HTA considerations when supplementing RCT with non-randomized data

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Disclaimer

The views presented here are my own and should not be considered the views of NoMA, EMA or all HTAs in general.
RWE, the new magic bullet

• Not in the HTA world
• Data sources other than RCTs have always been used.
RWE, the new magic bullet

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• A health technology assessment has to:
  - Incorporate all appropriate evidence into the analysis
  - Compare the new intervention with the full range of relevant alternatives
  - Reflect uncertainties in the conclusions of the analysis
HTA models have always relied on the use of f.e.

• Utility values have routinely been derived from large observational studies and surveys
  • If one has a Societal perspective this is unavoidable
  • NoMA has a mixed, societal/payer perspective, yet we tend to accept observational utilities over trial derived utilities (the patients perspective)

• Expected number of patients are often based on sources such as the Norwegian prescription database

• Non-drug related costs, related to national clinical practice are variables often derived from registries/expert opinion
Is RWE always acceptable?

- No but it can be:
  - Small populations
  - ATMPs
  - Orphan drugs (COMP)
  - Personalized medicine
  - Histology independent (agnostic)
How do you want it - the crystal mumbo jumbo or statistical probability?
The problem

• RCT
  Efficacy
  Does it work in experimental setting
  Population selected
  Placebo or a selected comparator

• Real world
  Effectiveness
  How does it work in medical practice
  Patients as they come
  Many alternative treatments
Models to ‘predict’ the future

- All models are wrong; some models are useful
  George E. P. Box; Norman R. Draper (1987)

- Health economic models predict the future based on available data from different sources
Models to ‘predict’ the future

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HTA: the basics

• The aim is to maximize the health of the total population within the given budget

• HTAs want value for money!

Choice

\[
\text{ICER} = \frac{\text{Incremental costs (A-B)}}{\text{Incremental benefit (A-B)}}
\]

Economic evaluation

‘the comparative analysis of alternative courses of action in terms of both their costs and consequences’

(Drummond McGuire, 2001)
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Data, we need data

• All HTA agencies need robust comparative (randomized) data

• Cost utility analyses (CUA) require even better data
  • To run a lifetime horizon model extrapolations is almost always required
  • Transition probabilities between health states must be informed by enough data
RWE Intensifying Across Product Lifecycle

Development
- Budget Impact
- Unmet need/disease burden
- Patient recruitment
- Understand standard of care
- Trial design

Growth Phase
- Post marketing commitments (safety etc.)
- Adherence
- Utilization/prescribing patterns
- Long-term clinical outcomes
- Differentiation in sub-populations
- Target populations
- Usage Difference

Mature Phase
- Effects of switching on outcomes
- Differentiate with or vs. protected formulation

Evidence Required
- Launch
- Pricing Review
- New Competition
- New Formulation/Indication
- Competitor Goes Generic

Red and blue lines represent Now and Past, respectively.
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Past

Now
Guidance

- NICE, TSD17 (The use of observational data to inform estimates of treatment effectiveness in technology appraisal: Methods for comparative individual patient data)
- Institute of Health economics Alberta
- FDA
  - Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices; Guidance for Industry and Food and Drug Administration Staff.
  - Use of Electronic Health Record Data in Clinical Investigations Guidance for Industry
- National HTA agencies