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

Pelham Barton
West Midlands Health Technology Assessment Collaboration

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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
• 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?