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The Sheffield RA Models

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Presentation

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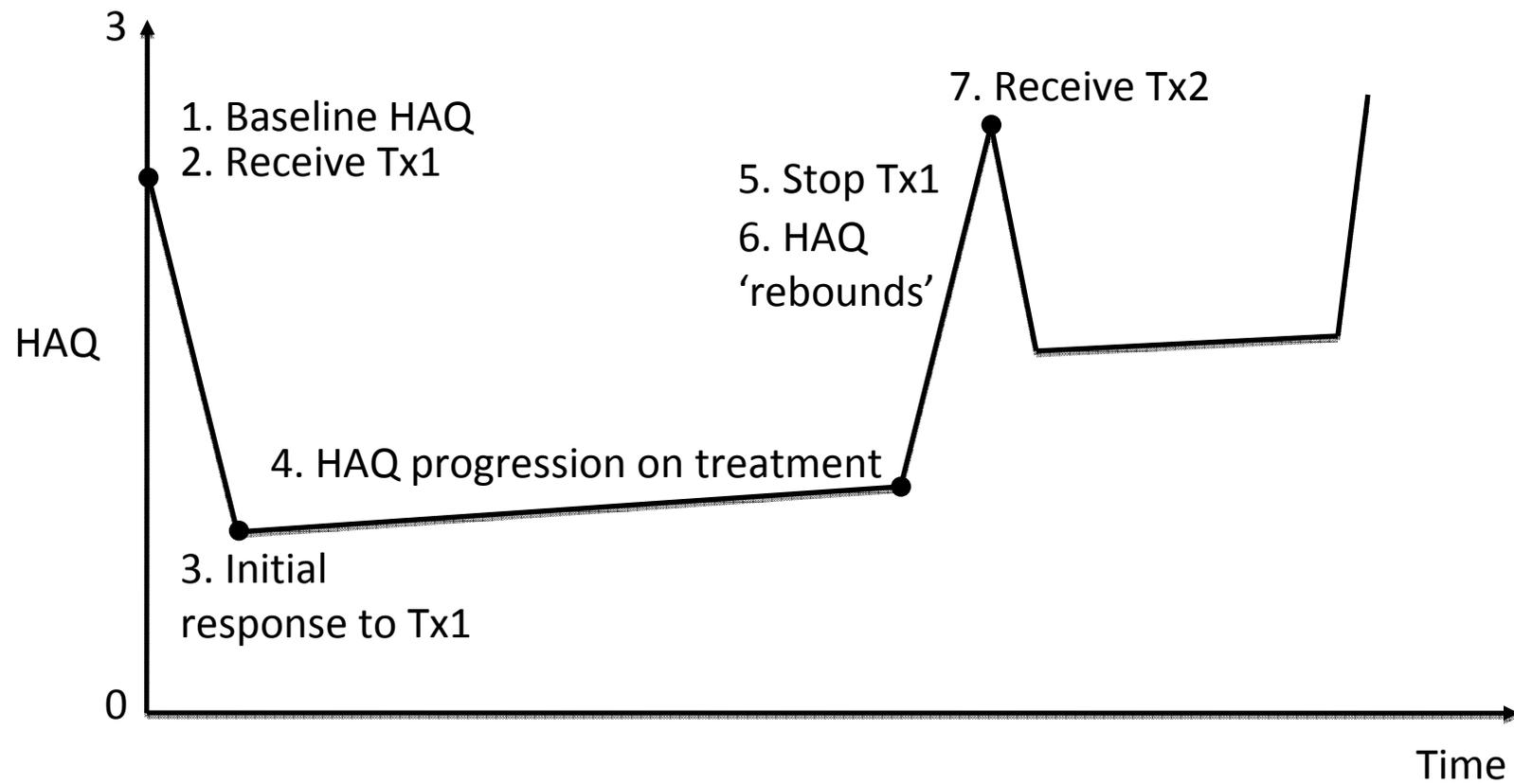
Introduction

- ScHARR - University of Sheffield
 - Health Research
 - Consultancy
 - NICE
- Our work in RA has come from all three
- ScHARR have produced more RA models than are mentioned today!
- Have an interest in musculoskeletal conditions (OA, OP, AS, PA)

The ScHARR Model(s)

- Individual Patient Sampling (IPS) model
 - Generates a simulated patient with a set of characteristics
 - Patient{age,gender,HAQ,disease duration,DMARDs,TNFs}
 - Evaluates patient's HAQ score over their lifetime
 - Estimates total cost and total QALYs
- Model runs 000's patients to estimate mean total cost and total QALYs
- Allows the comparison of alternative treatments
- Incorporates uncertainty

HAQ



Etanercept Model

- First model built at ScHARR
- Was consultancy work for Wyeth
 - submission document for NICE TA36
- Analysis in line with BSR “*two DMARDs first*” guideline recommendation
- Evaluates etanercept as third line therapy vs sequential DMARD therapy
- Etanercept £16,330 per QALY (£7k - £42k)
 - NICE appraisal: £27k - £35K per QALY

Etanercept Model

Parameter	Etanercept	DMARDs
ACR20 response (%)	Patient level trial data	RCT DMARD arms
Treatment withdrawal	Observational data	Observational data
ACR20 HAQ improvement	Patient level trial data	Trial data mean HAQ improvement •Adjusted for disease duration •Adjusted for ACR20 responders only
HAQ progression - responders	Trial evidence applied to DMARD base rate	Pooled analysis from systematic review
HAQ progression – non-responders	ERAS observational data	ERAS observational data
HAQ ‘rebound’ after withdrawal	Rebound equal to initial gain	Rebound equal to initial gain
Healthcare costs	Applied linear function between HAQ and costs •Evidence taken from Swedish and US studies	
Utility	Pooled relationship of HAQ to utility taken from four published studies	

BSRBR Model

- Was a research project using the British Society for Rheumatology Biologics Registry (BSRBR) dataset
- Evaluates TNF- α inhibitors as third line therapy vs sequential DMARD therapy
- BSRBR provided patient level data
 - DAS28, HAQ and SF-36 outcomes
- Patient level data allowed multivariate analysis for parameters
- TNF- α inhibitors £24k per QALY vs DMARD monotherapy

BSRBR Model

Parameter	TNF- α inhibitors and DMARDs
EULAR (non/moderate/good) response	BSRBR data
Treatment withdrawal	BSRBR data
EULAR HAQ improvement	BSRBR data
HAQ progression	Observational study data
HAQ 'rebound' after withdrawal	Rebound equal to initial gain
Healthcare costs	BSRBR data
Utility	BSRBR data

AHRQ Model

- Was a research project for the Medicare Prescription Drug Improvement and Modernization Act (MMA)
 - Supported by the US Agency for Healthcare Research and Quality (AHRQ)
- Evaluates infliximab, etanercept, adalimumab and anakinra in patients who had not failed a biologic
- Incorporates data from the National Databank for Rheumatic Diseases (NDB)
- Recommends the use of etanercept or adalimumab, and not infliximab or anakinra

AHRQ Model

Parameter	TNF- α inhibitors
Sub ACR20, ACR20 and ACR50	Published Mixed Treatment Comparison
Treatment withdrawal	BSRBR data – multivariate Weibull
ACR HAQ improvement	Multivariate analysis from the NDB
HAQ progression	Multivariate analysis from the NDB
HAQ 'rebound' after withdrawal	Rebound equal to initial gain
Healthcare costs	NDB HAQ to Medicare cost relationship derived
Utility	Multivariate analysis from the NDB – US EQ-5D

DMARDs Model

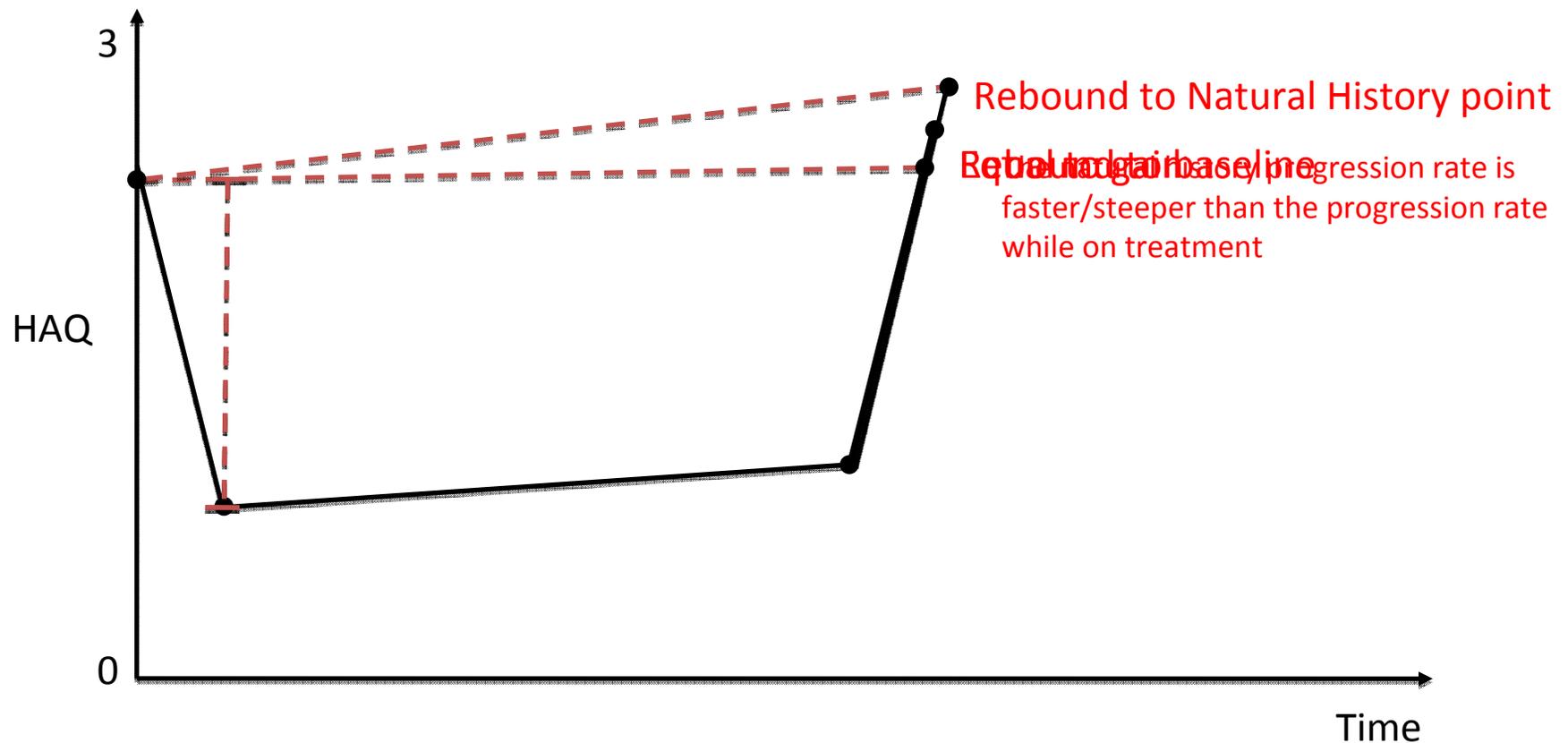
- A NICE Clinical Guideline project – health economics was undertaken by ScHARR
- Evaluates combination DMARD strategies vs monotherapy DMARDs in patients with early RA (pre-biologics).
- Fits into the “*two DMARDs before biologics*” decision space, as determined by NICE appraisals
 - Patient’s who fail on a combination progress straight to TNF- α inhibitors
- Costs and QALYs from BSRBR model ‘bolted on’ to provide a lifetime model
- Combinations that either titrate dosage downwards, or involve intensive triple DMARDs are likely to be cost effective compared to monotherapy

DMARDs Model

Parameter	Combination DMARDs	Monotherapy DMARD
Sub ACR20, ACR20 and ACR50 response	Mixed treatment comparison	Meta-analysis
Treatment withdrawal	Trial withdrawal rate with constant risk	
ACR HAQ improvement	AHRQ model analysis	
HAQ progression	Published observational analysis	
HAQ 'rebound' after withdrawal	Rebound equal to initial gain	
Healthcare costs	Resource Utilisation Norfolk Arthritis Register (NOAR) HAQ to Cost function	
Utility	Published HAQ to EQ-5D function	

Key Assumptions (1)

- Rebound



Key Assumptions (2)

- Rebound is important
 - Very little evidence available
 - It determines whether or not long term benefit is achieved by a treatment
 - If differential assumption, or differential progression rates...
 - KEY DRIVER FOR COST-EFFECTIVENESS!

Key Assumptions (3)

- HAQ
 - Used to track a patient’s “disease activity”
 - It is not a preference based measure
 - Ideal is for Health Related Quality of Life (HRQoL) instruments to be used (EQ-5D, SF-6D)
 - EQ-5D is preferred by NICE
 - HAQ correlates well with HRQoL’s
 - EQ-5D not widely used in international trials
 - Hence why ‘mapping’ from HAQ to EQ-5D is used, to meet NICE’s Methods Guide

Conclusions

- The Sheffield models continue to be used/refined
 - The HAQ based ‘structure’ allows a flexible model to be developed to meet a clients requirements
- Observational data plays a key role in populating RA models
- The decision space continues to get more complex
 - More treatment options, and more NICE guidance
- Expert input is key at all stages of model development
 - Conceptual modelling
 - Population of model
 - Validation of model

Thanks

- Thanks to ARUK/MRC HTMR for inviting me to speak
- Thanks to Nick Bansback, Allan Wailoo and Alan Brennan for their input

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