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

**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 20 condition specific utilities and the effect of using generic utility values. **Methods:** A Markov model with a lifetime horizon comparing symptom management with subcutaneous glatiramer acetate was based on a previously published study. The model has four EDSS health states and two reafferent transitions for specific specific and generic effect states. **Results:** The model was run with and without transitional costs. The cost differences were £9000 and £2000 with and without discontinuation of therapy. Costs and effects were discounted with 3%. For this study, QALYs were calculated with utility values from the MSIS-29, a sensitive condition specific utility instrument based on a Time Trade-off valuation of SF-12v2, 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 £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:** The aim of this study was 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 MFs 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 MF 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 OS (36.3 months; 95% CI: 27.5–31.0) 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 potential confounding factors, non-inferiority assumption is violated, and proposed method should be the method of choice.

**RM1**

**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 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 evidence is needed as part of robust evidence synthesis. This study evaluates the use of NMA 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 therapies 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 time points 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 developed to model the pharmacokinetics, concomitant drug use 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 (+/–10.5), number of oral medications 2.21 (+/–1.16), injectables 0.36 (+/–1.03), current HbA1c 9.4% (+/–0.8). The model shows that a lower number of daily diabetes medications per day, adherence, glycaemic control and Qol, while adjusting for confounding factors related to duration and type of medication, baseline HbA1c, age, concomitant drug use, and lifestyle factors. **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 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:** Survival data are available from published trials on first line metastatic renal cell cancer (1LmRCC) treatments. Survival on oncological treatments in pharmacoconomics is mainly estimated by fitting common parametric distributions over Kaplan Meier (KM) curves, assuming proportional hazards over time. Time-Related Effects Models (TREM) allow for an adjustment of hazard and survival functions based on time and other covariates 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 FR 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 MFs 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 MF 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 OS (36.3 months; 95% CI: 27.5–31.0) 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 potential confounding factors, non-inferiority assumption is violated, and proposed method should be the method of choice.

**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 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 (mCPRC) in which circulating Tumor Cells (CTC) were the response marker to first vs second line treatment. Techniques were compared on user-friendliness, input requirements, output 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 treatment and effects comprising the 2015-2035 cohort of 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 necessary for validation. RESULTS: Each patient's data was assessed by a neurologist 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 S2 patients while compared to healthy controls. CONCLUSIONS: In conclusion, our cohort study supports the hypothesis suggesting that a chromosome abnormality DRD2 gene is contributing to SZ pathogenesis. On the contrary, genetic stimulation to rethink SZ from a neurological as well as biological viewpoint and also to understand the phenotypes of these disorder in term 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 (NAVI GmbH, Munich), a non-invasive reflective confocal microscope (RCM), using followed dermoscopy for the diagnosis of melanoma. This research was conducted as part of a National Institute for Health and Care Excellence (NICE) Diagnostic Assessment Department systematic review (February 2013). METHODS: Two systematic searches on thermal and dermoscopic Therapy for the treatment of Dry Eye Syndrome, 3 literature applications of heat and vibration to the areas the eyes. Eye Syndrome was assessed as a safe and effective technology capable of improving the visual symptoms of patients. The safety and effectiveness of 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. RESULTS: 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.

PMD3

OBJECTIVES: Schizophrenia (SZ) is complex and multifactorial neuropsychiatric disorder. Schizophrenia is estimated to have the highest genetic and environmental loads of all psychiatric conditions. 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 45 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 performed. Each patient's data was assessed by a neurologist 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 S2 patients while compared to healthy controls. CONCLUSIONS: In conclusion, our cohort study supports the hypothesis suggesting that a chromosome abnormality DRD2 gene is contributing to SZ pathogenesis. On the contrary, genetic stimulation to rethink SZ from a neurological as well as biological viewpoint and also to understand the phenotypes of these disorder in term of biological pathways. Key words: Schizophrenia, DRD2 gene, chromosomal abnormalities

PMD2

A COST ANALYSIS OF OPEN SPINA BIFIDA DETECTION IN THE FIRST-TRIMESTER Taurus J, Mihai R, Cristea A, Costache I, Stefan E, Manolita C

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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. RESULTS: The sensitivity of the dermoscopy for the detection of spina bifida was 94.4% (CI: 90.6-97.1); the specificity was 86.4% (CI: 80.7-91.1). The positive predictive value was 12% (CI: 7.1-19.6); the negative predictive value was 99.2% (CI: 98.4-99.9). p<0.01. CONCLUSIONS: VivaScope following dermoscopy may increase the accuracy of the detection of malignant melanoma compared to dermoscopy alone. However, the absence of UK studies makes the generalisability of the results to UK clinical practice unclear.

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 inclusion in this systematic review 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.

HEALTH CARE TREATMENT STUDIES

MEDICAL DEVICE/DIAGNOSTICS – Clinical Outcomes Studies

RESEARCH POSTER PRESENTATIONS – SESSION I

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