Erasmus School of
Health Policy
& Management

Implications of ICH E20 for health technology assessment

Seamus Kent
Erasmus University Rotterdam

Erasmus University Rotterdam

HTA bodies and regulators…

1. …make different decisions
2. …have different preferences about clinical trial design
3. …use evidence from clinical trials in different ways

HTA bodies and regulators make different decisions and have different evidence needs

HTA bodies ask:

- What is the additional benefit of the new technology compared to the local standard of care on patient centered outcomes among patients eligible for treatment in routine care?
- Some ask: Do the additional benefits justify the additional cost (ie cost effectiveness)

They need evidence on:

- Size of treatment effect
- Against local standard of care
- In decision relevant population
- Patient centered outcomes (survival, QoL, clinical events)
- Long-term outcomes (ideally patient lifetime for CEA)

HTA bodies and regulators have different preferences about clinical trial design

Component	HTA preference	Adaptive trial impacts
Outcomes	Clinical events, overall survival, quality of life, (resource use/costs)	Lower quality evidence – role of secondary outcomes in adaptive trial design?
Outcome (effect)	Size of treatment effect for added benefit analysis; mean effect has dominant role in CEA	Potentially increase uncertainty.
Follow-up	Long-enough to observe all differences or reliable extrapolate	Potentially shorter follow-up; more extrapolation
Population, Intervention, Comparator (PIC)	PIC elements known in advance and relevant to local setting: eligible population, local standard of care	Changes to PIC elements during trial; challenges to relevance and process

HTA bodies and regulators use evidence from clinical trials in different ways

Evidence synthesis

Economic modelling

Evidence synthesis

HTA principles

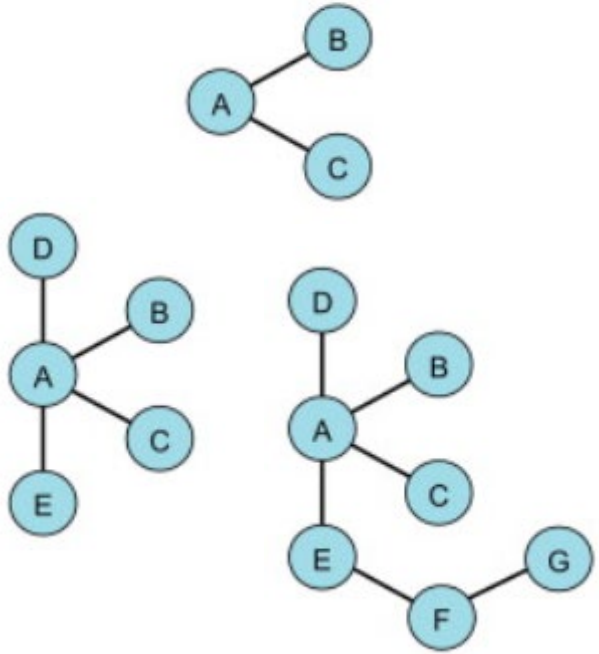
- Compare the new technology against local standard of care or best practice
- Consider all available evidence

Methods

- Use (network) meta-analysis and indirect treatment comparisons
- Relies on assumptions about similarity of trials

Potential impacts of adaptive trials

- Different populations
- Differences in interventions
- Varying data maturity levels (follow-up duration, events)



Jansen et al. 2011

Economic modelling

HTA principles

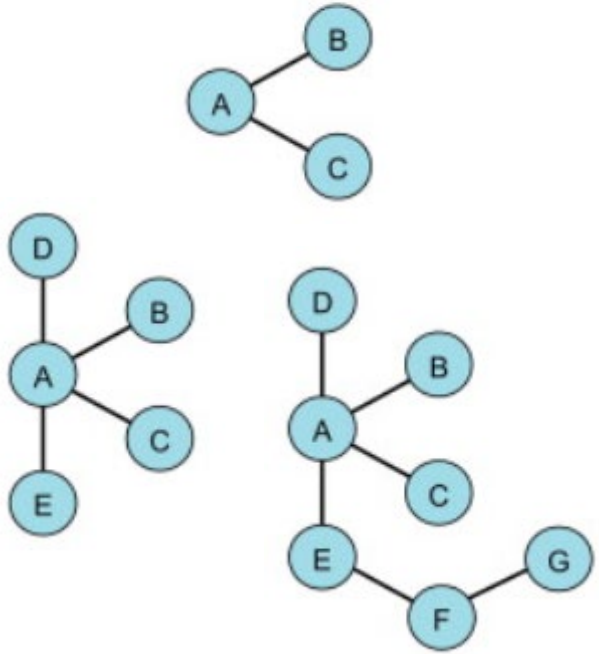
- Compare all differences in costs and effects during period in which incurred, usually over the patient lifetime

Methods

- Parametric time-to-event modelling
- Modelling surrogacy relationships

Potential impacts of adaptive trials

- Less mature data on relevant modelling endpoints
- Shorter follow-up -> greater need for extrapolation beyond trial -> major driver of uncertainty in health economic models
- Less precise estimates of treatment effects –> risks due to emphasis on mean cost-effectiveness



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