Development of the Birmingham Rheumatoid Arthritis Model: Past, Present, and Future Plans

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History

- First commissioned model (Birmingham Preliminary Model - BPM) as part of assessment of TNF inhibitors etanercept and infliximab (HTA vol 6 no 21)
- Important features of model established

Features of B P M 1

- Continuous time individual sampling model with lifetime horizon
- Inclusion of DMARDs after TNF inhibitors
- Time on treatment following Weibull distribution (modelled using tracker variables in TreeAge)

Features of B P M 2

- Population starting with early DMARDs (cancel out of analysis if divergence point not reached) – only need one starting population for different decision points
- Toxicity of one treatment may preclude its use in a later combination
- Rebound equal to HAQ improvement on starting treatment (subject to max HAQ of 3)

Features of B P M 3

- Costing of treatment and monitoring
- Additional costs early in treatment modelled as “one off” start-up cost
- Discounting to divergence point between strategies
- Delay in benefit of treatment and “tapering off” modelled as QALY losses at start and end of treatment

Limitations of B P M

- Quality of life on treatment taken as relative to natural history
- Long term progression on treatment necessarily parallel to natural history
- No severity-related mortality effects could be modelled
- No account of joint replacement or hospitalisation

B R A M First Version 1

- Developed as part of methodological TAR (HTA vol 8 no 11) ready for anakinra appraisal (HTA vol 8 no 18)
- Patient health state defined by HAQ score
- Only valid HAQ scores (points on discrete scale) allowed
- Short term improvement on starting treatment modelled as fixed decrease in HAQ

B R A M First Version 2

- Long term progression on treatment could now vary by treatment – allows assumption of constant HAQ while on TNF inhibitors
- HAQ dependent mortality now included
- Quality of Life modelled as linear function of HAQ (supported by data set)
- Joint replacement and hospitalisation modelled in methodological TAR only

B R A M First Version 3

- Still using starting population new to DMARDs but now patients not reaching divergence point are discarded and replaced
- Patient characteristics at divergence point preserved – small effect of variance reduction
- Switch from TreeAge to Borland Delphi gave 100-fold improvement in running speed

B R A M Second Version

- For adalimumab and review of etanercept and infliximab (HTA vol 10 no 42)
- HAQ improvement on starting treatment now based on variable multiplier
- Two stages of early withdrawal included
- Stopping rules included implicitly

B R A M Third Version

- For recent appraisal of adalimumab, etanercept, infliximab, rituximab, and abatacept following failure of first TNF inhibitor
- Coding included to accommodate probabilistic sensitivity analysis
- Switched to quadratic function from HAQ to quality of life (different statistical paradigm)

Needs for Future Modelling 1

- Assumption of fixed start up costs followed by constant annual costs difficult to sustain for infliximab and (especially) rituximab
- Need to change modelling so that each new prescription is an event in the model
- Continuous time modelling facilitates variable interval between treatments

Needs for Future Modelling 2

- Would like to include more detailed description of patient health
- Possibilities here include aspects not captured in HAQ and individual components of HAQ
- Would allow more realistic quality of life equation
- Issue – how do these vary over time on all treatments?

Needs for Future Modelling 3

- Possibility of explicit modelling of adverse events
- Joint replacement and hospitalisation

Any Questions?