65. Similarly, a 5-point lower MCS score among those with depression was associated with a 10% increase in MEs at age 25 but 4% at age 55. **CONCLUSIONS:** Differences in SF-12v2 scores, particularly PCS, had substantial impact on MEs, allowing enhanced interpretation of intervention-based improvements in SF-12v2 scores. In arthritis and depression, age significantly impacted the association between HRQL and MEs.

PP3
CONDITION SPECIFIC UTILITIES: IMPACT ON ICER IN A MARKOV MODEL FOR MULTIPLE SCLEROSIS

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OBJECTIVES: Perceived and observed insensitivity of the EQ-5D instrument in certain clinical areas has led to the development of condition specific preference based instruments, also for Multiple Sclerosis (MS). It is uncertain how these instruments perform in economic evaluations. This study investigates the effect on the incremental cost-effectiveness ratio (ICER) of using MS specific utility values rather than generic utility values. **METHODS:** A Markov model with a lifetime time horizon comparing symptom management with subcutaneous glatiramer acetate was based on a previously published study. The model has four EDSS health states and two relapse states, a one month cycle, accounts for age specific background mortality and discontinuation of therapy. Costs and effects were discounted with 3%. For this study, QALYs were calculated with utility values from the MSIS-PBM, a sensitive condition specific utility instrument based on a Time Trade-off valuation of MSIS-29, and EQ-5D utility values. Values were both taken from the UK risk sharing scheme. Deterministic and Monte Carlo simulation based probabilistic sensitivity analyses were used to assess impact on ICER. **RESULTS:** The mean ICER after 5000 simulations was USD 291.545 using MS specific utilities, and 180.633 using EQ-5D based utilities. **CONCLUSIONS:** This study used condition specific and generic utility values in a hypothetical Markov model for relapsing remitting MS patients and showed that the incremental cost-effectiveness ratio was 60% higher when applying the condition specific utilities. Contrary to what might be expected, the condition specific utility instrument was not better at demonstrating treatment value than the generic EQ-5D.

PP4
THE RELATIONSHIP BETWEEN GLUCOSE-LOWERING MEDICATIONS, ADHERENCE, AND OUTCOMES IN PATIENTS WITH TYPE 2 DIABETES

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OBJECTIVES: Adherent type 2 diabetes (T2DM) patients are more likely to have good glycaemic control than non-adherent patients, potentially resulting in better outcomes. We investigated the association between the number of glucose-lowering therapies, adherence and their impact on glycaemic control and quality of life (QoL). **METHODS:** Data were drawn from the 2013 Diabetes Disease Specific Programme, a large cross-sectional real-world survey of primary care physicians (PCP) and specialists and their patients consulting for diabetes. Physicians provided information regarding prescriptions, previous treatment and most recent HbA1cvalues. Patients completed the Morisky Measurement of Adherence Scale and the EQ-5D. Patients who had been on current treatment between 6 months and 5 years and had values for all variables were included. A linear Structural Equation Model was developed to explore the relationships between the number of oral and injectable diabetes medications per day, adherence, glycaemic control and QoL while adjusting for confounding factors relating to duration and type of medication, existing complications, concomitant conditions, demographic and lifestyle factors. **RESULTS:** 239 PCPs and 137 specialists across 5 EU countries provided data on 1209 T2DM patients. 58% patients were male, mean age 60.7 years (+/-10.3); number of oral medications 2.21 (+/-1.16); injectables 0.36 (+/-1.03); current HbA1c6.94% (+/-0.80). The model shows that a lower number of daily diabetes medications is positively associated with adherence [orals (β=-0.10, p<0.001), injectables (β=-0.049, p<0.001)]. Improved adherence is associated with a lower HbA1c (β=-0.10, p<0.001), lower HbA1cis associated with improved QoL (β=-0.019, p<0.001). **CONCLUSIONS:** Controlling for important clinical and demographic factors, a lower number of daily glucose-lowering therapies is associated with greater adherence which, in turn, is associated with better glycaemic control and improved QoL. Further research is required to investigate if these associations vary depending on the specific medication taken or other patient-related parameters not considered here.

RESEARCH ON METHODS STUDIES – II

RM5
NETWORK META-ANALYSIS OF SURVIVAL DATA USING FRACTIONAL POLYNOMIALS – AN EXAMPLE WITH FIRST LINE METASTATIC RENAL CELL CANCER TREATMENTS

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OBJECTIVES: Summary survival data are available from published trials on first line metastatic renal cell cancer (1LmRCC) treatments. Survival on oncological treatments in pharmacoeconomics is mainly estimated by fitting common parametric distributions over Kaplan Meier (KM) curves, assuming proportional hazards over time. Use of fractional polynomials (FP) allows for change of hazards over time and offers more freedom in distribution selection. This study aims to analyse existing survival data of 1LmRCC treatments through a network meta-analysis (NMA) and FP application. **METHODS:** A systematic literature review was performed to identify randomized clinical trials (RCT) of 1LmRCC treatments with progression

free survival (PFS) and/or overall survival (OS) as reported outcomes and to create a RCT network accordingly. Fixed and random effects FP models of first/second order were applied on these data and tested for goodness of fit using deviance information criteria. Finally, the best fitting model was used to estimate the hazard function, median PFS, median OS and uncertainty of treatment effect. **RESULTS:** Literature review found 8 RCTs and 5 RCTs which reported PFS and OS respectively, for 7 different mRCC treatments (interferon-alfa (IFN), bevacizumab+IFN, temsirolimus+bevacizumab, sunitinib, pazopanib, cediranib, placebo). The best fitting FP model was second order random effect model for both, PFS and OS NMA. Hazard functions varied significantly. Estimated median PFS was the longest with sunitinib (10.8 months; 95% credible interval (CI): 9.5-11.8), followed by pazopanib and temsirolimus+bevacizumab. Similarly, sunitinib was estimated with the longest median OS (28.8 months; 95% CI: 25.7-31.0) followed by pazopanib and bevacizumab+IFN. **CONCLUSIONS:** Synthesis of NMA evidence for 1LmRCC treatments identified sunitinib to be the treatment with favourable PFS and OS. When dealing with multiple sources, hazards proportionality assumption is violated, and proposed method should be the method of choice.

RM6
NETWORK META-ANALYSIS OF BIOLOGICAL RESPONSE MODIFIERS IN RHEUMATOID ARTHRITIS INCLUDING REAL WORLD EVIDENCE AT MULTIPLE TIME POINTS

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OBJECTIVES: Network meta-analysis (NMA) is widely used to compare multiple interventions of interest when head-to-head comparisons of active treatments are not available. Most NMAs pool data from randomised controlled trials (RCTs) on a single clinical outcome. However, in the case of chronic diseases such as rheumatoid arthritis (RA), outcomes are often reported at different time points and long-term real-world data (RWD) is routinely collected as part of national registries. Evaluation of models for the inclusion of different time measures in NMA, especially from both a regulatory and reimbursement perspective, is thus warranted and is considered here. **METHODS:** RCTs and observational studies evaluating biological agents in RA were searched using standard filters and electronic databases. Networks of RCTs were supplemented with RWD to include outcomes extracted for as many time points as possible. Multivariate NMA models were extended to incorporate repeated measures, adjusting for correlation between time points and bias of RWD. Sensitivity and scenario analyses were performed to test different network sizes, correlation structures and bias adjustments. **RESULTS:** Addition of RWD and studies reporting treatment effects at multiple time points significantly increased the evidence base for NMA in RA. The inclusion of RWD led to a reduction in the level of uncertainty around most of the effect estimates. Furthermore, the additional evidence from multiple times has potential of reducing uncertainty by 'borrowing' evidence and giving a fuller view of treatment effect over time, not just at a specific single time point. **CONCLUSIONS:** Initial evaluation of these models in NMA indicates that extending an evidence base to include repeated measures and RWD maximises study network sizes and can significantly impact the level of uncertainty in treatment effects. Further investigation of correlation and bias modelling is warranted, as too is the application of new NMA fractional polynomials model to RA.

RM7
SIMULATION OPTIMISATION OF TREATMENT SEQUENCES FOR RHEUMATOID ARTHRITIS

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OBJECTIVES: Using simulated annealing (SA) to inform the economic evaluation of treatment sequences for rheumatoid arthritis (RA). **METHODS:** A discrete event simulation (DES) model was built to estimate lifetime costs and Quality Adjusted Life Years (QALYs) of alternative sequences for the treatment of patients with severe RA. Thirteen Disease Modifying Anti-Rheumatic Drugs (DMARDs) can be used sequentially, with a theoretical maximum size of the decision space of over 10 billion unique sequences. This problem can be formulated as an optimisation problem – finding the treatment sequence that maximises net monetary benefit (NMB). However, it was not feasible to evaluate the NMB of every treatment sequence in the decision space. SA, a stochastic optimisation algorithm, was used to identify a sequence that was optimal, or near optimal. Given the evaluation of the NMB of some particular sequence by the DES model , the SA algorithm then selects a "nearby" sequence to evaluate. Better solutions are accepted, and worse solutions are sometimes accepted with a probability reducing as the algorithm progresses. This attempts to prevent the optimiser from getting stuck in a local optimum. Comprehensive tuning of the parameters of the SA algorithm was undertaken, and scenario analysis was performed. **RESULTS:** At a willingness to pay of £30,000 per QALY gained, the best performing sequence found was exclusively composed of conventional DMARDs. At £50,000 per QALY gained, the best performing sequence began with conventional DMARDs for the first four treatment lines, before beginning biologic DMARD treatment. The results were consistent when re-run, and when alternative specifications of the SA algorithm were used. **CONCLUSIONS:** SA is a commonly used optimisation method, but it has rarely been applied in HTA. In this instance, SA performed well and may be an appropriate method for health resource allocation decision-making where there is a large decision space.

RM8
COMPARISON OF TIMED AUTOMATA WITH DISCRETE EVENT SIMULATION FOR MODELING PERSONALIZED TREATMENT DECISIONS: THE CASE OF METASTATIC CASTRATION RESISTANT PROSTATE CANCER

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OBJECTIVES: The aim of this study is to compare the usefulness of two promising alternative modeling techniques, Timed Automata (TA) originating from