Reduction of bias or a burden? The use of individual-patient models for submission to HTA authorities

A NICE Appraisal Committee member's perspective

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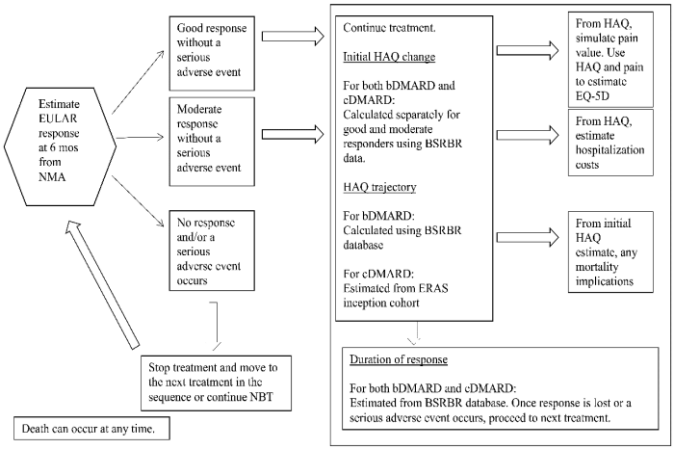
Committee requirements (my view)

- The model sufficiently reflects the decision problem it is trying to address
- Avoids inappropriate restrictive assumptions which are likely to matter
- Appropriate use of best available evidence
- Appropriate characterisation of uncertainty
- The ERG understands and trusts the model
- The appraisal committee understands and trusts the model

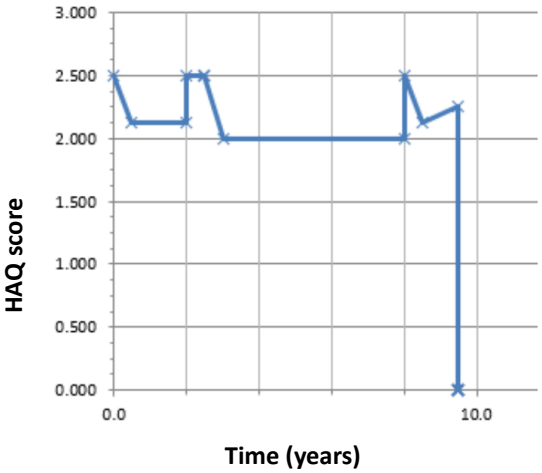
Example 1: bDMARDS for RA (TA375)



- DES
- Sequences
- Model centred around the HAQ
- Mortality risk, utilities and costs driven by HAQ

Stevenson et al, J Rheumatol, 2017

Example 1: Example HAQ trajectory

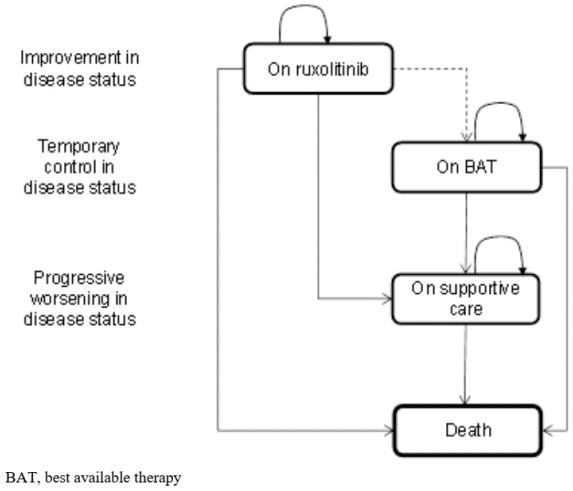


Example patient route

- Moderate response to 1st drug, discontinued at 2 years
- No response to 2nd drug
- Good response to 3rd drug, discontinued at 8 years
- Moderate response to 4th drug (cDMARD),
- Worsened and died at 9.4 years

DES required to accommodate preferred assumptions about HAQ & treatment impact

Example 2: Ruxolitinib for MF (TA386)



BAT, best available therapy

- DES
- Structured around pathway and HRQoL assumptions (+stopping rule)
- Similar to STM except estimates time to events
- Intermediate health state (SC)
- DES required to avoid tunnel states

NICE, TA386 Committee Papers, 2015

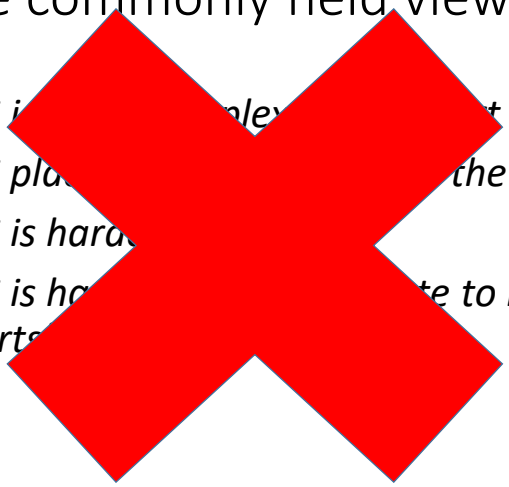
What did the NICE FADs say?

- **Example 1: bDMARDs for RA**
  - Barely a passing mention…
  - Includes discussion around plausibility of individual assumptions e.g. HAQ rebound, sequences, non-linear HAQ trajectory for cDMARDs
- **Example 2: Ruxolitinib for MF**
  - *"Novel"* approach - most oncology models use cohort structures
  - Justified given progressive disease
  - ERG report comments on value of flexibility in exploring structural uncertainty but notes that approach makes *"considerable demands of the limited data"*

Is the argument about methodology at all?

- Key issue is about how to handle *complexity*, rather than the modelling approach
- Complexity – e.g. where event risk or outcome is dependent on time since entry into an intermediate state
- Three options:
  1. Ignore it
  2. Loosen restrictive assumptions in cohort model
  3. Use an individual patient-level approach

Some commonly held views



- *"DES i… …ple… …t models"*
- *"DES pla… …the data"*
- *"DES is hard…"*
- *"DES is ha… …te to non-experts"*

Some recommendations

- Start with the problem, not the solution.
- Think about the "tipping point" – would DES be easier?
- When to think about using patient-level simulation:
  1) When you're about to make a huge assumption on the basis of convenience
  2) When you realise you're going to need a lot of health states
  3) When the prospect of programming that cohort model scares you
  4) When you've finally programmed that model, but nobody else understands it…

Discussion statement

- Neither cohort- nor patient-level models should always be preferred in all situations - model developers should adopt the simplest approach which retains the important complexities of the decision problem…

… sometimes this will be patient-level simulation