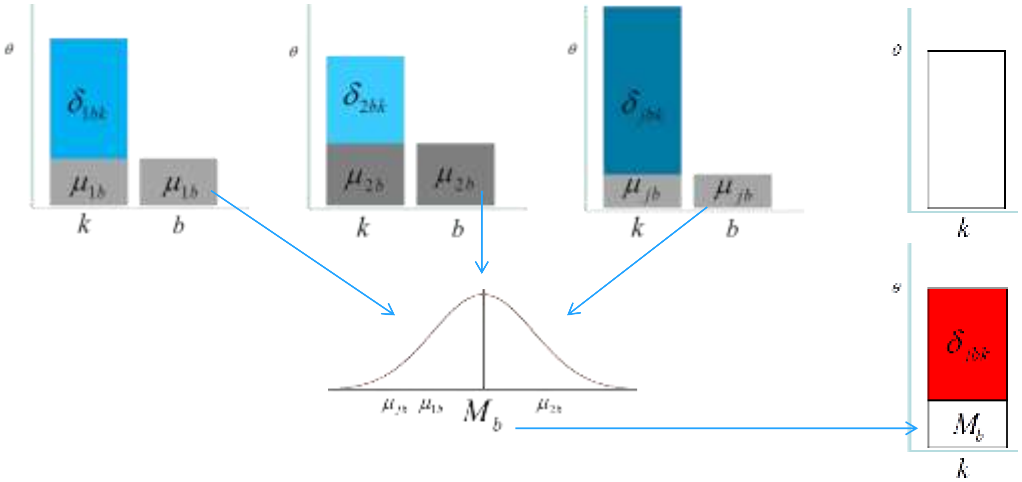
When you have only study level data: “Aggregate level matching” - network



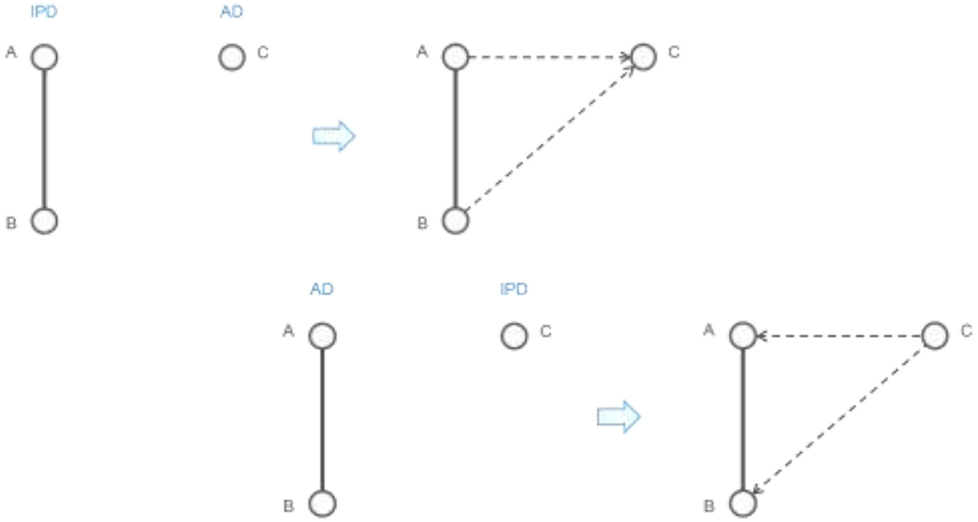
When you have only study level data: "Reference prediction"



Exchangeable effects regarding reference treatment



When you have individual patient data:
Population-Adjusted Indirect Comparison (2 Trials)

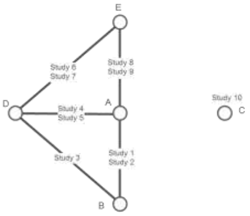


Population-Adjusted Indirect Comparison (2 Trials)

- 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