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, temisrolimus+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

informatics, and Discrete Event Simulation (DES) known in operations research, for modeling todays complex and personalized treatment decisions over time, involving multiple interactions and decision gates. **METHODS:** The usefulness of both modeling techniques was assessed in a case study on the treatment of metastatic Castration Resistant Prostate Cancer (mCRPC) in which Circulating Tumor Cells (CTC) may be used as a response marker for switching first to second line treatment. Techniques were compared on user-friendliness, input requirements, input possibilities, model checking facilities, and results. Input parameters were similar for both models, consisting of costs, QoL, treatment effectiveness, diagnostic performance, physicians' behavior and survival. Primary outcome measures were health outcomes, expressed in QALYs, and costs. **RESULTS:** Modelling was considered easier using TA, as this approach allows independent modeling of the actors and elements comprising the treatment process, such as patients, physicians, tests and treatments, and their mutual interaction and communication. Furthermore, the statistical model checking feature in the TA software was found to be a powerful tool for validation. Input requirements and possibilities were similar for both modelling approaches in this case study. Both modelling approaches yield comparable results. Using TA, CTC reduced first and second line treatment by, on average, 108.9 and 107.6 days, respectively. Using DES, treatment was reduced by 83.6 and 85.0 days. CTC therefore reduced healthcare costs by €28,998 and €21,992 according to TA and DES, respectively. **CONCLUSIONS:** Both Timed Automata and Discrete Event Simulation seem to be suitable for modeling complex and personalized treatment processes like that of mCRPC. Timed Automata is a new and interesting alternative modeling technique, as it allows explicit separation of model components and supports statistical model checking to validate models.

RESEARCH POSTER PRESENTATIONS – SESSION I

HEALTH CARE TREATMENT STUDIES
MEDICAL DEVICE/DIAGNOSTICS – Clinical Outcomes Studies

PMD1
SYSTEMATIC REVIEW OF THERMAL MASSAGE THERAPY FOR THE TREATMENT OF DRY EYE SYNDROME

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OBJECTIVES: The safety and effectiveness of Thermal Massage Therapy for the Treatment of Dry Eye Syndrome as a technology for treatment of dry eye symptom by stimulation of the obstructed meibomian glands through application of heat and vibration to the areas around the eyelids and the eyes were assessed. **METHODS:** For information search for systematic review considerations on Thermal Massage Therapy for the Treatment of Dry Eye Syndrome, 8 domestic databases including Korea Med and overseas databases including Ovid-Medline, Ovid-Embase and Cochrane Library were used. A total of 107 literatures were searched through search strategy. As the result, a total of 3 domestic and overseas literatures were included in the final assessment by applying the criteria for selection and exclusion to the 74 literatures after having excluded 33 overlappingly searched literatures. Each of the stages from literature search to application of selection standards and extraction of data were carried out independently by 2 assessors under the deliberation by the Sub-committee. Tools of Scottish Intercollegiate Guidelines Network (SIGN) were used for assessment of the quality of literature. **RESULTS:** Regarding the safety of the Thermal Massage Therapy for the Treatment of Dry Eye Syndrome, 3 literature reported conjunctivitis, temporary visual impairment, headache and abnormality in the area of contact as the procedure related complications or side effects. The effectiveness of the Thermal Massage Therapy for the Treatment of Dry Eye Syndrome was assessed by means of the ocular surface disease index (OSDI), break-up time (BUT), schirmer tear test (STT) and osmotic pressure of tear on the basis of 3 literatures. **CONCLUSIONS:** Thermal Massage Therapy for the Treatment of Dry Eye Syndrome was assessed as a safe and effective technology capable of improving the dry eye symptom by alleviating the obstructed meibomian glands through application of heat and vibration to the areas the eyes.

PMD2
A COST ANALYSIS OF OPEN SPINA BIFIDA DETECTION IN THE FIRST-TRIMESTER

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OBJECTIVES: The objective of this study was to examine the diagnostic accuracy of targeted sonomarkers in the first trimester for a simple screening method that improves outcome and has a positive cost/benefit ratio. **METHODS:** We analyzed 23 sonomarkers from 66 fetuses (6 cases of open spina bifida and 60 normal fetuses) to determine the most robust screening marker associated with spina bifida. We compared the variables between the two groups using Fisher's exact test or Mann-Whitney test. We evaluated the sensitivity with 5% FPR. We also performed receiver operating characteristic (ROC) curve analysis to determine which markers were significant to propose a simpler test. **RESULTS:** Some markers showed statistically significant differences between the two groups ($p<0.001$), but using both likelihood ratio and area under the ROC curve analysis, we demonstrated that the subjective Dry brain, Crush sign and BPD/AC ratio from axial views and numeric BS/BSOB ratio, FMF angle and Cisterna magna from sagittal views were significantly associated with the fetal risk of having OSB. **CONCLUSIONS:** Yet, subjective markers are usually dependent on the operator's experience. Contrary, the measurement of the BPD/AC ratio or the BS/BSOB ratio at 11-13 weeks is simple and could be easily incorporated into the routine scan. If this test accurately predicts open spina bifida in up to 100% of cases, it would cost for one diagnostic 200 Ron=44 Euro vs. the maternal serum alpha-fetoprotein test (250 Ron=55 Euro) or amniocentesis (2000 Ron=444 Euro) that are needed to early diagnosis of open spina bifida.

PMD3
CYTOGENETICS AND DOPAMINE RECEPTOR (DRD2) GENE POLYMORPHISM IN SCHIZOPHRENIA PATIENTS

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OBJECTIVES: Schizophrenia (SZ) is complex and multifactorial neuropsychiatric disorder.Schizophrenia is estimated to have the highest genetic and environmental loads and penetrance among the neurocognitive disorders. The essential role dopamine D2 receptor (DRD2) in dopamine signalling, DRD2 gene has been regarded as one of the top candidate genes for SZ. The intention of this study was to evaluate the chromosomal aberrations as well as disruption in the DRD2 gene among the SZ patients. **METHODS:** As a preliminary measure in the search for the chromosomal abnormalities of a gene or genes relevant to this illness, cytogenetic and molecular screenings using the Peripheral blood Lymphocyte of 45 SZ patients were obtained. Each patient were diagnosed by a neuropsychiatric professionals based on both DSM-IV(TR) and SCID questionnaire. Equal numbers of healthy controls were also analysed. **RESULTS:** In our study random numerical and structural aberrations were detected in chromosomes 6, 11, 15, 16 and 22 (15q13.3 and 22q11.2). In this study the comparison between the cases and control for the numerical as well as structural mutations showed a degree of ($P<0.001$) which was more in cases compared to control. Structural aberrations predominantly observed were deletions and micro-deletions of 22q11.2 and 15q13.3. Further, the disruption in the DRD2 gene which resulted into polymorphism was seen in SZ patients while compared to healthy controls. **CONCLUSIONS:** In conclusion, our cohort study supports the hypothesis suggesting that a chromosomal abnormality as well as disruption in DRD2 gene is contributing to SZ pathogenesis. On the contrary, genetics stimulate to rethink SZ from a neurological as well as biological viewpoint and also to understand the phenotypes of these disorder in terms of biological pathways. Key words: Schizophrenia, DRD2 gene, chromosomal abnormalities

PMD4
VIVASCOPE© FOR DIAGNOSING MELANOMA: A SYSTEMATIC REVIEW

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OBJECTIVES: Melanoma is the fifth most common cancer in the UK, accounting for 4% of all new cases of skin cancer. In 2011, 13,300 cases of malignant melanoma were diagnosed in the UK, out of which 2,200 people died from the disease. This systematic review evaluates the clinical effectiveness of VivaScope (MAVIG GmbH, Munich), a non-invasive reflectance confocal microscope (RCM), used following dermoscopy for the diagnosis of melanoma. This research was conducted as part of a National Institute for Health and Care Excellence (NICE) Diagnostic Assessment Report on VivaScope. **METHODS:** Electronic databases (MEDLINE, EMBASE and the Cochrane Library) were searched in October 2014 and updated in February 2015 to identify studies evaluating RCM following dermoscopy with histopathology as the reference standard in detecting malignant melanoma. Researchers were contacted for additional information on studies identified. Clinical experts were contacted for details on any unpublished studies. **RESULTS:** Of the 7,446 studies identified in the literature search, 10 were considered relevant to this review. However, none were conducted in the UK (1 Spain, 1 China, 1 Australia, 2 Brazil/USA, 2 Australia/Italy, 3 Italy) and the studies were considered too heterogeneous (e.g. differences in study design, patient/lesion level data, with/without comparator) for their results to be combined in a meta-analysis. Overall results indicate that RCM subsequent to dermoscopy may improve diagnostic accuracy of malignant melanomas compared to dermoscopy alone. One study (Alarcon et al. 2014) was deemed to be most representative of UK clinical practice and reported statistically significant differences in sensitivity (97.8% vs 94.6%, $p=0.043$) and specificity (92.4% vs 26.74%, $p<0.000001$), for VivaScope 1500 following dermoscopy compared with dermoscopy alone. **CONCLUSIONS:** VivaScope following dermoscopy may increase the accuracy of a diagnosis of malignant melanoma compared to dermoscopy alone. However, the absence of UK studies makes the generalisability of the results to UK clinical practice unclear.

PMD5
CLINICAL AND ECONOMIC IMPACT OF THE IMPLEMENTATION OF HPV 16/18 GENOTYPING TEST FOR CERVICAL CANCER SCREENING IN MEXICAN HEALTHCARE SYSTEM

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OBJECTIVES: HPV genotypes 16/18 are the most prevalent worldwide and are present in around 70% of all cervical cancer (CxCa) cases. This analysis aims to estimate clinical and economic impact of the implementation of HPV 16/18 genotyping test for CxCa primary screening at Mexican Institute of Social Security (IMSS) that is the main healthcare provider covering around 50% of Mexican population. **METHODS:** A cohort Markov model with a five-year time horizon was developed. A 300,000 women cohort was simulated since payer perspective. Two scenarios were evaluated: 1) cytology screening, where women are re-tested for ASCUS, ≥CIN1 are referred to colposcopy, cycle lenght is 1-year, if negative 3 consecutive cycles length changes to 2-years; 2) primary screening HPV genotyping, women HPV-16/18 are referred to colposcopy, other 12 high-risk HVP genotyping are referred to cytology with 12-months follow-up, and when negative a follow-up in 3-year cycle. Clinical and test performance data were taken from ATHENA trial and other published sources. Direct medical costs for cytology and CxCa treatments were obtained from local published sources. Costs for HPV genotyping test was given by the manufacturer. Costs are expressed in 2015 USD ($1USD=$15MXN). **RESULTS:** Due to cobas HPV genotyping sensibility, total number of CxCa cases would be 46% lower (221 vs 409, respectively) and would result in 44% less mortality events (8 vs 15, respectively) compared to cytology. To