**BACKGROUND**

- Disease progression models describe the evolution of a clinical endpoint over time.
- As a key element, health economic models usually contain a disease progression model to predict the effect of treatment over time.
- To predict outcomes under active treatment one needs to describe how treatments change disease progression.
- Extending disease progression models by individual level covariate effects (including treatment) allows to predict differences between populations and treatment groups.

**OBJECTIVE**

- To identify and assess disease progression models used in rheumatoid arthritis (RA) cost-effectiveness modelling.

**METHODS**

- We examined all studies identified in two recent systematic literature reviews on health economic decision models evaluating RA treatments (Ganz 2015, Scholz and Mittendorf 2014).
- We identified the elements in these studies describing disease progression and classified them by outcome measure affected and by model type.

**RESULTS**

Disease progression models were in most cases developed for the health assessment questionnaire (HAQ) score. The review identified four modelling frameworks: individual sampling models, discrete event simulation models, microsimulation models, and Markov cohort models. The reported individual sampling models and discrete event simulation models make assumptions about improvement of the HAQ when treated progression rates that can differ between treatments. A few of the Markov cohort models treat disease progression as separate states, depending on the patient’s type of response (e.g. remission, good, moderate or no response, measured by the American College of Rheumatology (ACR) response criteria or by the disease activity score 28 (DAS28)). Furthermore, they all assume a long-term deterioration in the HAQ score and a rebound effect when the treatment stops, i.e. for example a complete loss of the initial gain. Microsimulation and Markov cohort models use simpler structures with average annual HAQ tes of the DAS28 and estimate transition probabilities between such states over time. Disease progression of a radiographic score was modelled in one study, assuming a diseased deterioration of the radiographic score while being on treatment. No study modeled the impact of disease progression models on ACR response criteria. Finally, the two reviews did not include any cost-effectiveness analysis using decision trees that contained a disease progression model. See the table below for a summary of the identified models.

**REFERENCES**

**ENDPOINT** | **MODEL TYPE** | **DESCRIPTION** | **REFERENCE**
--- | --- | --- | ---
HAQ | Individual sampling model | “Sheffield Rheumatoid Arthritis Model”
- According to the type of response (measured by ACR), change in HAQ due to treatment
- Long-term HAQ progression, depending on treatment
- When treatment stops, HAQ “rebounds” (i.e. goes back to baseline, or loses initial gain, or increases to which it would have been without treatment) | Brennan (2004), Walloo et al. (2008)
Individual sampling model | - Patients follow certain disease course (spontaneous remission, slow or rapid progression)
- According to the type of response (measured by DAS28 and ACR), change in HAQ due to treatment
- Long-term HAQ progression, depending on response type and radiographic scores | Finckh et al. (2009)
Discrete event simulation model | “Birmingham Rheumatoid Arthritis Model”
- Fixed improvement of HAQ when treatment starts
- Rate of deterioration of HAQ over time, depending on treatment
- Loss of initial HAQ improvement when treatment stops | Barton (2011), Barton et al. (2004)
Microsimulation model | - Transition probabilities for five HAQ states, depending on treatment
- Annual HAQ progression rates, depending on treatment
- Radiographic damage affecting HAQ progression
- Loss of initial HAQ improvement when treatment stops | Kobelt et al. (2011)
Markov cohort model | - Transition probabilities for different HAQ states, depending on treatment and covariables
- Annual HAQ progression, depending on treatment
- Loss of initial HAQ improvement when treatment stops | Leander et al. (2013), Kobelt (2003), Kobelt et al. (2002)
DAS28 | Markov cohort model | - Transition probabilities for different DAS28 states (e.g. high or low disease activity), depending on treatment | Leander et al. (2013), Schipper et al. (2011), Welsing et al. (2004)
Radiographic score | Individual sampling model | - Decreased progression of radiographic score when patient is treated, depending on type of response (measured by DAS28 and ACR) | Finckh et al. (2009)

**CONCLUSION**

- Health economic decision models in RA include disease progression predominantly through the HAQ score.
- Discrete endpoints such as ACR20/50/70 are typically modelled directly and not linked to an underlying smooth disease progression process.