Wednesday Research Poster Presentations

POSTER SESSION V: Poster Display Hours – 8:45 - 14:00
Poster Author Discussion Hour – 13:00 - 14:00

POSTER SESSION V:

PRM: RESEARCH ON METHODS
PIN: INFECTION
PSS: SENSORY SYSTEMS DISORDERS

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### Research Poster Presentations – Session V

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**PRM1: COMPARISON OF VARIOUS SEVERITY ASSESSMENT SCORING SYSTEMS IN PATIENTS WITH SEPSIS**

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**OBJECTIVES:** To evaluate the predictive ability of six severity assessment scoring systems, namely, Acute Physiology and Chronic Health Evaluation (APACHE II), Rapid Emergency Medicine Score (REMS), Sequential Organ Failure Assessment (SOFA), Multiple Organ Dysfunction Score (MODS), Predisposition, Infection, Response and Organ Dysfunction (PIRO) and Mortality in Emergency Department Sepsis (MEDS) scores, in patients with sepsis. **METHODS:** A prospective cohort study, carried out in a south Indian tertiary care teaching hospital. Institutional ethics committee approval was obtained prior to the study. All patients diagnosed with sepsis according to guidelines the third International Consensus Definitions for Sepsis and Septic shock (Sepsis 3), who meets the inclusion and exclusion criteria were enrolled into the study. Patients were followed from the day of admission to till the day of discharge or death. Patient demographics, clinical characteristics, laboratory test data and comorbidities were recorded on the day of sepsis diagnosis. These parameters were used to calculate the severity scores and predicted mortality for each patient. ROC curve analysis was used to analyse the discriminative power (ability to differentiate between survivors and non-survivors) of various severity scores. **RESULTS:** A total of 193 patients were included in the study. The mean age was 57.2±15.3 (mean±SD) years. Majority of the patients were male, 125 (64.76%). Overall mortality was 108 (55.9%). The calculated AUCs were 0.86 (95% CI: 0.80-0.90) for APACHE II, 0.81 (95% CI: 0.75-0.87) for REMS, 0.80 (95% CI: 0.74-0.86) for SOFA, 0.74 (95% CI: 0.67-0.80) for MODS, 0.78 (95% CI: 0.71-0.84) for PIRO and 0.77 (95% CI: 0.71-0.83) for MEDS. Sensitivity and specificity for APACHE II was 81.5 and 75.3 respectively. **CONCLUSIONS:** In our study, APACHE II score proved to be the most superior of all the scores, as it considers not only the laboratory data but also chronic comorbidities and surgical status of the patient.

**PRM2: COULD EMBASE EMTREE INDEX SEARCH TERMS BE FOCUSED TO REDUCE NUMBERS TO SCREEN IN CLINICAL SYSTEMATIC REVIEWS?**

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**OBJECTIVES:** Embase is one of the most commonly searched bibliographic databases when undertaking systematic reviews of healthcare interventions. Using a combination of text searching and index searching is accepted best practice when designing Embase search strategies. As the number of Emtree index terms assigned to each Embase record has increased over time, there has been a corresponding increase in overall search result numbers and, therefore, the size of the workload for reviewers. The objective of this research was to investigate whether focusing Emtree indexing terms using the ‘restrict to focus’ function, so that only those articles where the index term is key to that article are retrieved, could reduce the number of records for screening without loss of included studies. **METHODS:** Embase searches conducted in three selected clinical reviews undertaken by the review team were retrospectively compared with searches in which the Emtree terms were focused. The subjects of reviews investigated were treatments for invasive fungal infections, type 2 diabetes mellitus, and acute lymphoblastic leukaemia. **RESULTS:** The data collected was analysed to identify total results with and without focusing Emtree terms, and to calculate the yield of included records. The focused searches retrieved 100% of the included papers in each review but results retrieved to screen were reduced by up to 30%. **CONCLUSIONS:** Focusing Emtree terms can potentially reduce screening burden in clinical systematic reviews without lowering retrieval of relevant records. Reducing the number of results in Embase searches without a loss of sensitivity could improve efficiency by reducing time spent and costs when undertaking systematic reviews.
**PRM3: A REAL WORLD EVIDENCE (RWE) APPROACH TO CHARACTERISING AN ULTRA-RARE DISEASE (URD) COHORT OF METASTATIC UVEAL MELANOMA (MUM) PATIENTS WITHIN NATIONAL HEALTH SERVICE ENGLAND (NHSE)**


**OBJECTIVES:** In Europe, primary UM is reported to affect 2.8 Caucasians/million population annually. ~90% of tumours involve the choroid, with the remainder confined to iris and ciliary body. Despite radical intra-ocular intervention(s), ~50% of patients develop metastatic disease, predominately in the liver. In the absence of therapeutic options, median time-to-progression and overall survival is ~2-3 and ~7-12 months, respectively. To inform a real-world understanding of mUM standard of care (SoC) treatment pathways, this study aimed to i) identify a cohort of mUM patients within the NHSE monopsony using the Hospital Episodes Statistics (HES) database; ii) compare the cohort characteristics and observations against clinical literature. **METHODS:** A mUM patient cohort were identified within HES (observational period: Apr2012-Jun2016, follow-up until Jan2017). Eligible patients had no cancer ICD-10 codes prior to their first inpatient admission for UM (C693 or C694); and at least another cancer code in the same or subsequent admission(s), indicating metastasis. Patients with C699 or D31 codes for their first inpatient admission (indicating unspecified or benign disease) and C693 or C694 in subsequent admissions were permitted if they had a subsequent C787 code (liver metastasis). **RESULTS:** Consistent with total NHSE epidemiological estimates, 450 mUM patients were identified in HES. Cohort characteristics: Mean age [65 years, range 0-97]; female [49%]; primary tumour involvement: choroid [n=391,87%] Vs. ciliary body [n=55,12%]; reported enucleation [n=177,39%]; “Liver” as first metastatic site [n=212,47%]; The most frequent sites of metastases in the cohort were: liver [n=255,57%], lung [n=115,26%], skin/soft tissue [n=82,18%], bone [n=63,14%] and lymph nodes [n=31,7%]. **CONCLUSIONS:** The cohort characteristics were consistent with published mUM literature. Only the overall involvement of liver metastases appeared discrepant to that reported ~90% in literature. This may be explained by a limited observation and follow-up period in our cohort. This RWE methodology provides supportive insight into SoC treatment pathways for URDs such as mUM.

**PRM4: EVALUATING ENDPOINTS AND CHANGING TRENDS IN ADVANCED STAGES OF CANCER RELATED CLINICAL TRIALS**

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**OBJECTIVES:** Properly selected endpoints are essential for clinical trials aimed at developing new drugs. This study uses ClinicalTrial.gov registry as data source in evaluating the use of endpoints and changing trends in phase II and phase III trials in advanced stages of breast cancer. **METHODS:** We searched phase II and phase III clinical trials of advanced breast cancer registered in ClinicalTrial.gov registry between October 2000 to September 2012, which was divided into two study periods (cohort A: October 2000 to September 2007 and cohort B: October 2007 to September 2012). The assessment of primary and secondary endpoints was conducted by two independent reviewers. **RESULTS:** In 398 phase II trials, there was a change in the most commonly used primary outcome measure from objective response rate in cohort A (60.6%) to progression-free survival in cohort B (40.7%). The trend was statistically significant with a decline in objective response rate selection (P < 0.001) and an increase in progression-free survival selection (P < 0.001). For 120 phase III trials, progression-free survival was the most frequently used primary outcome in both cohort groups (cohort A: 35.9%; cohort B: 66.1%; P < 0.001). **CONCLUSIONS:** This was the first study to assess endpoint selection in advanced breast cancer clinical trials over a decade. For both phase II and III trials, progression-free survival was the most frequently used primary outcome in general. However, in phase II trials studies, increasing trend in progression-free survival use in substitution of objective response rate was observed. As selection of proper endpoints is important for the success of clinical trials, changing trends should be considered when deciding upon primary and secondary outcome measures for the assessment of drug efficacy and safety.

**PRM5: COGNITIVE ASSESSMENTS ON PORTABLE DEVICES: A COMPARISON BETWEEN PHONES AND TABLETS**

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OBJECTIVES: Assessments of cognitive function are important endpoints in clinical research. It is often important to carry out such assessments in an everyday setting. In such cases, portability and ease of use are very important. Smaller devices are more portable, but screen size may become a limitation. The study examined whether a mobile test battery yields similar results on a mobile phone (6cm diagonal screen) and a tablet (18cm). METHODS: 39 healthy volunteers took part. aged 18 - 30 years, 20 female. The 20 minute test battery assessed attention, psychomotor functioning, memory, and comprehension. Tests were: Number Pairs, Arrow Flankers, Arrow Reaction Time, Memory Scanning, Shape Pair Learning; and Serial Sevens Subtraction. Outcome measures for each test were mean reaction time (RT) and percentage of errors (PE). The study used a two-period crossover design, with the two platforms in randomised order within a half-day session. Within each period, volunteers completed 5 practise assessments, then a final assessment that was used for the present analysis. RESULTS: Test scores were similar for the platforms. Differences between phone and tablet were all small, with effect sizes < 0.25, and there was no clear tendency for scores to differ overall between platforms. For RT scores, correlations between phone and tablet scores were in the range 0.54 – 0.82 (mean 0.71). For PE scores correlations were somewhat lower. One measure, Shape Pairs, showed a correlation of 0.14. Other PE scores were in the range 0.53 – 0.76 (overall mean 0.59). CONCLUSIONS: Taken together, these results indicate that there is good agreement between phones and tablets. The six tests, which assess a broad range of functions, can be used across a range of screen sizes from 6 – 18 cm with equivalent results, allowing great flexibility in the choice of portable devices for everyday assessments of cognition.

PRM6: USING CONVERGENT MIXED METHODS TO EVALUATE TREATMENT RISKS AND BENEFITS IN RARE DISEASE: AN EXAMPLE FROM A PHASE II REGISTRATION TRIAL IN METASTATIC MERKEL CELL CARCINOMA

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OBJECTIVES: Demonstrating treatment benefits for rare diseases within clinical trials is challenging. Mixed methods research (MMR) offers to overcome these challenges by combining quantitative and qualitative approaches, thus providing a better understanding of the available data. A convergent mixed methods design in the context of Merkel cell carcinoma, a rare type of skin cancer, during the JAVELIN Merkel 200 trial (NCT02155647) Part A, was used. We aimed to assess the concordance between a patient’s assessment of their own cancer health versus the objective measure of RECIST. METHODS: Nine of 88 patients from the trial were interviewed at baseline prior to receiving the study treatment avelumab, and at 13 weeks and 25 weeks after first avelumab administration. Key concepts of interest (COIs) identified from the baseline interviews were physical functioning, fatigue/energy, and pain. Patient perceptions of overall change in their cancer-related health status since starting study treatment was also recorded. During qualitative analysis, at each time-point, each COI was assigned a category describing the trend in change (e.g. newly emerged, no change/stable, improved, worsened, ceased/disappeared). In parallel, patients’ tumour status was determined by the overall response status, as per the clinical trial protocol. RESULTS: A high concordance between patient-reported qualitative data and tumour status was observed. All eight patients who responded to treatment perceived an improvement in their disease, while the single patient whose tumour progressed perceived no improvement in the COIs since starting the treatment. CONCLUSIONS: Embedding qualitative research in clinical trials is an innovative approach for characterization of treatment benefit meaningful to patients. This application of MMR can support clinician-reported outcomes to provide a more comprehensive picture of perceived benefits of treatment in rare diseases.

PRM7: VALIDATION OF SURROGATE ENDPOINTS IN MELANOMA THERAPIES AND USE IN HTA

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OBJECTIVES: The use of surrogate endpoints in oncology trials may allow for a smaller sample size, a shorter study duration, and a more rapid time to market, if proven to be valid. We aimed to investigate the validation of surrogate endpoints in melanoma trials, and their use in health technology assessments (HTA). METHODS: We conducted a targeted literature review to identify studies assessing the validity of surrogate endpoints in melanoma, using the key words ‘surrogate endpoint’, ‘correlation’ ‘regression’ and ‘melanoma’. Searches were conducted on MEDLINE, EMBASE and Cochrane Library (2012-2017), ISPOR, ASCO and ESMO congresses (2012-2017), and HTA websites (NICE, SMC, HAS, PBAC, IOWG and pCODR). RESULTS: Four meta-analyses and one phase III trial were identified that assessed the following surrogate measures for overall survival (OS): progression free survival (PFS), 1- and 2-year OS, recurrence-free-survival (RFS), early-tumour-response, time-to-progression (TTP), objective-
The design of appropriate and robust methodologies will be required to validate surrogate endpoints. The lack of relevant robust methodology, inclusion of non-evidence for surrogate validation. Reasons for rejection of surrogate endpoints included lack of appropriate and robust methodology, inclusion of non-comparable treatments, regimens or endpoints, exclusion of relevant trials, and lack of relevant sensitivity analyses. CONCLUSIONS: There is currently no clear consensus on how to validate surrogate endpoints. The design of appropriate and robust methodologies will be required to validate surrogate endpoints for use in solid tumour HTAs.

**PRM9: REVIEW OF SURROGATE ENDPOINT VALIDATION METHODOLOGIES AND APPLICATION IN SOLID TUMOUR HTAS**

**OBJECTIVES:** There are currently no universally accepted surrogate endpoints for overall survival in trials of solid tumours. We aimed to conduct a literature review of methods that have been utilised to validate surrogate endpoints, and assess how these methods have been applied in health technology assessments (HTA). METHODS: Using the key words ‘surrogate endpoint’, ‘correlation’ and ‘regression’, searches of MEDLINE, EMBASE, Cochrane Library, ISPOR, ASCO and ESMO (2012-2017) were conducted to identify studies reporting methodologies for validating surrogate endpoints. A number of national HTA agencies (NICE, SMC, HAS, PBAC, IQWIG and pCODR) were also searched to investigate the use and critique of these methods, with a focus on solid tumours. RESULTS: The foremost methodologies for surrogate validation reported in the literature include multi-trial approaches (meta-analytic analyses, informatics theoretic approach and surrogate threshold effect [STE]) and causal inference (causal association and principal stratification). Of the six HTA agencies investigated, only IQWIG and PBAC suggest preferred methodologies for the validation of surrogate endpoints, citing meta-analytic analyses and STE. A search for solid tumour HTAs examining the validity of surrogate endpoints returned eight results. Negative decisions were reported for axitinib in kidney cancer (PBAC), dabrafenib in melanoma (IQWIG), palbociclib in breast cancer (IQWIG), and pertuzumab in breast cancer (SMC and pCODR). Positive decisions were reported for imatinib in GIST (PBAC), pertuzumab in breast cancer (NICE) and vandetanib in thyroid cancer (pCODR), despite a lack of statistical evidence for surrogate validation. Reasons for rejection of surrogate endpoints included lack of appropriate and robust methodology, inclusion of non-comparable treatments, regimens or endpoints, exclusion of relevant trials, and lack of relevant sensitivity analyses. CONCLUSIONS: There is currently no clear consensus on how to validate surrogate endpoints. The design of appropriate and robust methodologies will be required to validate surrogate endpoints for use in solid tumour HTAs.
OBJECTIVES: Hypertension is the first rank of chronic disease found in Indonesian primary health care. Cardiovascular disease could happen from uncontrolled blood pressure as existing of drug related problems. This study was to investigate the prevalence and nature of drug related problems in outpatients with hypertension and reveal any association between DRPs and the therapeutic outcomes in these patients.

METHODS: This was a cross-sectional study. A total of 214 hypertension patients who fulfilled the inclusion criteria were recruited through outpatient clinic from seven primary health care in Yogyakarta province, Indonesia that collected during year 2016. The patient’s blood pressure was follow up for one to three month. During this period of therapy the patients could come to the clinic several times as the medication serve for around two to four week from the clinic. Patients’ data were assessed to identify DRPs using an evidence-based approach.

RESULTS: This study found about half of the participants (54%) had uncontrolled blood pressure. A total of 323 DRPs were identified. The average number of DRPs was 1.5. per patient and most of the patients (90%) have at least one DRP. The main DRPs affecting uncontrolled therapeutic outcome included sub optimal doses of medication prescriber, nonadherence to the medication, drug-drug interaction. Significant associations were found between poor blood pressure control and the existing of DRPs (p=0.000).

CONCLUSIONS: The number of DRPs among patients with hypertension was relatively high. These DRPs were associated with poor therapeutic outcome of hypertension patients. The improvement of clinical pharmacy services for all patients with hypertension is strongly recommended. Aneptic outcome included sub optimal doses of medication prescriber, nonadherence to the medication, drug-drug interaction. Significant associations were found between poor blood pressure control and the existing of DRPs (p=0.000).

PRM11: CLINICAL EVALUATION OF CEA, CA125, CA19-9 and CA72-4 IN GASTRIC CANCER PATIENTS WITH ADJUVANT CHEMOTHERAPY

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OBJECTIVES: In the clinical practice, we aimed to investigate whether tumor markers CEA, CA125, CA19-9 and CA72-4 can be used to evaluate the response to adjuvant chemotherapy, and to evaluate the diagnosis and prognosis value of 4 tumor markers in the patients of gastric cancer. METHODS: A retrospective study was performed of 216 gastric cancer patients who underwent a first line cisplatin chemotherapy and anti-angiogenic agents regimen. Statistical analysis was performed to identify the clinical value of these tumor markers in predicting the progression free survival and the response to adjuvant chemotherapy. RESULTS: Progression occurred in 78 of 216 patients and overall median progression free survival was 5-Months. For serum CEA, the median PFS was 4 versus 7 Months for elevated and normal groups (P = 0.01). The median PFS for normal and elevated CA199 and CA72-4 was 6 versus 4 months (P = 0.001). In the multivariate Cox regression model elevated pre-treatment level of CEA, CA199 and distant metastases were independent factors associated with increased risk of progression (p = 0.021, p = 0.000, p = 0.006). Furthermore, patients presented with combined three or four elevated tumor markers showed worse prognosis and shorter PFS (p = 0.001). The decrease of tumor markers CEA, CA199 and CA72-4 was significant after adjuvant chemotherapy (p = 0.006, p = 0.001, p = 0.002) especially in the disease control group (CR+ PR+ SD) (p = 0.03, p = 0.001, p = 0.002) and in patients using anti-angiogenic agents with first-line platinum-based chemotherapy (3-drugs therapy) (CEA, CA199 and CA72-4; p = 0.005, p = 0.006, p = 0.001). CONCLUSIONS: Our result suggests that elevated pre-treatment level of CEA and CA199 are correlated with high risk of progression and worse prognosis, while the use of anti-angiogenic agents with first-line platinum-based chemotherapy more effective in decreasing tumor markers level after adjuvant chemotherapy.

PRM12: NOVEL BIOLOGICS VERSUS CONVENTIONAL PREVENTIVE THERAPIES IN MIGRAINE: A FRAMEWORK FOR ECONOMIC EVALUATION

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OBJECTIVES: Erenumab, a calcitonin gene-related peptide receptor inhibitor (CGRPRi) developed for the prevention of migraine, has completed phase 3 studies. The goal of healthcare policy makers is to position this novel class of therapy to maximise the clinical and economic benefits in this highly prevalent and burdensome disease. We propose an economic modelling framework to assess the cost-effectiveness of CGRP Ri in migraine prevention. METHODS: We reviewed previous economic models of migraine preventives, assessed how well they represented outcomes of migraine patients and summarized key limitations. We then constructed a de novo semi-
Markov health state transition model, driven by clinical literature and expert opinion. **RESULTS:** Previous models differed in structure and clinical endpoints used. A common limitation was the aggregation of migraine frequency data into simplified health states based on response status or arbitrarily-defined categories of frequency. The proposed framework models the frequency of migraine days per 28 days (monthly migraine days [MMD]) as a continuous outcome, from which patient costs and quality-adjusted life-years are estimated. Patient-level variation in MMD is modelled assuming negative binomial and beta-binomially distributed panel data, to facilitate parametric indirect comparisons. Current preventives in migraine are associated with significant tolerability issues, therefore the model applies time- and treatment-specific discontinuation rates to account for the role of patient adherence in assessing cost-effectiveness. Utilities are modelled as a function of MMD, using EQ-5D values mapped from migraine specific instruments. In addition to drug acquisition and administration costs, medical resource use, acute medication use and productivity losses are also estimated, which are all linked to MMD frequency. **CONCLUSIONS:** By adapting previous modelling approaches based on expert opinion, we developed a modelling framework to assess the cost-effectiveness of novel preventive biologics in episodic and chronic migraine. By modelling migraine frequency as a continuous outcome, we address a key limitation of previous approaches.

**PRM13: STATISTICAL METHODS FOR CRITICAL CARE OUTCOMES**

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**OBJECTIVES:** To review statistical methods and their applications in situations involving multiple causes of failure when studying critical care outcomes (death and utilization of mechanical ventilation [MV]/extubation, hospital and intensive care unit length of stay). **METHODS:** A targeted literature search was conducted to identify methods that address issues of competing risk of death, censoring, and other statistical considerations applicable to the critical care setting. A total of 31 relevant articles were reviewed. To illustrate the performance of recommended methods, we conducted a simulation study to compare results from standard Cox and competing risk models. Relationships among time-to-event variables and covariates were defined a priori based on the relevant literature. Two standard Cox models were fit for time-to-event analysis (time from MV to cure and time from MV to extubation), which ignore subsequent events, such as death. We also conducted analysis of time-to-event by competing risks, with events of interest either time-to-cure or extubation duration, treating death as a competing risk. **RESULTS:** Based on our targeted literature search, we concluded that competing risks can be used instead of Cox survival models. Our simulations showed that Cox models appear to overestimate the effects of the treatment variable on the risk of cure by 7% and on the risk of extubation by 2% compared with competing risk estimates. Treating patients who died as if they were censored would lead to overestimation of the hazard rate in the standard Cox models. **CONCLUSIONS:** Competing events are common in critical care research. In this context, death is considered a competing event, which prevents other events of interest from occurring, and should not be treated as censoring. According to our literature search and simulation study, competing risk models should be used instead of standard Cox regressions in the presence of one or more competing risks.

**PRM14: METHODOLOGICAL ISSUES WITH KEY DRUG VALUE FRAMEWORKS**

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**OBJECTIVES:** A number of value frameworks (VFs) have been devised in the last years to assess the value of new drugs. The objective of this study was to discuss methodological soundness of selected VFs and to identify the main hurdles for real-life application of the elements incorporated in these VFs. **METHODS:** Targeted literature review using Ovid was performed to identify pivotal papers, commentaries and conference abstracts on VFs proposed by leading organisations i.e. ASCO, ESMO, ICER, NCCN, and MSKCC. Search results were supplemented with information from hand search of websites of these organizations. **RESULTS:** Targeted search resulted in 304 abstracts, of which 74 were analysed. VFs demonstrated notable heterogeneity in defining and measuring value, and several methodological limitations were reported. For instance, ASCO VF allows assessing the net health benefit only if therapies were compared in a head-to-head trial. Meta-analysis outcomes can be used with the ESMO scale, but it is not applicable to single-arm studies. While ICER methodology appears quite stringent and very close to that of the National Institute for Health and Care Excellence (NICE) in the UK, inherent limitations related to the use of QALY-based assessments remain. VFs which consider costs focus excessively on drug costs (ASCO, DrugAbacus) or ignore potential cost offsets (NCCN). Arbitrariness and transparency issues were reported for the majority of VFs, often because of thresholds used for grading treatment benefits (ASCO, ESMO), or even whole assessments (NCCN), being based on expert opinions. Not considering patient-reported outcomes or real-world evidence was also
a common issue of current VFs. **CONCLUSIONS:** Emerging VFs are subject of intensified debates among patients/citizens, the scientific community, and payers, feeding any potential VFs revisions. The use of these VFs in drug value assessment and their impact on the current decision-making processes remains a key question.

**PRM15: CURRENT AND POTENTIAL FUTURE CHANGES IN THE METHODOLOGY OF EMERGING VALUE FRAMEWORKS**

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**OBJECTIVES:** Growing interest of stakeholders in better informing value-based decision-making has led to the emergence of value frameworks (VFs), including those developed by ASCO, ESMO, ICER, NCCN and MSKCC. The aim of this study was to discuss current and potential future revisions of those VFs. **METHODS:** Search for articles on VFs was conducted in Medline via Ovid, supplemented with searching the websites of organisations developing VFs, or having an impact on health policy development. **RESULTS:** Authors of VFs are open to comments from various stakeholders, and have already implemented or are discussing changes in terms of attributes, scoring, stakeholder perspectives, purpose and eligibility criteria. For example, the ASCO VF was modified to include hazard ratio instead of median overall survival, and to consider all grades of toxicities rather than only high-grade. Moreover, the authors adopted a more patient-relevant perspective by considering quality of life and treatment-free interval, and confirmed possible future incorporation of patient-reported outcomes, when those are widely available. Changes in scoring methodology were also considered: ASCO adopted continuous efficacy scoring system. ICER included new cost-effectiveness thresholds for “long-term value for money” and ESMO considered revising weights/thresholds for health gain and toxicity assessment. Wider eligibility criteria are expected, since NCCN and ICER expressed willingness to assess non-drug technologies, e.g. radiation or medical devices. The purpose of VFs may also change and tools which currently aim to support therapeutic decisions (NCCN, ASCO), could be adapted for assisting policy/coverage decision-making. **CONCLUSIONS:** VFs paved a way to value-based decision-making for expensive therapies, but their implementation is challenging, due to the complexity of healthcare systems, treatment pathways, and value perception of stakeholders. Refinement of VFs and a dynamic approach aligned with drug life cycle will help to optimise VF use, and their potential impact on decision-making is likely to become clearer over time.

**PRM16: LONG TERM EFFICACY OF PERTUZUMAB FOR HER2+ METASTASIC BREAST CANCER ECUADORIAN POPULATION**

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**OBJECTIVES:** assess long-term efficacy of Pertuzumab in treatment of metastatic HER2+ breast cancer in Ecuador. **METHODS:** Globocan data was used to calculate HER2+ metastatic population on Ecuador and data from Cleopatra clinical trial and epidemiological data from the tumor registry at Munich were used to perform an overall survival (OS) and progression-free survival (PFS) extrapolation of 5 and 10 years. The probability of being alive or remaining in PFS was determined by OS or PFS probabilities obtained from CLEOPATRA study Kaplan-Meier estimates or parametric function that was fitted to data. Extrapolation beyond clinical follow-up period was performed by fitting parametric distribution to the observed OS and PFS times from the study period of the trial. This was done independently for each treatment arm (assuming independent shape). With results obtained we compared the number of Ecuadorian patients treated with current standard therapy Trastuzumab that will be still alive in 10 years against the number of Ecuadorian patients that will be still alive in 10 years if Pertuzumab was new standard treatment for metastatic HER2+ breast cancer. **RESULTS:** With annual metastatic HER2+ breast cancer incidence of 3 per 100,000 inhabitants Ecuador will have 580 women suffering from metastatic HER2+ breast cancer in 10 years. Considering current therapy, of the 580 women treated in 10 years, at the 10th year 278 women will be still alive and 138 won’t have progressed. With Pertuzumab, of the 580 women treated in 10 years, at the 10th year 340 women will be still alive and 189 won’t have progressed. Changing from Trastuzumab to Pertuzumab would save 62 more women and would avoid the progression of 51 more women in ten years. **CONCLUSIONS:** Pertuzumab could potentially change long-term outcome of HER2+ metastatic breast cancer in Ecuador by saving 24 more women in 5 years and 62 more women in 10 years.

**PRM17: CREATING INDIVIDUALIZED HBA1C TARGETS USING PREDICTIVE MODELING**

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OBJECTIVES: Glycemic targets (HbA1c) have been recommended to guide therapeutic treatment for patients with type 2 diabetes mellitus (T2DM) and reduce the risk of primary and secondary complications. In this study, we describe a methodology using predictive models to create individualized glycemic target ranges that are associated with a greater reduction of the risk for complications. METHODS: The study population includes adult members of Clalit Health Services with three-seven years T2DM duration, without concurrent serious chronic conditions (cancer, chronic infections, and cirrhosis). We built a predictive model to assess the future risk of common T2DM complications (macro/microvascular diseases, hypoglycemic events and all-cause mortality), based on the index HbA1c, while controlling for baseline demographic and clinical information. Individualized HbA1c target ranges were simulated in order to determine which specific range would minimize each individual’s risk of complications as identified by the predictive models. The final sub-analyses compared rates of complications associated with the model-based individualized HbA1c target range to rates of complications among those individuals whose index HbA1c was or was not within the target range. RESULTS: We developed a new methodology for the calculation of an individualized glycemic target. The obtained targets yielded 20% more individuals within the recommended range, compared to the standard guidelines, while maintaining the same outcome rates, and have the potential to more accurately identify those at risk for future outcomes. CONCLUSIONS: We successfully created a tool to calculate individualized HbA1c target ranges. Target ranges can potentially reduce the need for intensive intervention in some populations and highlight other populations at greatest risk. Validation of the tool using an independent external dataset is required. This study is the first attempt to generate an individualized glycemic control target tool based on predictive modeling and establishes how precision medicine can be incorporated into diabetes care management.

PRM18: MAXIMIZING THE VALUE OF WEARABLE BY THE REMOTE COLLECTION AND ANALYSIS OF RAW 100HZ DATA

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OBJECTIVES: This study was designed to look for patterns in raw accelerometer data potentially associated with a specific type of motor movement, namely scratching, to show that raw and aggregated data can be transmitted remotely outside of the traditional clinical setting. This research demonstrates that data from accelerometers has value beyond the traditional sleep and activity endpoints and could be used in remote studies. METHODS: Two healthy volunteers (A and B) were provided with accelerometers and hubs. The hubs were SIM enabled to allow for continuous data collection. Volunteer A wore the device for 24 hours and used a diary to identify 27 scratching events of approximately 30 seconds duration. Volunteer B wore the device for 8 hours and used a diary to identify 7 scratching events. RESULTS: Raw 100 Hz accelerometer data was transmitted remotely via the hubs to the centralized study center, from where it was further processed and analyzed. An analytical model was developed using the data from Volunteer A to identify scratching events at a 10 second epoch level. This algorithm achieved sensitivity and specificity values of 99 and 100%, respectively for Volunteer A. The algorithm was further evaluated on unseen (from the model’s point of view) Volunteer B and achieved sensitivity and specificity values of 99 and 86%, respectively. CONCLUSIONS: Accelerometer-based wearables are gaining acceptance in clinical trials as a means of generating objective endpoints for sleep and activity using validated algorithms. This study has shown that the application of suitable algorithms to raw accelerometer data has the potential to generate clinically relevant outcome measures associated with patient motor movement patterns, which can have significance in studies looking at tremor and itch and other clinical symptoms. The ability to generate and transmit raw data from a patient’s home facilitates the integration of this methodology into remote and virtual trials.

PRM19: PARAMETRIC MODELLING OF MIGRAINE DAY FREQUENCY IN MIGRAINE PREVENTION: A CASE STUDY OF ERENUMAB CLINICAL TRIAL DATA

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OBJECTIVES: The primary efficacy outcome of most clinical trials of migraine preventive drugs is change in migraine day frequency per 28 days (monthly migraine days [MMD]) relative to baseline for active treatment versus placebo. This analysis assesses parametric models of change in MMD for migraine preventives using data from erenumab clinical studies, with the objective of capturing intra- and inter-patient variability so trial observations can be modelled parametrically for the purposes of economic evaluation of migraine prophylactics. METHODS: MMD observations
from the double-blind phases of two studies of erenumab were used; one in episodic migraine (EM; NCT02456740), and one in chronic migraine (CM; NCT02066415). Data from the placebo groups were used to fit non-linear mixed-effects multilevel regression models to the changes in MMD over time, using the statistical software Stata. Negative binomial and beta-binomial models were fitted in each population using count-panel data, which allows better estimation of changes in MMD. These models have previously been shown to be suitable models of MMD frequency, and provide estimates of the distribution parameters that quantify the dispersion of the data. These parameters are assumed constant over time. Goodness-of-fit was assessed by the root mean squared error (RMSE) of the estimated values compared to trial observations, and visual inspection of the predicted distributions. RESULTS: Compared to the MMD distributions observed in the trials, the negative binomial and beta-binomial regressions generate RMSEs of 0.075 and 0.102, respectively, for EM, and 0.082 and 0.081 for CM. Predicted values showed a good visual fit to the trial observations through all the time points considered. CONCLUSIONS: Modelling MMD with regression models that accommodate over-dispersion in a longitudinal framework is a statistically valid method to model the variation in MMD both within and between individual patients. This has important applications in the economic evaluation of preventive medications and policy decisions in migraine.

**PRM21: AN ALGORITHM TO QUANTITATIVELY ESTIMATE EXTRAPOLATED LIFETIME SURVIVAL CURVES FOR ECONOMIC EVALUATION (EE) OF CANCER TREATMENTS WHEN ONLY AGGREGATED PATIENT DATA ARE AVAILABLE; WITH APPLICATION TO METASTATIC PANCREATIC CANCER**

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OBJECTIVES: Economic evaluations (EE) of cancer treatments extrapolate observed trial overall (OS) and progression-free survival (PFS) data to a longer-term time horizon by fitting distributions (eg, exponential, Weibull, Gompertz distributions) to time-to-event data. Visual inspection is commonly used to justify parametric selections, but is subjective. We propose an algorithm for selecting and quantitatively justifying parametric model selection for OS/PFS extrapolation when only aggregate patient data are available. We illustrate the algorithm with EE of FOLFIRINOX against gemcitabine in metastatic pancreatic cancer. METHODS: The algorithm includes seven steps: digitize treatment graphs; extract parametric functions; plot and visually inspect parametric distributions; assess goodness-of-fit; assess proportional hazard model; calculate EE; and propose results. Goodness-of-fit criteria include residual sum of squares (RSS), coefficient of determination (R2), and F-test. RESULTS: For OS, goodness-of-fit statistics were: for exponential, RSS=1.076, R2=0.983, F=1554.365; for Weibull, RSS=0.312, R2=0.987, F=1992.354; for Gompertz, RSS=1.325 R2=0.875, F=1081.550 (all pF<0.0001); with Weibull yielding best-fit. For PFS, goodness-of-fit statistics were: for exponential, RSS=0.869, R2=0.985, F=1112.542; for Weibull, RSS=0.218, R2=0.993, F=2299.226; for Gompertz, RSS=1.126 R2=0.912, F=820.238 (all pF<0.0001); with Weibull yielding best-fit. The PH assumption between treatments was valid. CONCLUSIONS: The application of different parametric models impacts EE estimates. While exponential-based analysis was associated with lower ICER/ICUR, per goodness-of-fit results the Weibull-based analysis was more accurate relative to trial data. Measures such as the Akaike (AIC) and Bayesian Information Criteria (BIC) require patient-level data. Thus, the proposed algorithm provides a systematic and quantitative
justification for parametric model selection and thus optimizing the validity of economic evaluations of cancer treatments when only aggregate patient data are available.

**PRM22: INCLUSION OF COMPARATOR SINGLE ARM TRIALS USED FOR EMA/FDA REGISTRATION IN THE NETWORK META-ANALYSIS USING MATCHING ADJUSTED INDIRECT COMPARISONS**

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**OBJECTIVES:** Several treatments have obtained accelerated approval by FDA based on single arm trials. This is especially the case for promising breakthrough treatments. Interest was in an approach for pooling these single arm aggregated data (AD) trials used for comparator registration with RCTs using own individual patient single arm/RCT data (IPD) forming relative effects. **METHODS:** Matching Adjusted Indirect Comparison for multiple trials. **RESULTS:** Using MAIC, a “pseudo” relative effect can be computed for each single arm AD trial versus the treatment assessed by the IPD data. If the own IPD data is not an RCT but a single arm trial, performing MAIC of the IPD trial to at least one RCT results in a linked network. Because the single arm IPD data are used multiple times, uncertainty estimates may be best obtained by procedures like bootstrapping. Although this approach can be used to model the relative effects, the quality depends on numerous characteristics of the included trials, like the availability of covariate information, the comparability of single arm AD and IPD, the maturity of the trial, the sample size, among other characteristics to be assessed before performing the MAIC, so that an approach to reasonably perform the MAIC was needed and is formulated. The approach will be exemplified. **CONCLUSIONS:** Mathematically, the promising AD single arm trial results used for comparator registration can be used in network meta-analysis using single arm IPD data. This provides insight in which of the treatments is the most important to compare the own product with and thus for the creation of the base case scenario in cost-effectiveness evaluations. However, whether the approach is acceptable will also depend on the promising value of the products for which registration is obtained based on single arm trial data.

**PRM23: COMPARATIVE EFFECTIVENESS OF VENETOCLAX IN VIEW OF A CLINICAL TRIAL WITH NO CONTROL GROUP**

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**OBJECTIVES:** Venetoclax is a new agent for treating chronic lymphocytic leukaemia (CLL) patients, especially with 17p deletion/TP53 mutation (17p/TP53), who have failed treatment with a B-cell receptor pathway inhibitor (BCRI). The NICE appraisal expressed several concerns in determining its efficacy: small number of patients and no control group. The study aimed to determine the most suitable comparator and comparative effectiveness for venetoclax reimbursement process in Slovenia. **METHODS:** A systematic review of clinical trials studying potential venetoclax comparators was performed to define their progression-free survival (PFS) and overall survival (OS). Publications on venetoclax were searched for hazard ratio (HR, venetoclax vs. comparator) for PFS. Additionally, due to immature data for venetoclax OS, the OS HR was obtained by calculation of ratio of 1-HR between OS and PFS (kOS/PFS) from randomized controlled trials on BCRI effectiveness involving larger number of patients. A clinical expert was consulted to present relevant treatment of 17p/TP53 CLL subpopulation in clinical practice. **RESULTS:** The literature review revealed several immunotherapies and BCRI (ibrutinib, idelalisib) as potential comparators. Idelalisib was the most suitable comparator based on venetoclax indication, existing prescribing restriction of ibrutinib and clinical expert opinion. An observational study Mato et al. (Ann Oncol. 2017 1;28(5):1050-1056) studying 683 CLL patients was found; in BCRI-failed population, similar to the target population in Slovenia, 26 were receiving venetoclax and 37 idelalisib. The PFS HR of venetoclax vs. idelalisib was 0.315 (95% CI: 0.106-0.939) and was applied for 17p/TP53 CLL subpopulation, assuming that HR is the same for all CLL genotypes. From clinical trials studying idelalisib vs. rituximab (NCT01539512) and ibrutinib vs. ofatumumab (NCT01578707) kOS/PFS of 0.85 and 0.73 were obtained, respectively. Finally, the calculated OS HR of venetoclax vs. idelalisib was 0.460. **CONCLUSIONS:** The comparative effectiveness expressed as HRs of venetoclax vs. idelalisib are 0.315 for PFS and 0.460 for OS.

**PRM24: A VALIDATION STUDY OF THE RANK-PRESERVING STRUCTURAL FAILURE TIME MODEL: CONFIDENCE INTERVALS, UNIQUE, MULTIPLE AND ERRONEOUS SOLUTIONS**

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**OBJECTIVES:** The rank-preserving structural failure time model (RPSFTM) is used for Health Technology Assessment submissions to adjust for switching of patients from reference to investigational treatment in cancer trials. It uses counterfactual survival (survival when only reference treatment would have been used) and assumes
that, at randomization, the counterfactual survival distribution for the investigational and reference arm are identical. The validity of the on treatment version of RPSFTM at various levels of cross-over was of interest. METHODS: The RPSFTM was applied to simulated datasets differing in percentage of patients switching, time of switching, underlying acceleration factor and number of patients, using exponential distributions for the time on investigational and reference treatment. RESULTS: There were multiple scenarios where two solutions were found: one corresponding to identical counterfactual distributions, and the other to two different crossing counterfactual distributions. The same was found for the hazard ratio. No multiple potential solutions were observed only when switching patients were on investigational treatment for <40% of the time that patients in the investigational arm were on treatment. CONCLUSIONS: Automatic estimation methods to obtain point estimates and confidence intervals for the acceleration factor may be used when the time that switchers stay on investigational treatment within the trial period is short. However, multiple solutions imply that automated estimation procedures are unlikely to work when switching patients stay significantly longer on investigational treatment than direct starters.

PRM25: SUBGROUP SPECIFIC MEDICINE: FINDING PATIENTS WITH POOR THERAPY RESPONSE

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OBJECTIVES: Personalized medicine aims at a better medical treatment by tailoring the treatment for the patient’s individual characteristics. One step towards personalized medicine is subgroup specific medicine that adjusts the treatment for groups of patients. This work aims at detecting patient subgroups, which react worse to a specific medication compared to the rest of the population. Therefore, we propose a framework that finds characteristics of patients that correlate with weak therapy results. METHODS: We used the health claims database of Arvato Health Analytics that contains diagnosis codes and prescriptions of 3 million German insurants for the years 2008-2015. First, we selected all patients suffering from rheumatoid arthritis (ICD-10 GM: M05, M06.0) and their respective medication intervals. We implemented a quality of life (QoL) metric for each interval based on the number of emergencies, admissions, side effects and outpatient/inpatient visits. Then, we applied subgroup mining to identify patient groups with significantly worse QoL result. Finally, we explored the characteristics that lead to this worse QoL outcome. RESULTS: Our analysis included n=36,756 RA patients. For female RA patients, the biologicals Etanercept (μQoL=1.05, p=0.03), Infliximab (IFX) (μQoL=0.93, p=0.003) and Adalimumab (μQoL=0.97, p=0.002) showed a poor QoL outcome. In contrast, Golimumab had no significant worse impact on the QoL of the female patients (μQoL=0.9, p=0.83). According to the product information of IFX, it is advisable to use IFX concomitant with Methotrexate (MTX). Although this has not been verified in clinical studies, our algorithm identified that RA patients using MTX react better to IFX than patients without MTX (μQoL=1.12, p=0.009). Furthermore, we determined poor QoL scores for patients >50 years taking Etanercept (μQoL=1.05, p=0.008) and Adalimumab (μQoL=1.02, p=0.0009) that has not been reported in literature yet. CONCLUSIONS: By this approach, we can guide the development of new drugs for the identified patient subgroups that react poor to approved medication.

PRM26: AN ANALYSIS OF TRANSLATION CHALLENGES WHEN ADAPTING THE PICTURE NAMING SUBTEST OF THE REPEATABLE BATTERY FOR THE ASSESSMENT OF NEUROPSYCHOLOGICAL STATUS (RBANS) FOR USE IN MULTINATIONAL STUDIES

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OBJECTIVES: The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) is a neuropsychological assessment consisting of twelve subtests, including the Picture Naming subtest. Examinees are shown a series of pictures and asked to name them. In a multinational study where the images cannot be adapted due to practical restrictions, a number of different methodological challenges arise. This comprehensive review suggests solutions to these challenges to ensure consistent and accurate scoring. METHODS: Existing translations of the subtest were reviewed by the language services provider’s linguistic validation team and lead members from the CRO scientific team. The issues were defined and categorized. Solutions and further considerations were provided for each category, prior to revision of the existing translations and development of new language versions of the RBANS for a new clinical study. RESULTS: The analysis resulted in the following distinctions of challenges: 1) Inclusion of alternative responses Regionalisms: examinee responses to an image would be considered correct in one region of a country but incorrect in another Target response variation: the picture presented to an examinee can elicit more than one correct response in the target language 2) Exclusion of alternative responses: Existing source alternative: multiple acceptable responses in English; only single acceptable response in target language 3) Necessary target language deviations: The picture presented is not culturally appropriate CONCLUSIONS: When adapting the subtest for use in other countries, a thorough analysis of possible variations in examinee responses for each picture is necessary. Alternative responses must be included in target languages where regionalisms or
common response target variations exist for an image. Alternative responses must be omitted when source response alternatives do not apply in the target language. Finally, translations of responses must deviate from the source when a culturally inappropriate image would otherwise elicit incorrect data.

**PRM27: IQWiG’S GENERAL METHODS 5.0 - WHAT’S NEW?**

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**OBJECTIVES:** The Institute for Quality and Efficiency in Health Care (IQWiG) is an independent, scientific institution that supports evidence-based decision making in the German health care system. IQWiG publishes their General Methods, which describe principles and scientific tools for document preparation, such as health technology assessments (HTA). In 2015, the Health Care Strengthening Act (HCSA), which promotes integrated care and the type and scope of potential evaluations in the statutory health insurance system, was passed and updates to the Fifth Book of the Social Insurance Code (SGB V) made, necessitating an update to the General Methods. The objective was to compare IQWiG’s General Methods version 5.0 which replaces version 4.2. **METHODS:** An overlay of IQWiG’s General Methods 4.2 and 5.0 was created in Word to identify the replacements and additions. **RESULTS:** The General Methods 5.0 includes new language to support a systematic approach to the evaluation of medical devices in high risk categories, which HCSA envisioned. Para. §139b SGB V was changed to include HTA reports based on public proposals. The General Methods 5.0 detail the topic choice and selection, as well as quality assurance. The HTA report should include benefit and risk assessment of an intervention, as well as economic, ethical, social, legal and organizational aspects, following international HTA definitions. The chapter on information acquisition was restructured and extended, detailing the approach in conducting systematic literature reviews. The General Methods 5.0 now detail when to perform a comprehensive or a targeted review, respectively search strategy development and data assessment. Minor changes in the meta-analyses section were implemented, in particular regarding the methodology choices following assessment of heterogeneity. **CONCLUSIONS:** IQWiG’s General Methods 5.0 include new paragraphs that align procedures and methodology with changes in German law. Expanded details are provided for the conduct of systematic literature review and meta-analyses.

**PRM28: USING AN INSTRUMENTAL VARIABLE APPROACH TO ESTIMATE CAUSAL TREATMENT EFFECTS IN AN OBSERVATIONAL COHORT OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE**


**OBJECTIVES:** Instrumental Variable (IV) approaches have been advocated to estimate causal treatment effects using observational data in the presence of unmeasured confounding. However, IV methods can be subject to weak instrument bias (and therefore attenuation of the causal effect towards the null). They also rely on strong assumptions, which cannot be tested from the data and have to be justified by background knowledge. **METHODS:** Using an observational cohort of 150 patients experiencing exacerbations due to Chronic Obstructive Pulmonary Disease (COPD), we used an IV approach to estimate the effect of treatment with prednisolone and antibiotics compared to prednisolone alone in terms of Forced Expiratory Volume (FEV) post treatment. Three potential IVs were considered: sputum colour, distance from facility and deprivation index. We also undertook a simulation study (based on the characteristics of the cohort study) to compare these IVs with regard to weak instrument bias and to assess the sensitivity of our analyses to violation of IV assumptions. **RESULTS:** The three potential IVs displayed varying degrees of strength in this cohort of COPD patients, and our simulation study confirmed that the impact that this variability had on our study estimates, and therefore conclusions, could range from minor to considerable depending upon the weakness of a particular instrument. **CONCLUSIONS:** IV approaches to estimating causal treatment effects from observational data are becoming popular. Finding a suitable IV is not always straightforward. Our study illustrates the potential dangers associated with weak (but valid) instruments or with instruments that violate core assumptions. We recommend that the impact on an analysis in any particular context should be explored using a simulation study approach.

**PRM29: USING ELECTRONIC HEALTH RECORDS AS A REAL WORLD COMPANION: A CASE STUDY IN A SINGLE ARM ONCOLOGY TRIAL**

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**OBJECTIVES:** This research aims to examine the use of electronic health record (EHR) data to derive effectiveness
evidence. **METHODS:** EHR data collected from January 1, 2011 and February 28, 2016 (control cohort) was combined with individual patient data (IPD) from two single-arm phase II studies (intervention cohort) to estimate treatment effectiveness. The data was harmonized by applying the inclusion and exclusion criteria from the trial to the EHR database. Prognostic variables were selected a priori and three different methods (propensity score matching (PSM), inverse probability of treatment weighting (IPTW), and Genetic Matching (GenMatch)) were applied and compared to address imbalances in measured confounders. A multivariate Cox proportional hazards model was used to compare OS. The hazard ratios (HR) were evaluated for each method. A sensitivity analysis evaluating the survival of the control cohort from EHR was conducted with an indirect comparison between the control cohort and digitized trial data from the control treatment. **RESULTS:** After applying the inclusion and exclusion criteria, the intervention cohort (n=183) and control cohort (n=72) were imbalanced in terms of measured confounders. The PSM method did not balance measure confounders (standardize mean differences (SMDs ≥25%) and the IPTW and GenMatch method improved imbalance (SMDs <10%) between the intervention and control cohort. The observed treatment effect on the risk of death of the PSM (HR=0.59, 95% confidence interval (CI) 0.36-1.74), IPTW (HR=0.64, 95% CI 0.48-0.88) and GenMatch adjusted analyses (HR=0.54, 95% CI=0.48-0.62) was similar favoring the intervention cohort. Median OS was similar between the EHR control cohort (15.6 months) and clinical control cohort (14.9 months). **CONCLUSIONS:** Our results demonstrate the utility of EHR data to estimate comparative effectiveness in a single-arm trial setting. PSM, IPTW, and GenMatch were used to address measured confounding; however the PSM result did not perform well due to small sample size.

**PRM30:** CONCEPTUALIZATION, DEVELOPMENT, AND INTERNAL AND EXTERNAL VALIDATION OF A ‘WHOLE DISEASE’ MODEL FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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**OBJECTIVES:** To conceptualize, implement, and internally and externally validate the Evaluation Platform in COPD (EPIC): a ‘Whole Disease Model’ of chronic obstructive pulmonary disease (COPD) that addresses policy and clinical decisions at different levels of care across the entire clinical pathway of the disease. **METHODS:** EPIC is a dynamic (open) population, Discrete Event Simulation model for COPD. COPD care pathways were conceptualized by a panel of clinical experts. Main features representing disease course are 1) prevalence of COPD based on an analysis of a large representative Canadian COPD cohort (CanCOLD), 2) individualized longitudinal trajectories of forced expiratory volume at one second (FEV1) from a dedicated analysis of the Lung Health Study (LHS), and 3) heterogeneous background exacerbation rate and severity from an analysis of a recent major COPD clinical trial (MACRO). COPD incidence equations were stochastically calibrated from the prevalence equations. To externally validate the model, we compared lung function trajectories, exacerbations, and mortality against four external cohorts (EUROSCOP, PanCan, TORCH, and UPLIFT). **RESULTS:** FEV1 trajectories showed robust internal and external validity: with 95% prediction intervals having actual coverage probabilities of 96%, 91%, and 90% in LHS, EUROSCOP, and PanCan, respectively. Simulated values for total exacerbation (1.34/PY, 1.30/PY), severe exacerbation (0.27/PY, 0.28/PY) and mortality rates (10%, 12.4%) were consistent with reported values in TORCH and UPLIFT respectively, considering uncertainty intervals around the mean. **CONCLUSIONS:** EPIC is a validated microsimulation model of COPD informed from multiple large clinical data. As a Whole Disease Model, it is capable of modeling the health and economic outcomes of many decisions in their interaction. By using an open-population, it can model realistic scenarios such as gradual market penetration and sub-optimal adherence. By considering disease heterogeneity, EPIC can be used to answer questions on efficiency and clinical utility of “personalized medicine” interventions such as biomarker implementation.

**RESEARCH ON METHODS - Cost Methods**

**PRM31:** COMPARING COSTS AND OUTCOMES BETWEEN COBLATION TECHNOLOGY AND MECHANICAL DEBRIDEMENT IN THE TREATMENT OF KNEE CARTILAGE LESIONS- A COST-EFFECTIVENESS ANALYSIS FROM A US PAYER PERSPECTIVE

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**OBJECTIVES:** Knee chondroplasty may be done using Coblation technology or mechanical debridement (MD) with a shaver. This study purposed to evaluate the cost-effectiveness of Coblation technology chondroplasty versus mechanical debridement in a patient population presenting with knee pain as a result of concurrent meniscus tear and an International Cartilage Research Society (ICRS) grade III focal chondral lesion. **METHODS:** A decision-analytic model comparing reimbursement costs and clinical outcomes between Coblation and MD in a patient
population after knee chondroplasty was developed. Medicare reimbursement costs, revision rates based on the frequency of repeat arthroscopy, osteotomy and conversion to total knee replacement and clinical outcomes data over a 4-year period post-surgery were obtained from published literature. Uncertainties surrounding model parameters were evaluated using one-way sensitivity analyses. Threshold analysis determined the point at which the model decision changes. Using a 3% annual rate, future costs were discounted and all costs were reported in 2016 US$. RESULTS: Compared with MD, over a 4-year period, Coblation chondroplasty resulted in net savings of $380 per revision avoided based on a lower revision rate (14% vs. 48%). This result was robust to sensitivity analyses while threshold analysis indicated that Coblation remains the least costly option assuming revision rates were raised from the reported rate of 14% up to 70%. Initial procedure costs for Coblation vs. MD were lower and outcome scores were significantly improved at 1 and 4-year following surgery CONCLUSIONS: Compared to mechanical debridement, Coblation technology is cost-saving, having lower total costs and better clinical outcomes following knee chondroplasty in a patient population with medial meniscus tear and ICRS grade III chondral lesion

PRM32: MEDICAL TRANSPORTATION COSTS IN FRANCE: WHICH SOURCE TO ESTIMATE THEM IN HEALTH-ECONOMIC ANALYSIS?

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OBJECTIVES: French Health Authority guidelines recommend to adopt a collective perspective in cost efficacy and cost utility studies. Consequently, medical transportation costs should be included in these studies. Medical transportation expenditures covered by the French Health Insurance were amounted to €4 billion in 2013. Nevertheless, detailed and specific data sources in France are limited to collect the medical transportation costs. The main objective is to determine a standardized method allowing to estimate medical transportation costs in French health economics analysis. METHODS: Medical transportation costs sources have been collected from efficiency opinions published by the French Health Authority (HAS). Then, these costs and their methodologies have been analyzed and completed by a literature search. RESULTS: Out of 31 efficiency opinions analyzed, 70% (22) revealed not to use any medical transportation costs or the specific methodology used for this cost was not mentioned. In the other 30% (9) efficiency opinions, a significant variation in transportation costs was observed ranging from €9.89 up to €96.90. One reference is mainly used. The Cour des comptes report, published in 2012, allows to determine the percentage of patients which is reimbursed by the French Health Insurance and the mean cost per transportation. Two methods can be distinguished, resulting in very different mean cost of transportation to use. The first takes into account the percentage of patients who is reimbursed by the French Health Insurance and patients who are not reimbursed. The second only considers reimbursed cost for all patients. CONCLUSIONS: Medical transportation cost estimation collected in efficiency opinions from HAS underlines a high degree of heterogeneity on these costs as well as a poor data source available in the literature or on database. Recommendations are needed to avoid this problem.

PRM33: BROADENING THE VALUATION SPACE IN HEALTH TECHNOLOGY ASSESSMENT: THE CASE OF MONITORING INDIVIDUALS WITH OCULAR HYPERTENSION

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OBJECTIVES: The economic evaluation (EE) component of health technology assessments (HTA) often defines value in terms of health related quality of life, with many HTA agencies requiring the use of EQ-5D based Quality Adjusted Life Years (QALYs). These approaches do not capture value derived from patient experience factors and the process of care. This thesis widens the valuation space beyond this limited perspective, taking account of such factors, using monetary values generated from a discrete choice experiment (DCE), incorporating these into a discrete event simulation (DES) and conducting a cost-benefit analysis (CBA). METHODS: The case study is monitoring individuals with ocular hypertension. Five strategies were compared using a DES: ‘Treat All’ at ocular hypertension diagnosis with minimal follow-up; Biennial monitoring (either in primary or secondary care) with treatment according to predicted glaucoma risk; and monitoring and treatment according to the UK National glaucoma guidance (either conservative or intensive). DCE based Willingness to pay (WTP) estimates for relevant health outcomes (e.g. risk of developing or progressing glaucoma and treatment side effects), patient experience factors (e.g. communication and understanding with the health care professional) and process of care (e.g. monitoring setting) were obtained. Conditional logit, mixed logit preference space and mixed logit WTP-space (rarely used within health economics) econometric specifications were used. These WTP valuations were aggregated in the DES, as fixed mean values or allowing variation between simulated individuals. RESULTS: While the standard cost-utility analysis (CUA) using EQ-5D implied ‘Treat All’ was most likely cost-effective, CBA with broadened valuation space identified, consistently across different econometric specifications, ‘Biennial hospital’ as the best choice. CONCLUSIONS: This thesis proposes an approach to broaden the valuation space that can be promptly
used for EE-HTA. Researchers should be attentive of the valuation space considered in their EE and choose wisely the EE approach to be used (e.g. CUA and/or CBA).

**PRM34: COST –EFFECTIVENESS OF OBINUTUZUMAB AS FRONTLINE TREATMENT FOR UNFIT PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA IN REPUBLIC OF MACEDONIA**

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**OBJECTIVES:** According to the results from the CLL-11 trial, obinutuzumab+chlorambucil (G-Clb) is superior to rituximab+chlorambucil (R-Clb) leading to an 13.8 month increase in median progression-free survival (PFS), longer time to next antileukemic treatment, higher rates of complete response and improved health-related quality of life in previously un-treated chronic lymphocytic leukemia (CLL) patients with comorbidities. The value of obinutuzumab as first line treatment for unfit CLL patients in Republic of Macedonia has not yet been reported. **METHODS:** Cost effectiveness analysis was performed using decision-analytic Markov model. Health states considered were PFS, disease progression and death. Transitional probabilities of each state in the model were based on the rates observed in CLL-11 study. Costs (2016 Euro) were collected from official, national health system data. Only direct costs (drug price, treatment administration and monitoring and post progression therapy) were included. Health states utilities were derived from the literature. Outcomes (discounted at 3% annual rate) were measured in quality adjusted life years (QALY) and costs and reported per patient as incremental cost per QALY gained ratio (ICER). Probabilistic sensitivity analysis (PSA) assessed the uncertainty around key model parameters (varied over range ±25%) and their impact on the base-case results. The model used a time horizon of 20 years. **RESULTS:** An incremental gain of 0.25 QALYs was estimated for GClb compared to R-Clb at additional cost of € 7357.85 per patient. Corresponding ICER was 29 436.00 € /QALY. The associated cost per relapse for G-Clb compared to first line therapy was significantly lower compared to R-Clb (G-Clb vs. R-Clb= 4815.6 € vs. 6946.1€). Sensitivity analyses showed the robustness of the base case results. The PSA demonstrated that the probability of cost effectiveness was 84% for G-Clb compared to R-Clb. **CONCLUSIONS:** G-Clb represents a cost - effective treatment strategy for unfit CLL patients in R.Macedonia.

**PRM35: ASSESSMENT OF HEALTHCARE COSTS OF INFANTS IN EXCLUSIVE BREASTFEEDING VERSUS MIXED OR ARTIFICIAL BREASTFEED.**

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**OBJECTIVES:** We aimed to analyse whether breastfeeding is related to lower healthcare costs **METHODS:** We included women admitted to the hospital to give birth between June and August of 2014. Women with multiple births, mothers requiring special hospital admission due to complications at birth, infants admitted to the neonatal unit, and children given up for adoption were excluded. Socioeconomic data, type of breastfeeding (exclusive breastfeeding, formula feeding, or mixed), consumption of health resources made by the child at birth, at discharge, at 1 month and at 6 months were collected. Health costs were estimated using official unit cost sources. The project was evaluated by the Ethics Committee of the hospital. **RESULTS:** We included 236 women, mean age 32.3 (SD = 5.3). At baseline, 69.5% would have started exclusive breastfeeding and 15.2% mixed or formula. At 6 months, only 19.5% indicated to maintain exclusive breastfeeding while 28.4% indicated mixed and 45.8% artificial breastfeeding. The total healthcare cost of infants without exclusive breastfeeding amounted to €1,044 (CI95%: 718.5-1,370.4) versus €652.8 (CI95%: 496.2-809.4) for infants in exclusive breastfeeding at month. At six months, €882.4 (CI95%: 702.6-1,062.2) and 385.4 (CI95%: 166.2-604.63). There was a higher consumption of health resources (€497.1 in primary care (€163.6), hospital (€217.1) and pharmacy (€24.5) in children without exclusive breastfeeding. **CONCLUSIONS:** Children who received exclusive breastfeeding versus mixed or formula required fewer health resources and had lower healthcare cost related. Exclusive breastfeeding seems to be an option to save resources to the NHS in addition to achieving health benefits for infants.

**PRM36: PHARMACOECONOMIC EVALUATION OF SORAFENIB AS FIRST-LINE TREATMENT FOR ADVANCED HEPATOCellular CARCINOMA**

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**OBJECTIVES:** Sorafenib significantly improve the overall survival of patients with advanced hepatocellular carcinoma (HCC). Conducted research aimed to assess the pharmaco-economic implications of sorafenib as first-line treatment for advanced HCC in comparison with best symptomatic treatment without systemic chemotherapy also
known as supportive care (BSC). **METHODS:** A Markov model was developed with three health states included: progression-free survival (PFS), progressed disease, and death in order to estimate the outcomes and costs in 10-year time horizon. ((TreeAge Pro 2016 Suite Inc.Williamstown, MA). The clinical data and utility values used in the pharmacoeconomic model were taken from the pivotal SHARP study with the data from the placebo arm used as a proxy for BSC. Based on this approximation and the results obtained from the GIDEON study in Republic of Macedonia approximately 25 patient per year are eligible for sorafenib treatment. The drug acquisition cost of sorafenib was calculated based on the mean dose per day and mean treatment duration used in the study. A range of other health state costs was integrated in the model, GP and specialists’ visits, laboratory and radiological tests, hospitalizations and specific medicinal procedures. Official publicly available data in R. Macedonia for medicinal unit cost were used in the model. Discount rate for all cost and outcomes was 3%. Sensitivity analyses evaluated the impact of several essential variables. **RESULTS:** The incremental cost-effective ratio was €14,363.00 per QALY for sorafenib versus best supportive care (BSC). The sensitivity analysis confirmed that the results were sensitive to the overall survival estimates, the cost of BSC and the utility values. **CONCLUSIONS:** Sorafenib is not a cost-effective option as a first-line treatment for patients with advanced HCC. Reduction in the price of sorafenib, or appropriate assistance program should be considered to improve the cost-effectiveness of advanced HCC treatment.

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**PRM37: WORK ACCIDENT COSTS. SECURITY, HEALTHCARE AND HUMAN RESOURCES DEPARTMENTS LINKS.**

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**INTRODUCTION:** Workplace accidents are important in the day-to-day of a productive society. Security, Healthcare and Human Resources Departments (SHHS) struggle to show that they are not part of a company merely to follow rules, laws and regulations that might be established, but that they are a group of people, a team, with the same goal: warn the employees of a company about the risks and consequences of work-related accidents. **OBJECTIVES:** Show the importance of SHHS, presenting work accident costs. **METHODS:** In the present work, two types of expenses in a food company were considered: the costs of lost hours due to work accidents with leave of absence in a one year period; and the costs with medical supplies, medicines and worker’s health. **RESULTS:** A total of 12 workers required a leave of absence after work-related accidents. The period of absence of these 12 workers totaled 1,568 days. Average worker’s salary = $1,500.00 Brazilian reals. A total of 220 hours worked/month. $6.80 Brazilian reals/hour/worker. Daily hours of work = 8.5 hours. A total of 13,328 lost hours/year. Therefore, the costs of lost hours due to work accidents totaled $90,900.00 Brazilian reals. The costs with medical supplies, medicines and worker’s health totaled $11,055.89 Brazilian reals. These costs were calculates with invoices from the drug stores and from the company that provides emergency care services. The highest corporate cost and the Accident Insurance Factor (Fator Acidentário Previdenciário) totaled $1,190,749.00 Brazilian reals. **CONCLUSIONS:** Occupational physicians need more information about the emergency care costs of work-related accidents. Today, the integration between Healthcare, Security and Human Resources is necessary before the post-report awareness of the cost and expenses of the accidents occurred.

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**PRM38: ASSESSMENT OF QUALITY OF HEALTH ECONOMIC STUDIES IN NON-ALCOHOLIC FATTY LIVER DISEASE**

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**OBJECTIVES:** Decision-analytic modelling have been carried out to simulate the natural history of non-alcoholic fatty liver disease (NAFLD) and the estimate cost-effectiveness and health outcomes of various therapies. Objective of the present investigation was to scan the published literature to assess the landscape of decision analytic models in NAFLD. **METHODS:** A systematic search of English articles on PubMed/Medline and Web of Science was performed. Studies that performed a formal decision-analytic modelling approach or a cost-effectiveness analysis of alternative interventions and diagnosis for NAFLD were included. Studies considering NAFLD as an event or complications of different condition were excluded. Studies were evaluated using Quality of Health Economic Studies (QHES). **RESULTS:** Seven studies were included. Of these, 4 were conducted in USA, 1 each in Australia, Canada, while 1 was multinational. A total of 6 studies included societal, third-party payer perspective and healthcare system, and discounting was 3-8%. Decision analytic models (Markov, state transition, and probabilistic), and cost utility analysis were employed in all the included studies. Disease progression was modelled through clinical staging in 4 studies where non invasive screening strategies were compared with invasive and imaging techniques. Treatment effect was modelled in 2 studies. Only 1 study calculated incidence and remission rates by calibrating against real-
world prevalence rates. All studies employed sensitivity analyses to assess the impact of model input uncertainty on outcomes across a wide range of values. Based on the QHES scale, 6 studies were high quality (75-92) and 1 study was fair quality (71). Overall quality of the study was higher (mean 82.14±7.98).

**CONCLUSIONS:** There is paucity of health economic modelling studies in NAFLD. The analysis illustrates the enormity of the clinical and economic burden of NAFLD, which is likely increase as incidence of NAFLD continues to rise.

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**PRM39: THE DESIGN OF ECONOMIC EVALUATION AND BUDGET IMPACT ANALYSIS OF BIOSIMILARS: A QUALITATIVE STUDY**

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**OBJECTIVES:** This study aims to discuss principles for economic evaluation and budget impact analysis of biosimilars. **METHODS:** Via 14 in-depth interviews, experiences of Belgian stakeholders with reimbursement of biosimilars were evaluated and insight was gained into their views on the design of an economic evaluation and budget impact analysis for a biosimilar. These stakeholders included representatives of the HTA body, the medicines reimbursement agency, health insurance agencies, researchers, physicians, and pharmaceutical companies. A grounded theory approach was used to analyse the data. **RESULTS:** No consensus was found on which technique of economic evaluation is deemed appropriate in the reimbursement decision of a biosimilar. The preference for a cost-minimization analysis was dependent on the view of the interviewee on potential differences between the originator and the biosimilar. Other interviewees suggested to perform a full cost-effectiveness analysis. When the reference product is not reimbursed, a full economic evaluation was considered appropriate. Not only for biologics or biosimilars, but for all medicines, frequent revisions on reimbursement decisions were advised. The interviewees seemed to agree that a budget impact analysis should be performed for the biosimilar. Ideally, the impact on the total healthcare budget is determined, however, differences outside the pharmaceutical budget might be limited. Evolutions in volume and price, and market entry of new products can be taken into account, but many uncertainties exist when making these assumptions. **CONCLUSIONS:** Among stakeholders, no consensus exists on how to perform economic evaluation and budget impact analysis of biosimilars to support reimbursement decisions. Varying levels of knowledge and experience of stakeholders with biosimilars and health economics resulted in differing opinions.

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**PRM40: EXPLAINING WAITING TIMES FOR SCHEDULED SURGERY USING A HIGH-DIMENSIONAL FIXED EFFECTS MODEL**

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**OBJECTIVES:** This study analyses waiting times for patients submitted to surgical treatment in the Portuguese National Health Service (NHS), using all patients (amounting to more than 2.5 million observations) from 2011 to 2015. It tries to evaluate whether there are variables besides need or severity of the patients that explain variations in waiting times. **METHODS:** Our study adds to the existing comprehensive literature on waiting lists using a methodology that offers more robust results. A High-Dimensional Fixed Effects model is estimated allowing a set of fixed effects to control the unobserved heterogeneity, since recent literature shows that these models perform better than the conventional models. **RESULTS:** Controlling for the fixed effects (year, hospital of origin, county of residence, main procedure code, initial priority and age) that were shown to be significant, the results indicate that, on average, men have a shorter waiting time than women (about 3%). Waiting times are higher in the population aged 1 to 22 years. Patients aged over 69 years have waiting times that seem to gradually decrease. Children under one year old are those who also have lower waiting times. Patients who were reported to have cancer wait less for surgery. Although hospital transfers occur in only 0.25% of cases, the results show that they are relevant to significantly reduce waiting times. The fixed effects also confirm that a higher level of priority is associated with shorter waiting times and that the organizational structure of hospitals explains some variation in waiting times. **CONCLUSIONS:** Despite controlling for a variety of fixed effects, significant differences were found in waiting times. On the one hand, it is shown that there is a prioritization of patients on waiting lists, on the other, there are differences that appear to indicate a discriminatory conduct.

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**PRM41: HEALTH INSURANCE PERSPECTIVE AND COLLECTIVE PERSPECTIVE: THE DIFFERENCES IN THE COLLECTION AND VALUATION OF COST DATA IN FRANCE**

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**OBJECTIVES:** In France, the French National Authority for Health (HAS) considers two perspectives in economic evaluations, the health insurance perspective to estimate the costs incurred by health insurance, and the collective
Perspective (all payers) to estimate costs incurred by the entire society. The objective is to present an inventory of available data to collect and value cost data, according to the perspective chosen (health insurance or collective). METHODS: Cost items most frequently found in economic evaluations include: treatment of interest, treatment administration, medical examinations, consultations, hospital admissions, medical transportation and adverse effects management. For each of these items, review of the data available for the cost valuation in France, according to the health insurance perspective and the collective perspective, was carried out. RESULTS: According to the perspective adopted, the use of available data for cost valuation is variable. In terms of health insurance perspective, cost valuation is based on health insurance rates and reimbursement rates. In a collective perspective, costing raises questions about the quality of the available data as well as their representativeness for the pathology studied, which creates uncertainty about the estimation of costs. This is the case when estimating the costs of hospitalization in the private sector from the national cost study (ENC), in very few hospitals participates (26 in 2015). This is also the case when estimating cost of medical consultations including extra fees, based on aggregated data at a national level by specialty, introducing uncertainty as to the representativeness with respect to the pathology studied. CONCLUSIONS: The valuation of costs in health insurance perspective is based on an official nomenclature and that is why it is easier than the valuation in a collective perspective whose data available for certain cost items can introduce uncertainty.

PRM42: A UNIFORM PROBABILISTIC APPROACH TO MANAGE UNCERTAINTIES REGARDING VACCINE EFFECTIVENESS AGAINST SEROTYPE 3, 19A, NTHI AND HERD EFFECT IN THE BASE CASE OF A COST-EFFECTIVENESS ANALYSIS COMPARING NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D (PHID-CV) WITH 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINES (PCV13) IN INFANTS

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OBJECTIVES: Cost-effectiveness analyses (CEAs) are increasingly requested by Health Care Authorities to take rational decisions on resource allocation. Single endpoint observations (EoS), used as inputs for CEAs may vary considerably depending on available sources. When comparing vaccines, the selected source for vaccine effectiveness/efficacy (VE)-inputs has a significant impact on CEA-outcomes (CEAOs). Probabilistic approaches, addressing values within a plausible VE-range instead of single EOs are gaining importance to manage parameter uncertainties and to outbalance interpretations of CEAOs. The aim of this study is to understand the importance of input-uncertainties according to different sources, when comparing non-typeable Haemophilus influenzae protein D (PHID-CV) and 13-valent pneumococcal conjugate vaccines (PCV13). METHODS: Plausible VE-ranges for serotype (ST)3, ST19A, non-typeable Haemophilus influenzae (NTHI; only against acute otitis media) and net herd protection were based on 95%CI from controlled efficacy/effectiveness studies. A published static Markov model comparing both vaccines for Canada was adapted to use EOs or uniform probabilistic VE-estimations (UPVs) within their plausible ranges. Endpoints: 1.5%-discounted averages and percentiles 2.5 and 97.5 (%ile2.5; %ile97.5) for incremental direct costs (ΔDC, k€) and Quality-Adjusted-Life-Years (ΔQALYs), excluding(excl.) and including(incl.) a probabilistic sensitivity analysis (PSA) for other inputs. RESULTS: Presented are ΔDC(%ile2.5; %ile97.5); ΔQALYs(%ile2.5; %ile97.5) using EOs: -23,521(na ;na); 365(na ;na) excl.PSA and -23,569(-25,354; -21,976); 384(-176;1,036) incl.PSA, using UPV (excl.PSA) for VE_ST3: -23,534(-23,574; -23,495); 367(361;373), for VE_ST19A: -23,524(-23,604; -23,444); 365(352;378), for VE_Herd: -23,531(-24,115; -22,942); 367(264;470), for VE_NTHi: -23,073(-25,124; -20,973); 203(-555;943) and using UPVs for all_4_VEs: -23,078(-25,259; -20,959); 216(-563;966) excl.PSA and -23,111(-25,765; -20,596); 219(-678;1,189) incl.PSA. CONCLUSIONS: This study allowed to understand the importance of the choice of VE-assumptions for CEAs: overall CEAO was not significantly impacted by the choice of VE against ST3 and ST19A and for herd effect. Varying VE against NTHI however affected the variability of CEAO the most. PHID-CV remained dominant over PCV13 independently of using EOs or UPVs.

PRM43: HORIZON SCANNING IN ONCOLOGY – RAPID SCANNING APPROACH IN SLOVAKIA

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OBJECTIVES: Horizon scanning is in place in many European countries, as well as outside of the Europe. Slovakia didn’t formalize that approach yet, but extreme pressure on healthcare budget has resulted in the implementation of the pilot project. METHODS: Rapid scanning was chosen as the most appropriate method for the pilot project. Prioritisation meeting was held at Slovak Medical University. Experts chose the area for scanning, agreed on method and form. Subsequently, all pharmaceutical companies were contacted to report expected new oncological indication registration for already registered molecules or for newly developed molecules. Finally we completed the table report by a literature overview using systematic research from pre-selected sources. The selected period was years 2017-2019. RESULTS: The report contained 31 molecules in 46 indications. 14 were already registered between 2012 and 2016. 4 new indications are expected the treatment of oncological diseases to molecules that are already registered.
18 new molecules were expected to be registered for the treatment of oncological diseases, 1 of them as the extension of the indication to the molecule, which is expected to be registered in 2017. 4 molecules reported new indications in the period after 2019. 3 already registered molecules were reported without time frame. The return of the questionnaires was 57%. The table was completed by 40 more molecules, 2 of them were excluded due to marketing authorization withdrawal and 15 were excluded due to inappropriate period. CONCLUSIONS: The report completed by the data from the search created the baseline for next steps – final prioritization based on burden of disease and potential impact on patients and budget impact. This shall result on planning of managed entry processes.

**PRM44: THE IMPORTANCE OF PERSPECTIVE WHEN EVALUATING THE ECONOMIC VALUE OF VOCATIONAL REHABILITATION**

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**OBJECTIVES:** The NICE reference case recommends economic evaluations take an NHS and Personal Social Services (PSS) perspective. This is appropriate if all of the associated costs and benefits are captured, however less so, when a proportion lie outside of healthcare. We aim to explore the importance of perspective in the FRESH trial. This trial assessed the feasibility of delivering a full scale trial evaluating the (cost) effectiveness of Vocational Rehabilitation (VR), an individualised return to work programme, amongst Traumatic Brain Injury patients in comparison to usual care, across three trauma centres in England. METHODS: This feasibility study compared alternative methods of collecting and valuing resource use data, which included taking two perspectives: NHS and PSS, plus a societal perspective. Several methods were used to estimate time off work costs, for example using national average hourly wage rates compared to participant reported earnings, as well as valuing presenteeism through the Workers Productivity and Activity Impairment instrument compared to bespoke questions. RESULTS: When societal costs were considered, such as government employment services, time off work and out of pocket costs, the broader costs accounted for 61.77% of total costs in the VR group, compared to 80.90% within usual care. Though these percentages varied according to methods used, they demonstrate that within any full-scale economic evaluation conducted, it is likely that the largest cost-drivers will occur using a societal perspective. Taking a broader perspective adds complexity to an evaluation in terms of appropriately capturing the data and in identifying sources of unit costs. CONCLUSIONS: Using a limited perspective where significant costs and benefits are believed to lie outside healthcare could lead to erroneous estimates of value for money and poor value from public funding. Further research is required to inform how such wider resource items should be measured and valued.

**PRM45: IDENTIFYING COST EFFECTIVE METHODS OF HEALTH TECHNOLOGY ASSESSMENT FOR DEVELOPERS – THE NEED FOR FAST AND FRUGAL EVALUATION**

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**OBJECTIVES:** “Early” or Supply-side Health Technology Assessment (HTA) is potentially useful during technology development. Supply-side HTA aims to inform investment and study-design decisions made by developers and investors. Supply-side HTA analysis can improve decision making and increase the net return on investment, and hence justify its own costs, in two ways: 1) by increasing the achievable price, market share or development costs for technologies that are ultimately successful, and 2) by reducing development costs, possibly by facilitating earlier termination of development, for technologies that are ultimately unsuccessful. Given the large number of candidate products, high rates of failure and fast pace of development, ‘fast and frugal’ methods are required for supply-side HTA to be cost-effective. This study aims to identify ‘fast and frugal’ methods for supply-side HTA and propose a ‘fast and frugal’ framework for supply-side HTA. METHODS: A wide-ranging cross-disciplinary pearl-growing literature review was undertaken. Methods of supply-side HTA were grouped according to their aim, methodology and resource requirements. A framework of activities in supply-side HTA was developed. Studies where authors had sought to apply ‘fast and frugal’ methods were identified and adaptations were noted. RESULTS: 81 studies were found exemplifying methods of supply-side HTA. Cost-effectiveness analysis was the most frequent method applied, expert elicitation and user-feedback methods were also well represented. One ‘fast and frugal’ application of a quantitative method (‘headroom’) was identified and one qualitative toolkit. There was a lack of studies using early stage qualitative methods. A framework for supply-side HTA was developed encouraging explicit qualitative steps before a quantitative model is developed. Possible adaptations to supply-side methods to enable ‘fast and frugal’ approaches were noted. CONCLUSIONS: Both qualitative early-stage and ‘fast and frugal’ supply-side methods may be valuable to developers and warrant further development.
**PRM46: WHICH INFORMATION SOURCES SHOULD BE USED TO IDENTIFY STUDIES FOR SYSTEMATIC REVIEWS OF ECONOMIC EVALUATIONS IN HEALTHCARE?**


**OBJECTIVES:** The key economic evaluation (EE) databases, NHS EED and HEED, have closed. Which databases do we now need to search to identify economic evaluations for models and systematic reviews (SRs)? We assess which databases are now the best sources of EEs and whether typical search strategies are effective. **METHODS:** A quasi-gold standard (QGS) set of economic evaluations was formed from studies included in SRs of EEs undertaken to inform HTA. 9 databases were searched for each QGS reference. Yield for each database, and combination of databases, was calculated. MEDLINE search strategies reported in source SRs were re-run to assess their performance in finding EEs. **RESULTS:** We built a QGS of 351 records from 46 reviews. Embase had the highest yield (0.89), followed by Scopus (0.84) and MEDLINE and PubMed (both 0.81). The HTA database identified the highest number of unique records (13/351), despite a low overall yield (0.1). All 9 databases combined retrieved 337/351 records. The most efficient combination of databases which could be searched to find records for all 337 references was Embase, Scopus, HTA Database and (MEDLINE or PubMed). 10/29 (34.5%) of re-run strategies missed at least 1 of the included records available in MEDLINE (25 records missed in total). Only 1 of the missed records was due to failings of search terms used for the economics concept. **CONCLUSIONS:** For most SRs Embase, HTA Database and either PubMed or MEDLINE are likely to be sufficient to identify EEs included in bibliographic databases. Additionally searching a multidisciplinary database may be useful, particularly in non-clinical topics. Beyond this, supplementary search techniques may be more efficient than extensive database searching. Weaknesses in reported MEDLINE search strategies were identified which impacted retrieval; these weaknesses appear to be associated with population and intervention concepts, rather than the economics concept.

**PRM47: SINGLE DISTRIBUTION, TWO-PART, AND TWO-COMPONENT FINITE MIXTURE MODELS FOR PREDICTING SMOKING-RELATED INDIRECT COSTS IN US WORKING ADULTS**


**OBJECTIVES:** Indirect costs data typically include a high proportion of zeros that cannot be adequately modeled with a single distribution. The current study examined predicted total costs associated with work impairments using different models applicable to such distributions. **METHODS:** Data on employed US adults (18-64 years old) were analyzed from the 2013 National Health and Wellness Survey. Self-report was used to define smoking status (never smoked, quit, attempting to quit, and currently smoke) as a predictor. Costs due to work productivity loss were derived from Work Productivity and Activity Impairment questionnaire-based measures on percentage absenteeism and presenteeism, and calculated using weekly wages by age and sex from the US Bureau of Labor Statistics (2014). Given excessive zeros (60%) in the cost data, two-part (first part logit, second part negative binomial [NB]) and two-component finite mixture (first component constant, second component truncated NB) models were used to predict costs as a function of smoking status, controlling for respondent demographics and health characteristics. Model fit statistics (Akaike and Bayesian Information Criterion [AIC and BIC, respectively] and mean squared error [MSE]) were compared with those from a single-distribution generalized linear model (GLM) with NB distribution, which is also suited to highly skewed, count-like distributions. **RESULTS:** Among 36,883 working adults, the two-part model had the best fit statistics (AIC=359159; BIC=359355) compared with the mixture (AIC=394788; BIC=395001) and the GLM (AIC=391201; BIC=391312) models, and also the smallest MSE (105454117 compared with 105482560 and 21486386573, respectively). Overestimation of costs among those with zero cost was greatest in the single-distribution GLM (average predicted costs=$5306.76) compared with those from two-part ($5293.13) and mixture ($5293.04) models. **CONCLUSIONS:** In a broadly representative US population of working adults, two-part modeling was found to better represent high zero-skewed indirect cost data compared with two-component finite mixture and single-distribution models.

**PRM48: ACCOUNTING FOR CAPACITY CONSTRAINTS IN ECONOMIC EVALUATIONS OF STRATIFIED MEDICINE: A SYSTEMATIC REVIEW**


**OBJECTIVES:** Stratified medicines are viewed as promising interventions to safely, effectively and cost-effectively target treatment to eligible sub-groups of patients. However, the adoption of stratified medicines into practice has been slower than anticipated. Regulatory approval and reimbursement of stratified medicines creates an immediate demand for companion-diagnostic tests which were either not previously available or not prognostically useful. Health system capacity constraints can slow the implementation of stratified medicines and potentially influence their relative
cost-effectiveness. This study aimed to identify if, and how, previous economic evaluations of stratified medicines had accounted for capacity constraints and the potential impact on relative cost-effectiveness. **METHODS:** A meta-review conducted in February 2017 used an electronic search of the EMBASE and MEDLINE databases to identify all previous systematic reviews of economic evaluations relevant to stratified medicines. Primary economic evaluations of interventions of a test-treat strategy were then collated from the published reviews. All extracted data were tabulated and a narrative analysis was used to identify whether studies had discussed potential capacity issues and whether they had used formal methods to account for these in the analysis. **RESULTS:** This study yielded 47 systematic reviews of economic evaluations of stratified medicines. From these reviews 185 primary economic evaluations of test-treat strategies were identified (from 2007 to 2010). Of these, 30 (18%) evaluations discussed potential capacity issues: limited health budgets; lack of quality laboratory and testing processes; ease of use of the test and results; and need for clinical and economic evidence in implementation. Methods used to account for capacity constraints included: capturing inefficiencies in trials or models; sensitivity analysis; and scenario analysis. **CONCLUSIONS:** Capacity constraints may impact the short-term cost-effectiveness of stratified medicines but few economic evaluations account for such constraints. Methodological developments are needed to take account of capacity constraints such as dynamic cost-effectiveness models or value of implementation analysis.

**PRM49: REPORTED LIMITATIONS IN ECONOMIC MODELS FOR TREATMENTS OF SCHIZOPHRENIA: A SYSTEMATIC LITERATURE REVIEW**

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**OBJECTIVES:** Many pharmacoeconomic models in schizophrenia are available. Our objective was to overview the reported limitations of these models. **METHODS:** Pharmacoeconomic models in schizophrenia published after 2000 were identified through Medline, Embase and grey literature. Author-reported limitations relative to model structure, model input and others aspects were extracted. **RESULTS:** After screening 1889 records, 67 references were selected: 87% reported limitations in structure, 88% in input and 13% in others. Limitations relative to structure primarily focused on treatment strategies (n = 22), cost (n=30) and clinical outcomes (n=27). Limitations on treatment strategies mostly concerned incomplete treatment option (dose change, combinations or switch not accounted for), switch pattern (number of lines, timing, treatment for switch) and comparators (first generation antipsychotics, clozapine, paliperidone, quetiapine, zotepine not considered). Limitations relative to costs included lack of indirect costs (lost productivity/employment, violence, caregiver burden) and lack of costs for adverse event. Limitations relative to clinical outcomes were mostly lack of consideration of some adverse events (tardive dyskinesia, akathisia, sexual dysfunction, metabolic syndrome, diabetes, cardiovascular event) and clinical outcomes (partial-response/response rate, PANSS, suicide). Limitations relative to inputs primarily focused on clinical estimates (n=35). Limited data mostly included relapse/response, adherence/discontinuation, adverse event, dose distribution and drug cost. Mostly reported limitations were source type (assumption, clinical trial, observational studies, database analysis, evidence-synthesis studies). Others also reported limitations on quality of source data (non-evidence-synthesis: small sample, short duration; evidence-synthesis: limited included studies, heterogeneity), and source geography (other countries, non-nationally-representative). Other reported limitations included incomplete uncertainty analysis (probabilistic sensitivity analysis, multivariate analysis, expected value-of-perfect-information) and not accounting for heterogeneity. **CONCLUSIONS:** Current pharmacoeconomic models in schizophrenia reported several common and specific limitations upon model conceptualization in terms of treatment strategy and outcome, and model inputs. Although these are only reported limitations, they provide possible questions for future models to address.

**PRM50: COST-EFFECTIVENESS ANALYSIS OF CHIDAMIDE VERSUS CHEMOTHERAPY ON THE TREATMENT OF PERIPHERAL T - CELL LYMPHOMA PATIENTS IN CHINA**

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**OBJECTIVES:** Chidamide, a new subtype-selective HDACi, has been approved by CFDA as a new drugs for PTCL. This study was to assess the cost-effectiveness of Chidamide vs. chemotherapy in Chinese PTCL patients from a payer’s perspective. And to estimate the budgetary impact on health insurance fund after Chidamide adopted to national reimbursement drug list (NRDL). **METHODS:** A cost-effectiveness model and a budget impact model was constructed to assess the cost-effectiveness of Chidamide and chemotherapy in the treatment of PTCL and to
estimate the potential budget impact once Chidamide is included in the national reimbursement drug list (NRDL).

Utility value and clinical data were obtained from published literature and from the II phase clinical trial of chidamide. Cost data were collected from Chinese leading hospitals (Ruijin hospital, Beijing cancer hospital, Jiangsu Province Hospital etc.). The model calculated incremental cost effectiveness ratio (ICER) and increased health insurance fund in budget impact model. In the model, 4 scenarios were established to compare the two treatment regime (the 4 scenarios were defined with various combinations of market shares and pricing). A one-way sensitivity analysis was conducted for all parameters. **RESULTS:** Compared with chemotherapy, the ICER value for Chidamide was 107,419 Chinese Yuan (CNY)/QALY, which is lower than WHO recommended 3*GDP threshold (148,053 CNY/QALY, with 2015 Chinese GDP 49,351 CNY). The one-way sensitivity analysis demonstrated that the model result was not significantly impacted with all parameters increase or decrease 10% on the basis value, indicating the robustness of the model. After Chidamide adopted to NRDL, the budget impact model showed the health insurance fund would increase 111,271,753.9, 134,696,484, 127,532,620, 120,480,978 CNY per year respectively in the 4 scenarios. **CONCLUSIONS:** Chidamide is a cost effective treatment of PTCL in China compared to chemotherapy and will result very moderate increase on the insurance fund.

**PRM51: PREDICTING BUDGET IMPACT: A MIXED-EFFECTS MODEL APPROACH**

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**OBJECTIVES:** In the past decade, many new oncology drugs entering the market have raised concerns on affordability. At market authorization (MA), data on budget impact is limited. Uncertainty around budget impact pose substantial financial risks to payers. This analysis aims to test a novel method for budget impact estimation. This method has the potential to provide payers with a tool that would allow them to quantify the uncertainty around budget impact and the associated predictions. **METHODS:** Budget impact data were derived from the Danish Health Data Authority, covering nationwide intra- and extramural turnover per drug and featuring annual data from 1996-2016. Only novel oncology products with a European Public Assessment Report published in 2008 or later were included. A mixed-effects model was used. Fixed effects include logarithmic time since MA and time interactions with product type and therapeutic area. Random effects are composed of a random slope for logarithmic time per drug. Starting point of the prediction is time of MA with 0 drug uptake. We used k-fold cross-validation to assess primary model performance, as the mean absolute percentage error (MAPE), indicating the difference between the actual and predicted values. **RESULTS:** 34 drugs were included for model building and validation. The MAPE was 190% (interquartile range of 26% – 113%), the median was 70%. Data is highly skewed due to a limited number of drugs with a very high deviation between actual- and predicted budget impact. **CONCLUSIONS:** Our results are generally in line with broad budget impact predictions performed by agencies regulating drug reimbursement. Further specification of covariates, improved handling of outliers and increased granularity could improve the model so that it can provide payers with improved insight in budget impact development and the associated risks.

**PRM52: SYSTEMATIC REVIEW OF COHORT-LEVEL ECONOMIC MODELS FOR ANTIPSYCHOTICS IN SCHIZOPHRENIA**

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**OBJECTIVES:** Cohort-level (CL) models, including decision trees (DTs) and Markov models (MMs), are broadly used in economic evaluations of antipsychotics in schizophrenia. Our objective was to compare main characteristics of these CL models in literature, to have a better understanding of their structural simplifications assumptions. **METHODS:** Cohort-level cost-effectiveness studies of antipsychotics in schizophrenia using DTs or MMs published after 2000 were identified through Medline, Embase, congresses websites and grey literature. Main characteristics were extracted including population, treatment strategy(ies), economic outcomes and timeframe. **RESULTS:** After screening 1889 records, 41 DTs and 56 CLMMs were identified. Half of the DTs considered chronic schizophrenia (n=15); other studies considered acute phase, outpatient/hospitalized or young patients with schizophrenia. Possibility to switch was considered in 18 studies, up to 4 lines. They were mostly cost-utility analyses (n=19), and cost-effectiveness analyses (n=21) considering cost per (day of) relapse avoided. The timeframe was usually 1-year (n=32). Two thirds of the CLMMs considered general schizophrenia, whereas others targeted specific subgroups, such as chronic/acute, inpatient/outpatient, responsive/partially-responsive/treatment-resistant, young patients, and non-adherent schizophrenia. Possibility to switch was considered in 33 studies, with number of treatment lines ranging from 2 to 5. There were 33 cost-utility and 19 cost-effectiveness analyses, considering cost per (day of) relapse/hospitalization avoided or cost per month/week without symptom. Timeframes varied a lot: 5-year (n=22), 1-year (n=11), 10-year (n=10) and lifetime (n=10). **CONCLUSIONS:** No significant difference was found between DTs and CLMMs for antipsychotics in schizophrenia, except that longer timeframes
and cost-utility analysis were more used in CLMMs. Overall, these models considered simple structures to address specific research questions. It remains unclear whether these models can be generalized to address broader research questions from health technology assessment perspective: it is likely that use of microsimulations can provide estimations closer to expectations and requirements, and flexibility to approach real-life.

**PRM53: THE IMPACT OF THE LEARNING CURVE ON COSTS AND EFFECTS OF NOVEL MEDICAL DEVICES. EVIDENCE FROM REGISTRY DATA**

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**OBJECTIVES:** The existence of a learning curve (LC) might affect the early performance of novel medical devices, but its actual inclusion in the HTA processes and reimbursement decisions is limited and largely unexplored. The aim of the present study is to empirically estimate the effect of the LC on different outcomes, and to assess whether its inclusion has the potential to affect economic evaluations and HTA reports. **METHODS:** Methods to estimate the LC were systematically identified from a literature review. A biodegradable vascular scaffold (BVS) for coronary angioplasty, and a transcatheter aortic valve implantation (TAVI) procedure were used as case studies exploiting real-world registries of consecutive patients. The effects of the LC were estimated on cost data, procedural outcomes and clinical outcomes, fitting multivariate linear and non-linear parametric models. In addition, a two-stage linear regression model was adopted to estimate the minimum learning threshold before reaching a plateau. **RESULTS:** The learning effect was sensitive to the type of device, and the type of outcomes considered. No effects of LC were found for the BVS on either costs, procedure times and major adverse cardiac events, whereas for TAVI, experience was associated with lower procedure times and improved mortality at 12 months. Procedure length of TAVI reached a plateau after approximately 50 procedures. **CONCLUSIONS:** At the center and clinician level, LC may influence the early performance of novel devices affecting both costs and patients’ outcomes. Incorporation of the LC in economic evaluations and HTA reports can be relevant for certain types of technologies, and may even affect coverage decisions. Based on the number of procedures needed to gain sufficient experience, it might also inform the design of health service provision that maximize health gains. Data allowing the estimation of the LC from clinical studies and real-world registries should be made available.

**PRM54: MONTECARLO MODEL AS A TOOL IN ESTIMATION OF ECONOMIC BURDEN OF A DISEASE THROUGH THE PREDICTION OF BIOLOGICAL CHARACTERISTICS OF TUMOR IN BREAST CANCER**

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**INTRODUCTION** The third-party payer whom provide health services around the world need mathematical and methodological tools to estimate the future expenditures related health services in different populations. We use breast cancer data to generate a predictive mathematical model as help to estimate the health services’ cost in the context of a developing country as Mexico. **OBJECTIVES:** To evaluate the concordance between observed and calculates expenditures in the treatment of a sample of breast cancer patients attended in a Mexican public health institution. **METHODS:** We reviewed the clinical records from 407 breast cancer women to calculate through micro-costing, the total expenditure in health during their treatment. After that was generated the Montecarlo mathematical predictive model to try to estimate the health services expenditure in a 100 women hypothetical sample, simulating the clinical characteristics, as primary tumor size, clinical stage, histologic features, lymphatic ganglia, surgery, radiotherapy and chemotherapy kind, metastases, metastasis anatomic localization, and recurrence treatment. Chi squared and student T test for independent samples were used to estimate p value between studied patients and hypothetical population. **RESULTS:** Were not found statistical differences between clinical stage (p=0.865), tumor receptors (p=0.893), and kind of metastases between patients sample and hypothetical sample (p=0.699). The mean cost for the breast cancer women sample was $251,454.43 MXN, and for hypothetical sample $329,503.85 MXN (p<0.05), however we did not find differences in surgical procedures cost (p=0.441) **CONCLUSIONS:** The Montecarlo predictive model could be a useful tool to estimate the health services expenditure and to calculate a budget close to real cost.
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**OBJECTIVES:** Determine the optimal method of modeling a zero-inflated outcome by comparing generalized linear models (GLMs) that vary based on the distribution (negative binomial and Tweedie) and the inclusion of an offset. **METHODS:** Participants of the 2016 EU5 (France, Germany, Italy, Spain, and the United Kingdom) administration of the National Health and Wellness Survey who self-reported cardiovascular disease (CVD; n=3,685) were compared to those without CVD (controls; n=76,915) on costs derived from counts of hospitalizations, emergency room, and primary care provider (PCP) visits occurring in the preceding six months. Four different GLMs were fit for each outcome; negative binomial and Tweedie models with and without using an offset. The negative binomial is widely used, but the Tweedie distribution is a reasonable option because it allows for more flexible modeling of zeros and extreme values. Using an offset allows for the modeling of self-reported counts directly. Fit indices (lower scores are better) included the Akaike information criterion (AIC), mean absolute error (MAE), and root mean square error (RMSE). GLM parameters comparing CVD and control groups on the aforementioned outcomes were also reviewed to determine if modeling options affected statistical significance. **RESULTS:** GLMs utilizing offsets outperformed models without them for all cost outcomes (average improvement of 210,638, €83, and €23,149 for AIC, MAE, and RMSE, respectively). Among those utilizing offsets, Tweedie outperformed on MAE and RMSE (average improvement of €253 and €70,209, respectively) while the negative binomial models had a slightly lower AIC (average improvement of 4,231). Additionally, Tweedie model parameter estimates had smaller confidence intervals and detected a significant effect of CVD on PCP visit costs (p<.05). **CONCLUSIONS:** GLMs with a Tweedie distribution and offsets are the preferred choice because they demonstrated better fit and impacted substantive interpretation of model parameters.

**PRM56: WHAT IS THE SCOPE AND QUALITY OF ECONOMIC EVIDENCE AVAILABLE FOR ATOPIC ECZEMA? A SYSTEMATIC REVIEW**

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**OBJECTIVES:** Atopic eczema is a chronic inflammatory skin disease, resulting in itchy, dry skin. Whilst the clinical effectiveness evidence for eczema is collated in the Global Resource of Eczema Trials (GREAT) database there is currently no such resource for economic evidence. Therefore, we undertook a systematic review with the aim of identifying the scope and quality of economic research for atopic eczema. **METHODS:** A systematic literature search was conducted on 22nd May 2017. Studies eligible for inclusion were primary empirical studies either reporting the results of a cost of illness study or evaluating the cost, utility or full economic evaluation of prevention or interventions for eczema. Two reviewers independently assessed studies for eligibility and performed data abstraction collecting details of the study characteristics, costing and outcome methods, and quality assessment. Methodological quality was assessed using the CHEERS checklist. Further details can be found on PROSPERO (CRD42015024633). **RESULTS:** 77 studies were found, of which 33 (42.9%) were judged to be full economic evaluations, 26 (33.8%) were cost of illness studies, 12 (15.6%) were cost analyses, 5 (6.5%) were utility or willingness to pay studies, and one (1.3%) was a feasibility study. The interventions: tacrolimus, pimecrolimus, and barrier creams had the most economic evidence available (19 studies). Partially hydrolysed infant formula was the most commonly evaluated prevention (10 studies). The time frame for analyses ranged from 3 weeks to 14 years. According to the CHEERS checklist, the studies were of reasonable reporting quality with the majority of studies fulfilling more than 70% of criteria. **CONCLUSIONS:** The current level of economic evidence within eczema is much lower than that available for clinical outcomes. The limited range of interventions evaluated and the heterogeneity of methods used in the existing evidence suggest further economic research is needed to support commissioners making health funding decisions.

**PRM57: CLASSIFICATION OF CAUSES OF HOSPITALIZATION FOR HEART FAILURE PATIENTS IN COST-EFFECTIVENESS AND COST-UTILITY EVALUATIONS OF PHARMACOTHERAPEUTIC, SURGICAL, AND MANAGED-CARE INTERVENTIONS: SYSTEMATIC REVIEW**

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**OBJECTIVES:** Most heart failure (HF) patients are hospitalized frequently and for a variety of causes. The operational definition of these causes may affect cost-effectiveness and cost-utility estimates. We aimed to systematically review causes of hospitalizations and their definitions used in economic evaluations (EE). **METHODS:** We searched
PubMed for the 1994-2017 period for English-language cost-effectiveness/utility studies with HF as primary disease using decision tree analysis, markov modeling, monte-carlo simulation, trial-based models, or other models enabling determination of (quality-adjusted) life years (LY/QALY) and incremental cost-effectiveness/utility ratios (ICER/ICUR). HF hospitalization reasons included: HF, cardiovascular (CV), any-cause, HF&CV, procedure, or not-specified. Studies were classified as focused on pharmacotherapeutic, managed-care, or surgical interventions. **RESULTS:** Of 1400 records, 1145 were excluded per title and abstract: 331 irrelevant publications; 521 cost-analysis/budget impact reports; 192 studies reporting LY/QALY but not ICER/ICUR, or not comparing treatments economically. Of the 255 reports assessed full-text, 192 were excluded for not reporting ICER/ICUR, yielding 63 studies. Of the 25 pharmacotherapeutic EEs, 11 defined hospitalization cause as HF, 3 CV, 3 HF&CV, 6 any-cause, 2 not-specified (others 0). Of the 16 managed-care EEs, 5 defined cause as HF, 1 CV, 6 any-cause, 4 as not-specified (others 0). Of the 22 surgical EEs, 5 defined cause as HF, 1 CV, 6 any-cause, 9 procedures, 1 as not-specified (others 0). Omnibus contingency-table analysis yielded p=0.002. **CONCLUSIONS:** There is significant variation in the definitions of cause of hospitalization of HF patients in EEs in general as well as across and within intervention types. Because differential costs and utilities may be associated with definitions, the cause used in EEs may vary in terms of the estimated ICER and ICUR and thus affect decision-making regarding treatment or resource allocation.

**PRM58: THE DYNAMICS OF CHILD MENTAL HEALTH CARE**

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**OBJECTIVES:** We aim to estimate the persistence of mental health care for a population of Dutch children born between 2000 and 2012. The relationship between mental health and care is complex, with multiple mechanisms affecting both individual mental health and the amount of care an individual receives. Therefore, we develop a theoretical model to provide a structural interpretation for the true state-dependence of child mental health care. **METHODS:** We use administrative data from the Psychiatric Case Registry Northern Netherlands (PCR-NN), which is a longitudinal record of patient contacts with psychiatric institutions between 2000 and 2012. The sample contains 206,283 patient contacts corresponding to 20,193 individuals. We transformed the PCR-NN into a dynamic panel data set, and obtained consistent and unbiased estimates by using difference General Method of Moments (GMM). **RESULTS:** All estimation results show a positive coefficient smaller than unity, which indicates that the process is stable. An exogenous increase of 10 care moment in the present year is associated with approximately 4 additional care moments in the future. In addition, we find that the role of spurious state-dependence is small. Estimates are robust to numerous sensitivity analyses. **CONCLUSIONS:** Through the structural interpretation of the model, we can conclude that the persistence of health is likely stronger than the combination of the healing effect of care and the rate at which health problems lead individuals to receive care, but that the process is stable. In other words, if children experience an exogenous adverse mental health event, they will receive an increased number of care moments for a few years, but this effect will weaken over time so that eventually they will receive a base level of care again.

**RESEARCH ON METHODS - Databases & Management Methods**

**PRM59: CONVERSION OF A FRENCH ELECTRONIC MEDICAL RECORD (EMR) DATABASE INTO THE OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP COMMON DATA MODEL.**

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**OBJECTIVES:** The Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) provides a structure for organizing and standardizing patient data coming from disparate data sources. OMOP-CDM has never been implemented on French data. This study describes the conversion and evaluation of the French Disease Analyzer database (DA) to the OMOP-CDM model. The converted database (DA-OMOP) was validated by replicating a published study performed with an equivalent EMR database (Longitudinal Patient Database, LPD). **METHODS:** DA database (QuintilesIMS, EMR France) is an electronic medical record database of 1200 General Practitioners in France. DA data were mapped into CDM following the OMOP V5 specification and converted into different domains using correspondence tables to convert native language into common language. Accuracy and completeness of the information were evaluated. Conversion was tested with the replication of a published study regarding antithrombotic treatments in patient with Atrial Fibrillation (AF) conducted with LPD (QuintilesIMS, EMR France). Results obtained with DA-OMOP were compared with those obtained with DA native and LPD **RESULTS:** In total 99% of disease codes, exams, procedures and devices codes and 88% of drug codes were converted. Missing codes (12%) were related to homeopathy and OTC treatments. In DA-OMOP, mean age of 
AF patients was 74.4 years, (versus 74.6 in DA and 74.6 in LPD), 58.4% were men (versus 58.4% in DA and 59.5% in LPD) and 81.3% had a CHADs score ≥1 (versus 81.6% in DA and 83.1% in LPD). Additionally, 51.9% of thromboembolic high risk patients (45% in LPD) were not treated or inadequately treated according to ESC guidelines and 62.5% of patients with a score CHADs=0 (against 66.4% in LPD) were overtreated. CONCLUSIONS: Agreement between DA-OMOP results and those of LPD indicates a satisfying convergence and provides a robust validation for DA-OMOP. This will enable the integration of French data set into the international OMOP network.

PRM60: IS IT POSSIBLE TO ACCURATELY IDENTIFY RARE DISEASES USING NATIONAL HOSPITAL DISCHARGE DATABASES?

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OBJECTIVES: Generation of accurate data in a timely manner is often challenging especially for rare diseases. Data from administrative discharge databases, as an alternative to prospective studies, may be important and valuable but has methodological limitations. This study (HO-15-16391, funded by GSK) aimed at evaluating the feasibility of describing the hospital burden of Pulmonary Arterial Hypertension (PAH) in France using the French National Hospital discharge database (PMSI). METHODS: An exploratory analysis was performed from the PMSI databases. All 2013 hospital stays with ICD-10 codes for PAH (I27.0, I27.2) whether principal or associated diagnosis were extracted. Only incident adult patients were selected (not hospitalized with PAH in 2011-2012) and followed during 1 year. RESULTS: 38,834 patients were extracted in 2013. A more discriminating algorithm was defined with medical experts to get a specific selection of the study population. The presence of lung transplantation, prostacyclin administration and right heart catheterization at inclusion or during follow-up were tracked as potential surrogates for PAH. Concomitant diseases such as chronic left heart failure, chronic lung diseases, thrombo-embolic diseases, left valvular surgery were excluded as causes of other pulmonary hypertension group. The last criteria for true PAH was the presence of at least one PAH-related stay after diagnosis. In total, 384 incident patients were included. This cohort is consistent with the estimation from the French PAH national registry in terms of number of patients and demographic characteristics. Lack of clinical information prevented us from exploring specific sub-groups (NYHA functional classes). CONCLUSIONS: The PMSI database is an accessible and relevant source of data, especially for diseases mainly managed in hospital. Its exhaustiveness allows to overcome the low frequency of events that is specific to rare diseases and thus to gain a representative picture of the hospital burden of disease. Nevertheless, clinical information is limited and requires assumptions validated by medical experts.

PRM61: REGULATORY & REIMBURSEMENT DECISIONS DATABASE FOR INNOVATIVE DRUGS TO IMPROVE CONSISTENCY OF DECISION-MAKING

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OBJECTIVES: To create a reimbursement applications database for innovative drugs. Particularly, the further goal is to promote case-based analogical precedent-conscious reasoning and evidence-based decision making in Poland. METHODS: Information was gathered from documents published by the Agency for Health Technology Assessment and Tariff System (AHTAPol) and the Ministry of Health (MoH) between January 2012 and June 2017. Information from statements of AHTAPol’s Transparency Council (STC), recommendations of AHTAPol’s President (RPA) and MoH’s reimbursement decisions (MoHD) was extracted. RESULTS: The prepared database includes 470 reimbursement applications corresponding to 334 brand names and 288 unique substances. Applications were submitted by 100 companies. The database consists of 60 categories and includes the following: applicant name, product description, indication, market authorisation type, detailed process timelines, requested reimbursement mode, STC, RPA, MoHD, discrepancy between requested conditions and MoHD, information from BIA and ICER value if applicable, and key findings from available clinical analyses. CONCLUSIONS: Health care systems based on public money should treat all applicants equally if the conditions for the decision are similar and should provide equal access to benefits for patients with similar needs. The database gathers information on all precedent decisions of marketing authorization and public payer practices of similar products or similar indications. This approach opens up the possibility for improvement of transparency and decision-making practices not only in Poland, but in each country.

PRM62: COMPARISON OF ICD-9 TO ICD-10 CROSSWALKS DERIVED BY PHYSICIAN AND CLINICAL CODER VS. AUTOMATED METHODS

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OBJECTIVES: Coding algorithms are critical for identifying patient samples, comorbidities, and outcomes in studies of claims or electronic medical record data, but algorithms developed with International Classification of Diseases, Ninth Revision (ICD-9) codes are obsolete in current data. The present study sought to compare ICD-9 to ICD-10 crosswalks from General Equivalence Mappings (GEMs) and compare them to crosswalks derived by a clinician and clinical coder, to evaluate whether automated methods are sufficient for deriving ICD-10 algorithms. METHODS: Ten conditions from various therapeutic areas were selected for comparison. Existing ICD-9 algorithms were entered into GEMs to derive ICD-10 crosswalks, and a physician and clinical coder completed a questionnaire to guide the development of ICD-9 to ICD-10 crosswalks for the same conditions. Differences between the crosswalks were summarized using descriptive statistics and the theoretical impact of the differences were assessed qualitatively. RESULTS: Crosswalks identified by the physician/coder were typically far more inclusive than those from GEMs. Crosswalks from GEMs were missing a mean of 147.7 codes (median: 45; range: 19–462) compared to those from the physician/coder, while the physician/coder crosswalks missed far fewer (mean: 11.3; median: 5.5; range: 0–53) compared to GEMs. Crosswalks for diabetes, diabetic neuropathy, hypoglycemia, and peripheral vascular disease had the most discrepancies (>130) while crosswalks for acute myocardial infarction and hypertension had the fewest (<25). Generally, conditions with the most discrepancies included those with various etiologies, conditions with a variable clinical definition, those that may be a side effect of medications, and those that require procedure codes to supplement identification. CONCLUSIONS: The use of GEMs alone is likely not sufficient for identifying appropriate ICD-10 crosswalks from ICD-9 algorithms, but any algorithm should be reviewed by researchers prior to use in a study. Future research could include the validation of crosswalks after an examination of patient charts.


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OBJECTIVES: Little information is available on the role of the general practitioner (GP) in colorectal cancer (CRC) care. Therefore, the objective of this study was to establish a link between the Netherlands Cancer Registry (NCR) and the GP Database of the PHARMO Database Network and creating a CRC-GP population. METHODS: A linkage was performed between the NCR - a population-based registry of newly diagnosed cancer patients in the Netherlands - and the GP Database of the PHARMO Database Network which comprises data from electronic patient records registered by GPs, including information on diagnoses/symptoms, laboratory test results, referrals and healthcare product/drug prescriptions. After pairing records in both databases on gender and birth year, a linkage weight was calculated based on: first initial, first letter last name, 4-digit zip code and presence/absence of cancer related events as singular variables. Patients diagnosed with CRC between 1998-2014 were selected, resulting in a CRC-GP population. The representativeness of this population to the total NCR population was evaluated by comparing the distribution of gender, age at tumour diagnosis, tumour stage and tumour site. RESULTS: In total, there were more than 19,000 CRC patients in the linked CRC-GP population, of which 66% were diagnosed with colon cancer, 30% with rectum cancer and 4% with rectosigmoid cancer. These patients were representative for the cancer patients included in the total NCR. The difference in percentage between these two populations showed that patients who were linked tended to be somewhat younger (68.2 years vs. 69.7 years) and were slightly less often diagnosed with an advanced tumour stage (19% vs. 21%). CONCLUSIONS: The linked CRC-GP population is representative of the total NCR population. The CRC-GP population will create more insight into the role of the GP in CRC care and will give more opportunities to monitor the patients before, during and after cancer diagnosis.

PRM64: LEVERAGING ELECTRONIC HEALTH RECORDS TO MEET THE REAL WORLD EVIDENCE NEEDS OF HTA: A UK PERSPECTIVE

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OBJECTIVES: The inclusion of real world evidence in HTA submissions has become increasingly desirable. In the UK, databases containing data collected in primary care represent a ready source of real world data however they continue to be underutilised in this field. We sought to review the use of such databases in NICE technology assessments (TAs) and provide recommendations regarding their use in future submissions. METHODS: The NICE website was searched for keywords relating to the main primary care databases in the UK. All NICE TAs identified through this search were screened and information on the data source and the way the data was used in the submission were extracted. Comments on the data by the evidence review group (ERG) and committee were also
extracted and reviewed. RESULTS: A total of 13 NICE TAs were identified. Between 2007 and 2010, data from primary care databases were used in 3 NICE TAs to support arguments regarding the prevalence of asthma and prescribing patterns in asthma and fracture prevention. The ERG/committee did not comment on this data. Between 2011 and 2016, data from primary care databases were used in 10 NICE TAs, with 3 in 2015 and 3 in 2016. In each of these cases the data were used to inform a small number of parameters in an economic model. The data were generally well received by the ERGs/committees. Criticisms of the data typically occurred where the results had been repurposed from a published study. CONCLUSIONS: The use of data from UK primary care databases in NICE submissions is increasing. The planning of database studies to support market access should begin early in the drug development process and, through collaboration between the trial team, economic modellers and database experts, can be used to inform a multitude of parameters in the economic model.

PRM65: A REVIEW OF CLINICAL OUTCOME ASSESSMENT LABELING IN EUROPE AND IN THE UNITED STATES (2013-2016)

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OBJECTIVES: A review of approvals by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for 2000 to 2012 showed that respectively 21% and 26% of new drugs had patient-reported outcome (PRO) labeling. Our objectives were to expand the review to all clinical outcome assessments (COAs) for 2013 to 2016, and to identify: a) the endpoint positioning for each COA used, b) the therapeutic areas with highest number of products with COA labeling, and c) the type of instruments supporting PRO labeling. METHODS: The EMA and FDA websites were systematically explored to identify all approvals from 2013 to 2016. The PROLABELS database was used for COA labeling identification. All corresponding labels and reviews were reviewed. RESULTS: From 2013 to 2016, 407 and 244 new drugs were approved by the EMA and the FDA respectively. 37% of the FDA approvals had a COA labeling compared to 44% of the EMA approvals. 85 FDA drugs (21%) and 83 EMA drugs (34%) had a PRO labeling. Products (FDA/EMA) with other COA labeling were distributed as follows: ClinROs (67/52), PerfOs (27/32) and ObsROs (11/2). PROs were used as primary endpoints in 27% of all EMA and FDA products with a COA labeling, ClinROs in 48%, PerfOS in 59% and ObsROs in 40%. The highest number of products with a COA labeling were found in: respiratory tract diseases (n=43), nervous system diseases (n=34) and mental health disorders (n=26). Skin and connective tissue diseases were in the fourth position with 25 products and neoplasms at the fifth position with 24 products. PRO instruments used were often “legacy” instruments, i.e., SF-36 (22 products), St George’s Respiratory Questionnaire (15 products), and Health Assessment Questionnaire (14 products). CONCLUSIONS: From 2013 to 2016, COAs played an important role in the evaluation of treatment benefit.

PRM66: IDENTIFICATION OF REAL WORLD DATA SOURCES IN CANCER IN THE NORDIC COUNTRIES

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OBJECTIVES: The objective of this study was to systematically identify and assess cancer data sources that collect patient-level data in the five Nordic countries: Denmark, Finland, Iceland, Norway and Sweden. METHODS: A comprehensive review of literature was conducted using the Embase and MEDLINE bibliographic databases. The searches were conducted in November 2016, limiting records to the past five years. Records were included only if a Nordic based cancer related data source was mentioned in the title or abstract. Administrative health registries were not considered in this study. Altogether, 4797 records were screened by title and abstract. In addition, targeted internet searches and a review of grey literature were conducted. RESULTS: In total, 1592 records were included and further reviewed. The majority, 87%, of included studies reported epidemiological and clinical main outcomes, whereas treatment patterns were reported in 4%, patient-reported outcomes in 4%, and resource use related outcomes in 2%. The remaining 3% of studies reported other outcomes, such as validity assessment. Altogether, 195 cancer data sources were identified out of which 84 were in Sweden, 55 in Denmark, 27 in Norway, 12 in Finland, 6 in Iceland, and 11 covering multiple Nordic countries. The types of data sources identified were national and specified cancer registries including quality registries in cancer (n=100), biobanks (n=38), prospective cohort studies (n=34), cancer screening registries (n=13), and other registries that collect patient-level data in cancer (n=10). CONCLUSIONS: A multitude of real world cancer data sources was identified in the Nordic countries. These results strongly emphasize the available opportunities of utilizing Nordic real world data in cancer, on the one hand, to meet payer requirements in post authorization treatment effectiveness, safety and resource use, and on the other hand, to pursue innovative research combining the rich data from biobanks, cancer registries and population-based administrative health databases.
PRM67: INCREASING CLINICAL DATA QUALITY THROUGH INTERACTIVE DATA VISUALIZATION

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OBJECTIVES: To focus on critical data and to allow prompt detection for data inconsistencies on Early Access Program (EAP) studies and Non-Interventional Studies (NIS), by setting up a Risk Based Data Management (RBDM) approach with anticipated and periodic Visual Data Quality Review. METHODS: Test phase ran from July to December 2013 and RBDM was implemented since 2014 on Primary Data Collection NIS (PDC-NIS), Secondary Data Use NIS (SDU-NIS) or EAP studies. Visualization meeting are planned every 3 months from patients inclusion up to database lock. Data visualization is supported by TIBCO Spotfire® version 5.5 to release a visual presentation of clinical data. This visualization is based on SAS derived database resulting from the raw data. In order to standardize data visualization across studies, common database structure and derivation rules have been defined. RESULTS: Since 2014, 15 studies with RBDM were implemented: 13 PDC-NIS, 1 SDU-NIS, 1 EAP, 8 (53%) studies were carried out in oncology, 3 (20%) rheumatology, 2 (13%) anemia, 1 (7%) hematology and 1 (7%) HER2 diagnostic testing. Annualized meeting rate per study is in average 6 data visualization. Data review meeting duration decreased from 8 hours (before RBDM) to 2 hours using spotfire®. In average 52 graphs are presented to describe clinical data: 3.1% of graphs for demographic characteristics, 8.7% for patient’s vital status, 12.5% study treatment, 8.4% early termination, 20.2% for laboratory data, 11.5% safety data and 27.8% dedicated to study specificities. All graphics produced allows interactivity from macro to micro visualization. CONCLUSIONS: Added value of RBDM allows highlighting inconsistencies on clinical data faster and earlier than with classical data review. Moving from static (paper review) to interactive visualization allows a significant saving in time to clean and lock database combined with high data quality. Interactivity is a key element by selecting subsets of data and identifying easily outliers.

PRM68: A SNAPSHOT OF MEDICATION ADHERENCE ACROSS THREE EUROPEAN COUNTRIES: APPLICATION OF COMMON METHODOLOGY

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OBJECTIVES: Drug-utilization studies applies different methods to various data types to describe medication-adherence. Comparison of results of these studies is difficult due to differences in the methods applied, data-sources and selected populations. This study, performed under the umbrella of Action-Group-A1 on adherence of European-Innovation-Partnership on Active-and-Healthy-Aging, evaluates medication adherence and persistence to chronic therapies across different European settings applying a harmonized method of data extraction and analysis. METHODS: Information were retrieved from pharmacy-claims databases of three European countries: Spain (EpiChron-Cohort), Ireland (HSE-PCRS), Italy (Campania-LHU). Subjects aged >65 years, newly initiated antidiabetics, statins, bisphosphonates (ATC III-level) between 7/1/2010 and 12/31/2010 were identified and followed over 12-months. The first dispensing defined the index-date and treatment group. Main outcome measures was adherence (medication possession ratio, MPR) and persistence on index treatment. MPR <80% was considered as non-adherence. Subjects were defined as persistent until discontinuation (gap >60 days between two subsequent index treatment refill). All country-specific datasets were prepared employing a common data input model. Outcome measures were calculated for each country and then pooled using random effect models. RESULTS: Total number of subjects analyzed was 33,490. Pooled estimates: i) antidiabetics cohort: 30.33% of subjects with MPR<80% (95% confidence interval: [25.53; 35.60], I2=95%, p<0.0001); rates of non-persistence 46.80% (95% C.I.: [36.40; 57.49], I2=98.7%, p<0.0001); ii) statins cohort: 52.45% of subjects with MPR<80% (95% C.I.: [33.43; 70.79], I2=99.9%, p<0.0001); iii) bisphosphonates cohort: 61.35% of subjects with MPR<80% (95% C.I.: [52.83; 69.22], I2=97.5%, p<0.0001); rates of non-persistence 60.24% (95% C.I.: [45.35; 73.46], I2=99.2%, p<0.0001). CONCLUSIONS: Our study showed high degree of heterogeneity among countries in adherence and persistence rates. The extraction and aggregation of data into a common data model allowed to calculate the drug use parameters by means of a systematic and uniform approach.

PRM69: I-O OPTIMISE: DEVELOPING A UNIQUE MULTINATIONAL REAL-WORLD EVIDENCE-BASED RESEARCH PLATFORM IN ONCOLOGY

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OBJECTIVES: To focus on critical data and to allow prompt detection for data inconsistencies on Early Access Program (EAP) studies and Non-Interventional Studies (NIS), by setting up a Risk Based Data Management (RBDM) approach with anticipated and periodic Visual Data Quality Review. METHODS: Test phase ran from July to December 2013 and RBDM was implemented since 2014 on Primary Data Collection NIS (PDC-NIS), Secondary Data Use NIS (SDU-NIS) or EAP studies. Visualization meeting are planned every 3 months from patients inclusion up to database lock. Data visualization is supported by TIBCO Spotfire® version 5.5 to release a visual presentation of clinical data. This visualization is based on SAS derived database resulting from the raw data. In order to standardize data visualization across studies, common database structure and derivation rules have been defined. RESULTS: Since 2014, 15 studies with RBDM were implemented: 13 PDC-NIS, 1 SDU-NIS, 1 EAP, 8 (53%) studies were carried out in oncology, 3 (20%) rheumatology, 2 (13%) anemia, 1 (7%) hematology and 1 (7%) HER2 diagnostic testing. Annualized meeting rate per study is in average 6 data visualization. Data review meeting duration decreased from 8 hours (before RBDM) to 2 hours using spotfire®. In average 52 graphs are presented to describe clinical data: 3.1% of graphs for demographic characteristics, 8.7% for patient’s vital status, 12.5% study treatment, 8.4% early termination, 20.2% for laboratory data, 11.5% safety data and 27.8% dedicated to study specificities. All graphics produced allows interactivity from macro to micro visualization. CONCLUSIONS: Added value of RBDM allows highlighting inconsistencies on clinical data faster and earlier than with classical data review. Moving from static (paper review) to interactive visualization allows a significant saving in time to clean and lock database combined with high data quality. Interactivity is a key element by selecting subsets of data and identifying easily outliers.
**OBJECTIVES:** I-O Optimise, a pan-European initiative aimed at developing a multinational research framework, leverages existing real-world data sources (RWDS) to provide ongoing timely insights into the evolving lung cancer landscape. The goal, ultimately, is to improve outcomes for lung cancer patients. As RWDS’ structure, content and scope vary, database-mapping has been undertaken to explore RWDS’ suitability for addressing specific research questions. **METHODS:** RWDS were identified via literature searches, interviews with researchers and I-O Optimise affiliates and review of existing QuintilesIMS initiatives. RWDS were shortlisted based on population representativeness, disease coverage (non-small cell lung cancer [NSCLC], small cell lung cancer [SCLC] and mesothelioma), data quality/completeness, source type, estimated size and other attributes. Final selection was based on: pan-European coverage, research goal alignment and timely data availability. **RESULTS:** In addition to SCAN-LEAF (pre-identified Scandinavian RWDS), 490 RWDS were identified with 124 (25.3%) shortlisted. Of the shortlisted, 15 (12.1%) are under appraisal, 91 (73.4%) have completed appraisal, 4 (3.2%) are under assessment and 14 (11.3%) are fully assessed. Of the assessed RWDS, 7 (50.0%) have progressed to a comprehensive appraisal of research goal alignment and capacity (Germany, Italy, Netherlands, Portugal and UK); All 7 address clinical outcomes and treatment/practice patterns, 6/7 address pharmacovigilance, 5/7 address healthcare resource utilization and 1/7 addresses patient-reported outcomes. These 7 RWDS plus SCAN-LEAF will provide ~395,000 NSCLC, SCLC and mesothelioma cases. **CONCLUSIONS:** A structured assessment of RWDS facilitated development of a flexible collaborative research framework. The challenges of conducting such initiatives were also revealed, as most available RWDS proved unsuitable. Drawing together diverse RWDS enables examination of a wide range of research questions, reflects the diversity of real-world clinical practice and provides standardisation that allows insights to be drawn across data sources. I-O Optimise has the potential to elucidate real-world management of lung cancer in Europe, complementing ongoing clinical trial-based research.

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**PRM70: MISCLASSIFICATION OF DIABETES TYPE I IN GERMAN CLAIMS DATA**

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**OBJECTIVES:** The two major subtypes of diabetes, type I and II, are based on different pathogenic processes. Their correct diagnosis is important for a proper treatment of patients, assignment to appropriate disease management programs (DMP) and correct billing of medical costs. However, health claims data shows many patients diagnosed with both type I and II. Based on the prevalence of having both types, this number should be much lower, suggesting erroneous coding. To identify miscoding we propose an algorithm that distinguishes type I and type II diabetics. **METHODS:** We used the health claims database of Arvato Health Analytics containing diagnosis codes and prescriptions of 3 million German insurants for 2008-2015. We extracted all patients showing type I or type II diagnoses. We classified patients without insulin treatment as type II. Patients with a clear majority of diagnoses for either type I or II were classified accordingly. Furthermore, we identified a group of less certain type II diabetics without continuous insulin treatment or with continuous treatment of oral antidiabetics. For evaluation we applied the algorithm to two German health claim data sets from 2011 to 2015, one containing all insurants, one only participants of diabetes type I DMPS. **RESULTS:** 88.1% of the insurants with a type I diagnosis (45,632 of 51,812) also had a type II diagnosis. Reducing the population to double diabetics with at least 2 outpatient or 1 inpatient diagnoses in one year, 40.2% had no insulin prescription. We classified 12.4% as type I, 70.6% as type II. Among the DMP participants, 62.5% had additional type II diagnoses. According to our method, 4.8% were assigned incorrectly to the DMP. **CONCLUSIONS:** The algorithm indicates that many type I diabetes diagnoses are incorrect, as the patients show clear signs for only type II. Subsequently, reasons for the wrong diagnoses coding should be identified and reduced.

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**PRM71: USING OBSERVATIONAL DATA FROM REGISTRY IN COST-EFFECTIVENESS EVALUATION OF METASTATIC CASTRATION RESISTANT PROSTATE CANCER IN FRANCE**

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**OBJECTIVES:** Cost-effectiveness evaluations in oncology based on data available at the time of initial approval can
be challenging. Available clinical data are often limited to interim immature survival data; inclusion criteria may limit the external validity of results; evidence limited to one head-to-head comparison limits network meta-analysis (NMA) feasibility. Re-evaluation using real world evidence can solve these issues. However, several shortfalls need to be considered when estimating comparative effectiveness. This study explores potential solutions in the context of real-world evidence on metastatic Castration Resistant Prostate Cancer (mCRPC) in patients pre-treated by docetaxel. METHODS: A three-state survival model was constructed to estimate the cost-effectiveness of post-docetaxel mCRPC treatments in France and populated with data from the Janssen European Prostate Cancer Registry (NCT02236637). Baseline characteristics, progression-free survival and overall survival were obtained for abiraterone acetate plus prednisone (AAP) (n=199), enzalutamide (n=98) and cabazitaxel (n=145). Survival was extrapolated based on the NICE guidelines. Alternative methodologies were tested to take into consideration the differences in patients' characteristics between each treatment arm, including a cox model, adjusted HR, evidence from published NMA based on arm equivalence assumptions, adjusted HR based on propensity score matching and restricting analysis to a subgroup of patients presenting the same characteristics. RESULTS: Variation in the results was observed with the different methodologies tested. However, AAP and enzalutamide were always the two optimal treatments; cabazitaxel was dominated (the most expensive and less efficient treatment) on the efficiency frontier. In some cases, AAP was more expensive and efficient than enzalutamide with Incremental Cost-Effectiveness Ratios (ICERs) between 2,400 and 46,000 €/QALY. In other cases, enzalutamide was either dominated or more expensive and efficient than AAP with ICERs between 60,000 and 130,000 €/QALY. CONCLUSIONS: Despite the associated shortfalls, using registry data to estimate comparative effectiveness in CE evaluation is feasible and yielded coherent results despite the different methodologies used.

**PRM72: THE PERSONALISED REIMBURSEMENT MODELS (PRM): REAL WORLD DATA COLLECTION TO PROVIDE INNOVATIVE PRICING SOLUTIONS IN FRANCE**

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**OBJECTIVES:** Oncology medicines reimbursed in France have one fixed price whereas benefits vary across patient groups. Herceptin®, anti-HER2 targeted therapy, obtained reimbursement successively for metastatic breast cancer (2002), adjuvant setting (2006) and neo-adjuvant setting (2012). Consequently, its price decreased regularly on a volume based agreement ignoring the scaling of patients clinical benefit. The Personalised Reimbursement Models (PRM) project is an infrastructure validated by the French National Data Privacy Committee to collect real life data of HER2+ breast cancer (BC) patients receiving Roche targeted therapies since January 2011. The French PRM database has been active since 2015. It provides fully available datasets extracted from chemotherapy prescriptions, which gives the opportunity of modeling reimbursement agreements for Roche BC drugs next indications. METHODS: BC patients at 105 centers recorded in the Electronic Pharmacy Record system with at least one HER2 targeted Roche therapy administration since January 2011. PRM scenarios have been simulated to reflect the impact of price rebate of trastuzumab regarding its indications. RESULTS: From >18,000 HER2+ BC patient files extracted, 13,535 patients from 97 centers were analyzed, accounting for around 45% of all 2011-2016 French HER2+ BC. 7,658 patients had at least one prescription for 2015 or 2016 and at least one treatment line initiation for 5,347 of them within this period (respectively 3,728 (64%) / 2,128 (36%) early / advanced treatments). 49,372 trastuzumab injections are recorded in the database for 2016; 31,030 (63%) were related to early treatments and 18,342 (37%) to advanced treatments. According to price decrease over time, PRM agreements could have resulted in 40% price difference for Herceptin between early and metastatic indications. CONCLUSIONS: PRM database provides a reliable reference basis for substantial and relevant price agreements in HER2+ breast cancer drugs opening innovative pricing solutions based on in real life care practices that could be extended to new therapies in breast cancer

**PRM73: IDENTIFYING PATIENTS WITH LUPUS NEPHRITIS IN THE UNITED KINGDOM (UK) CLINICAL PRACTICE RESEARCH DATALINK (CPRD)**

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**OBJECTIVES:** Systemic lupus erythematosus (SLE) is a rheumatic disease affecting many organs. Lupus nephritis (LN), which is kidney inflammation linked to SLE, is a potentially severe SLE complication, yet data from the UK
regarding the characteristics and outcomes of LN patients is lacking. As such, investigations of LN patients in databases such as the UK CPRD can help to fill this evidence gap. It is thought that the prevalence of LN in SLE patients is between 20-60%; however, identification of LN patients in CPRD using two read codes specific for LN identified only approximately 3% of SLE patients as having LN. The aim of this work was to develop a disease phenotyping algorithm for LN to increase sensitivity of identifying LN patients in CPRD data. METHODS: Using a linked dataset of CPRD and Hospital Episode Statistics (HES), we assessed whether additional LN patients could be identified by 1) including secondary care data and 2) by utilising a wider range of potentially relevant codes for LN encompassing screening, diagnosis, and management with the 4 coding systems used in CPRD: Read (primary care diagnoses and procedures), British National Formulary (primary care prescriptions), ICD-10 (secondary care diagnoses) and OPOS-4 (secondary care procedures). RESULTS: More than 128 additional Read codes and 12 ICD-10 codes potentially reflecting LN were identified. The frequency of use of all potential LN codes and combinations of codes in SLE patients will be presented, with results highlighting whether or not linking HES data to CPRD increased the proportion of LN cases identified. The development of a phenotype algorithm to identify LN patients from these codes will also be presented. CONCLUSIONS: This work will increase sensitivity of identifying patients with LN in CPRD data to aid future studies involving this patient group.

**PRM74: ROCHE ONCOLOGY DATA IN OPEN ACCESS: AN INNOVATIVE STEP FOR SCIENTISTS**

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**OBJECTIVES:** The objective was to share oncology data from several studies sponsored by Roche based on several thousands of patients insuring both patient data privacy and actionable data access to the scientists’ community. **METHODS:** Twelve French local NIS were anonymised in accordance with the G29 article methodology. First, raw data from 12 NIS were pooled. Then, to ensure anonymization, multiple actionable aggregated data were generated. Aggregate generation did not contain less than 10 patients for a modality (if necessary was combined with the closest modality to achieve at least 10 patients per modality). Pooled variables were patient characteristics at study inclusion: demographics, disease and medical history, concomitant treatments, biological data, vital signs. No individual data was generated, therefore no minimum and maximum was displayed, only quartiles with mean, standard deviation and median. Local authorizations for data privacy were performed and acceptance notice was received in March 2016. The data covering period was from 2003 to 2013. Data was made available to the entire scientific community on the Internet through a 6 month data challenge organized by a collaborative scientific program Epidemium. **RESULTS:** Data access was granted to an open community of scientists and analysts based on 12 French Non-Interventional studies, more than 1000 sites and 7761 patients: 255 (3%) with follicular lymphoma, 765 (10%) with colo-rectal cancer, 4040 (52%) with neoplastic disease (2969 (38%) solid tumor and 1066 (14%) malignant hemopathy), 793 (10%) with lung cancer, 1908 (25%) with breast cancer. The multi-aggregation algorithm resulted in delivering 240 actionable aggregates, corresponding to 1560 modalities. Mean age was 62.8 ± 12.2 years and 4658 (60.1%) women were included. **CONCLUSIONS:** Discussions with local authorities helped building a multi-aggregation algorithm which resulted in both ensuring data privacy with a lower wealth of data exploitation than individual data and actionable open access to scientists.

**PRM75: ASSESSING THE VALUE OF DECISION TREES AS A METHOD FOR IDENTIFYING PATIENT SUBGROUPS**

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**OBJECTIVES:** Standard methods of identifying patient subgroups typically require pre-specifying attributes of interest, potentially overlooking important attributes. This study assessed the value of decision trees as a method for empirically identifying patient subgroups and to evaluate the decision tree and visualization functionality in SAS Enterprise Miner. **METHODS:** Electronic Medical Record (EMR) data from a panel of US Medical Retina Clinics were used to create a dataset of patients whose eyes were treated using anti-vascular endothelial growth factor (anti-VEGF) products. The decision tree algorithm used variables such as baseline visual acuity (VA) and number of doses to partition the patients into subgroups which were homogenous in their subsequent VA (outcome measure). To ensure that the decision tree remained interpretable, users specified constraints e.g. maximum tree depth and minimum number of observations in terminal nodes. Users also injected clinical domain knowledge by specifying a variable and split point on which to enforce a split at any point in the tree. **RESULTS:** Homogenous subgroups generated by the tool largely conformed to the known strata of patient eye segments, including stratification at the approximate VA threshold for legal blindness and threshold for driving eligibility in the US. It also corroborated existing evidence on the positive association between loading dose and subsequent VA. **CONCLUSIONS:** Decision trees and exploratory tools, such as SAS Enterprise Miner, provide an intuitive visual representation of data and are
capable of identifying insights that may be overlooked through conventional, pre-specified statistical analysis. The method lends itself towards exploring multiple pathways to outcomes without the constraint of a specific hypothesis.

PRM76: ADJUSTING FOR SELECTION BIAS IN EVALUATING TWO-DOSE HUMAN PAPILLOMAVIRUS VACCINE COVERAGE AMONG ADOLESCENTS IN THE UNITED STATES

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OBJECTIVES: Recent changes to the recommended human papillomavirus (HPV) vaccine schedule include reduction from a 3- to 2-dose schedule (if initiated before age 15) and inclusion of a 9-valent vaccine (HPV9). To assess potential impact on vaccine coverage, we examined 2-dose coverage and timing among adolescents and explored the use of survival analysis methods to estimate coverage and identify factors associated with receipt of the second dose. METHODS: Data from the 2015 National Immunization Survey-Teen were analyzed. Among 13-17 year-olds who initiated the series before age 15, the time to the second dose and factors associated with receipt of the second dose were estimated with and without adjusting for follow-up time. RESULTS: Among those who initiated before age 15, 88% initiated with the quadrivalent vaccine, 59% initiated at age 11-12 years, and 84% received a second dose. Among adolescents who received 2+ doses, median time between the first two doses was 3.0 months. Kaplan-Meier estimated median time between doses was 3.9 months. Logistic regression results indicated adolescents who initiated with HPV9 were less likely to receive a second dose (OR: 0.4, P < 0.0001); however, this was not observed in the Cox model (HR: 1.1, P = 0.5). Initiation at age 9-10 was associated with a greater likelihood of receiving a second dose (OR: 6.1, P < 0.0001). The effect was substantially smaller in the Cox model (HR: 1.2, P = 0.025). CONCLUSIONS: Standard methods for examining dose timing do not account for follow-up time, resulting in underestimation of dose timing and overestimation of the effect of vaccine type and age on receipt of a second dose. Substantial selection bias could affect individuals who initiated with HPV9 due to the limited duration of follow-up time. This research highlights the importance of using methods that account for variable follow-up time.

PRM77: ANALYSIS OF USING IRP AS A LAUNCH PRICE SETTING MECHANISM

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OBJECTIVES: International Reference Pricing (IRP) is a common mechanism used by payers worldwide to set and manage medicine prices. The study objective is to determine whether countries apply formal IRP rules, investigate any differences across regions and verify if the medicine price has any correlation to the application of an IRP rule. METHODS: Leveraging real world data from GPI pulse®, we selected Eribulin, Dapagliflozin and Dornase alfa which represent low to high price bands across France, Germany, Netherlands, Switzerland, Jordan, Lebanon, Canada, Brazil and Japan. Launch prices were analysed against projected prices simulated by the application of formal IRP rule. Post AMNOG prices in Germany and historical exchange rate fluctuations were taken into consideration. The analysis investigated two key areas: 1. % differential between the simulated price at launch using IRP and the real price at launch 2. Correlation between the application of IRP rules against the country, region, and medicine price. RESULTS: The analysis shows that Middle Eastern countries are less likely to exercise IRP rules when launching a medicine while Brazil, Canada and Japan are likely to apply IRP depending on the price of the medicine. European countries tested in the study are most likely to apply IRP rules consistently with no dependency on the medicine price. It is worthwhile noting that for value driven countries such as France and Germany, the application of IRP was directly linked to HTA assessment outcome. CONCLUSIONS: Although countries may define IRP rules as formal, there is significant variability in the application of the rule leading to inconsistency across countries. Factors correlating to the application of a rule include to the region, price of medicine and value assessment. A careful review of country nuances is important and should be taken into consideration when considering the commercial impact during launch and revenue forecasting.

PRM78: COMPARISON OF VARIOUS META-ANALYSIS TECHNIQUES

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OBJECTIVES: Meta-analysis is a statistical approach to systematically integrate and interpret several analyses from similar studies to draw a single conclusion. The objective of this study was to review meta-analysis methods and their assumptions, apply various meta-techniques to empirical data, and compare the results from each method. METHODS: Proper meta-analysis includes 5 basic steps: identify relevant studies, extract summary data from each paper, compute study effect sizes, perform statistical analysis, and interpret/report the results. A retrospective analysis on the efficacy of the Bacille Calmette-Guerin vaccine for tuberculosis (TB) was performed.
using data from 13 trials and 3 different meta-analysis techniques. First, a fixed-effects model was applied, followed by a random-effects model; lastly, results of meta-regression with study-level covariates were added. In each trial, a vaccinated group was compared to a non-vaccinated control group. Odds ratio was calculated based on the number of subjects contracting TB in the treated and control populations. Overall and stratified results by geographic latitude were reported. RESULTS: All techniques showed statistically-significant protective effects from the vaccination. However, once covariates were added, efficacy diminished. Independent variables, such as the latitude of the location in which the study was performed, appeared to be partially driving the results. CONCLUSIONS: Meta-analysis is useful in combining results from various studies and drawing general conclusions. However, with numerous assumptions, methods, and reported statistics available, understanding and identifying the appropriate study and model selection are important in ensuring the correct interpretation of results.

PRM79: GUIDANCE FOR DEVELOPING A STUDY PROTOCOL OF A CAUSAL COMPARATIVE EFFECTIVENESS ANALYSIS IN “BIG DATA”: THE CASE OF WHEN TO START STATIN TREATMENT

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OBJECTIVES: Within DEXHELPP, a large project on decision support tools for health-policy planning, causal relations are estimated from routine data as source to gain information outside the artificial setting of clinical trials. Common challenges occurring with real world evidence are confounding, missing/misclassified data, no clear treatment assignment, dynamic treatment regimes, and switching. The aim of this project is to describe a causal (counterfactual) approach for analyzing such datasets gaining insight when to start statin treatment to prevent cardiovascular disease (CVD). METHODS: We determined three comparative strategies, starting statin treatment when the ESC-SCORE exceeds 1%, 5%, and 10%. We assess potential time-independent and time-dependent confounding and selection bias using directed acyclic graphs (DAGs). We generate a study protocol following the “target trial” approach, describe data structure needed for the causal assessment, and provide solutions where necessity and availability of data deviate. RESULTS: Individuals between 40 and 75 years of age and no history of diagnosis of stroke or myocardial infarction (MI) within the last month enter the study at the time they first exceed the risk-threshold of 1% and are followed up for 5 years. Replicates of all patients are assigned to each treatment arm. A per protocol analysis is applied. Individuals who do not follow the assigned treatment protocol are censored at the time of protocol violation. As censoring is informative and time dependent confounding is present, inverse probability of censoring weighting is performed. The Austrian GAP-DRG database contains ICD9/ICD10 codes from 2006-2013. As the ESC-SCORE requires continuously measured values which do not exist for all variables, rules are designed to estimate the risk score. CONCLUSIONS: DAGs and a protocol following the “target trial” approach are important tools to guide the database structure, data assessment, and the choice of the analytic strategy in deriving causal effects from big data.

PRM80: REAL WORLD EVIDENCE IN GLAUCOMATOUS DISEASES: EMR DATA IS INDISPENSIBLE FOR UNDERSTANDING PATIENT JOURNEYS AND OPTIMIZING CARE

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OBJECTIVES: Very little is known about patient characteristics, treatment patterns and outcomes of contemporary patients with glaucomatous disease in the UK. We invited ophthalmology centers who are users of a uniformly structured electronic medical record (EMR) system (Medisoft, Leeds UK) to establish a real-world evidence platform in glaucoma. METHODS: EMR data, including visual field (VF) examination results, were collected from patient eyes with glaucomatous diseases at 6 centers in the UK. Patient eyes were included if a diagnosis code of primary open angle glaucoma (POAG), ocular hypertension (OHT) only and suspected glaucoma (SG) only was recorded in glaucomatous diseases at 6 centers in the UK. Summary statistics on intracocular pressure (IOP) at index date (≥6 months). RESULTS: Six clinics contributed 63,376 unique patients and 119,294 eyes (52% females in both), among which a POAG, OHT or SG diagnosis was recorded 31,890, 32,507 and 30,398 times, respectively. Overall, 21,601 eyes were included in the POAG cohort with 17,964
and 14,860 in the SG only and OHT only cohorts, respectively. At index the mean IOPs (Goldmann applanation tonometry) were 18 mmHg (SD 6), 22 mmHg (SD 5) and 18 mmHg (SD 4) for POAG, OHT and SG patients respectively. Mean IOP values for eyes with incident diagnoses were 20.1 (SD 6.7) for POAG, 23.5 (SD 4.3) for OHT, and 17.8 (SD 4.3) for SG, and 17.3 (SD 5.3), 20.8 (SD 5.1) and 17.2 (SD 4.1) for non-incident patients, respectively. CONCLUSIONS: Structured EMR systems can greatly facilitate real-world ophthalmology studies on a much larger scale than single center studies. We expect further unique evidence on clinical practice and treatment patterns from the platform.

PRM81: OVERCOMING THE LIMITATIONS OF CLAIMS DATA: LINKAGE OF CLAIMS DATA WITH SECONDARY DATA SOURCES IN GERMANY

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OBJECTIVES: Claims data analyses offers several strengths like high actuality of the data and health resource utilization under real-life conditions independent from a predefined study purpose. Furthermore claims data provide the full picture of reimbursed healthcare costs from a Statutory Health Insurance perspective, at least in the German setting. Nevertheless, researchers have to face certain limitations, e.g. lag of clinical data or patient reported outcomes. To overcome these limitations, claims data can be linked to other primary or secondary data sources. Aim of this study was to give an overview of opportunities and challenges of linking claims data with other data sources in Germany. METHODS: All publications available in PubMed until June 2017 using data linkage between German claims data and further primary or secondary data sources were included in this study by searching for "link*" in combination with "sickness fund", "health insurance", "claims", and "German". Study focus, study periods of the applied data, claims and further data sources, as well as the reasons for linking data sources were analyzed by two independent researchers. RESULTS: The search resulted in n=92 studies, of which n=23 were included in the analysis after abstract screening. An increasing application of data linkage with claims data can be observed over recent years. Most studies focused on disease specific research questions. Primary data collection via questionnaires (n=8) was used predominantly as linked data source. Data linkage was motivated by being able to link missing/unavailable information to the claims database (n=12). CONCLUSIONS: Data linkage constitutes a promising opportunity to overcome limitations of claims data research although the application of data linkage in German healthcare studies is a rarely utilized approach by now. Most of the studies used primary data to close information gaps of claims data, however several challenges have to be addressed to leverage this opportunity.

PRM82: ETHICAL CONSIDERATIONS: CONDUCTING RETROSPECTIVE NON-INTERVENTIONAL MEDICAL RECORD REVIEW STUDIES IN EUROPE

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OBJECTIVES: Ethics requirements in retrospective non-interventional medical record reviews (NIMRR) are highly variable by country. National requirements range from none to multiple submissions requiring approvals. At the site-level, requirements range from non-existent to mandatory approvals and contracts. Differences in country-specific ethics processes can delay data collection and thus provision of timely research. In this study, we sought to quantify variability in ethics-related aspects of NIMRRs. METHODS: Based on internal project data, we evaluated variability in ethical and regulatory procedures for 13 (12 oncology, 1 psychiatry) NIMRRs completed across 15 countries in Europe. RESULTS: Sixty-one national notifications/submissions were reviewed and approved across 8 countries; 21 single-site submissions were approved across 3 countries; and 56 notifications/submissions to all participating sites were approved in 6 countries, resulting in >7,300 medical records abstracted. Five countries did not have established ethics requirements for conducting anonymized retrospective reviews. Among those that did, the timeline from ethics initiation to launch of data abstraction for national-level activities ranged from 1 day (United Kingdom) to 15 months (France). For site-level submissions, the timeline from ethics initiation to launch of data abstraction ranged from 2 months (Spain/Germany) to 12 months (Portugal/Italy). CONCLUSIONS: Retrospective NIMRR studies are an effective way to gather clinical characteristics, treatment patterns, outcomes, and health care resource utilization data in real-world settings where existing data sets are unavailable, inadequate, or inaccessible. Evaluating country-specific ethics requirements and their associated timelines is a critical early step in country selection, study design, and project planning. Review timelines were generally consistent by country. National and site-based submission timelines varied substantially. More consistent regulations between countries, or a centralized approval process in Europe, would allow research to progress in a more efficient and predictable manner. Timely analysis of real-world clinical data leads to a better understanding of current practices, needs, and gaps, which ultimately benefits patients.

RESEARCH ON METHODS - Modeling Methods
**PRM83: A SYSTEMATIC REVIEW OF CALIBRATION IN POPULATION MODELS**

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**OBJECTIVES:** Population-level health policy models are often complex, especially when a dynamic cohort is simulated. Parameter calibration may be needed if parameters are unknown or unmeasurable, or to handle parameter uncertainty. This study provides an overview of parameter calibration methods used by models of this type and of the reporting on calibration. **METHODS:** A systematic review was performed. The search strategy combined a keyword search for population models in MEDLINE with a hand search starting from review publications. Data were extracted by two authors in standardized tables. The extracted characteristics were model type and analysis technique, calibrated parameters, target data, calibration strategy, search algorithm, goodness-of-fit measure, stopping rule and acceptance criterion, in line with recommendations in published studies. Formal methods used in the calibration of any model were summarized. **RESULTS:** We included 37 models in the review. For 25 of those, model parameters were calibrated or adjusted. 13 of those models used informal methods for adjustment without specifying an optimization algorithm, goodness-of-fit measure, or acceptance criterion. The remaining 12 models reported comprehensively or on some aspects of the calibration method. Three studies describe Bayesian updating as their calibration strategy. One model used a similar likelihood based procedure to rank and select parameters sets. One model used the score function method in connection with a formal optimization procedure for calibration. Three models specified search algorithms. These were hierarchical random grid search, simulated annealing and quasi-Newton optimization. Five studies specified a goodness-of-fit measure and an acceptance criterion. **CONCLUSIONS:** Half of the models proceed in an informal way to calibrate model parameters or do not report on calibration methods. Models detailing a more formal approach chose each their own distinct method. Comparability and transparency of published population models can be improved by a standardized reporting according to the items in our extraction table.

**PRM84: HOW CAN MIDDLE-INCOME COUNTRIES GET A VALID ESTIMATE OF COST-EFFECTIVENESS OF A DRUG MORE EFFICIENTLY AND EFFECTIVELY?**

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**OBJECTIVES:** The results of cost-effectiveness analyses (CEAs) are often generalised between countries. However, the accuracy of their results is remaining uncertain when these countries have important differences in their economies. The aim of this study is to investigate compatibility between the results of a previously published CEA in Iran and a middle-income country (MIC) with the results of transferred studies from high-income countries (HICs). **METHODS:** We systematically searched and selected model-based CEAs in HICs which were designed in the same method with an original country-specific CEA in Iran. The transferability of these studies to Iran was assessed using van Haalen method. Two methods were used to estimate incremental costs. In the first method, costs were corrected using consumer price indices and transferred to the Iran setting using purchasing power parities (PPP). The second method involved estimating initial trastuzumab costs and combining it with the incremental downstream costs. For both methods, incremental effects were adjusted estimating Quality-adjusted life-years (QALYs) based on differences in life expectancy from age at treatment onset. Cost-effectiveness results were compared with the results of an Iran-based CEA. **RESULTS:** Five of the nine CEAs identified passed van Haalen method. The transferred incremental cost-effectiveness ratios (ICERs) of the first method (€43,390/QALY(USA); €11,077/QALY(UK); €7,526/QALY(USA); €6,261/QALY(Portugal); €4,013/QALY(Belgium)) did not match the ICER of the Iranian CEA (€16,773/QALY). However, we could estimate a closer ICER (€16,473/QALY vs €16,773/QALY) with the second method. **CONCLUSIONS:** This study introduces a method to facilitate transferring the results of CEAs from HICs to MICs which is more efficient than the current methods. When there is a major economic gap between
countries, costs of expensive drugs should not be transferred using relative PPPs. The second method may be a solution to estimate a rough ICER in MICs while a country-specific CEA is recommended for a reimbursement decision-making.

**PRM85: FINDING UNDIAGNOSED PATIENTS WITH HEPATITIS C VIRUS: AN APPLICATION OF STATE-OF-THE-ART MACHINE LEARNING METHODS**

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**OBJECTIVES:** The hepatitis C virus (HCV) is a chronic, life-threatening disease which is substantially under-diagnosed. Accelerating time to diagnosis can lead to earlier treatment and improved patient outcomes. This was a retrospective database study to develop an algorithm which could be used to identify undiagnosed patients with HCV based on routinely collected patient data. The effectiveness of non-parametric machine learning methods was also compared with more conventional parametric methods. **METHODS:** Data were extracted from US prescription and open-source medical claims between 2010 and 2016. Outcomes for HCV patients were coded as 1; outcomes for non-HCV patients were set to 0. Index date for HCV patients was the first observed date of diagnosis, ensuring only pre-diagnosed predictors were used. The most recent activity was used as the index date for non-HCV patients. Features captured information on demographics, treatments, procedures and symptomatology, including temporal associations between the timing of events and the index date. Binary classifiers were estimated based on conventional parametric methods – unconstrained logistic regression and logistic regression with penalty – and non-parametric machine learning methods - random forest, gradient boosting and an ensemble of classifiers based on logistic regression. Five-fold cross-validation was used to identify optimal hyperparameters which included a differential misclassification penalty. Predicted Positive Value (PPV) at 50% sensitivity was used to evaluate model performance based on hold-out data. **RESULTS:** The sample comprised 120,000 HCV and 60,000,000 non-HCV patients. PPV (based on a HCV to non-HCV ratio of 1:34) was 72.3%, 70.8%, 65.0%, 52.1% and 51.7% for the ensemble, gradient boosting, random forest, logistic regression with penalty and unconstrained logistic regression, respectively. **CONCLUSIONS:** The evidence suggests that algorithms leveraging routinely collected real-world data could be an effective way to screen for undiagnosed HCV patients. State-of-the-art machine learning approaches also substantially out-performed conventional approaches, highlighting the potential value of these methods.

**PRM86: THE IMPACT OF HUMAN PAPILLOMAVIRUS VACCINE IN TAIWAN: A TRANSMISSION DYNAMIC MODELLING APPROACH**

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**OBJECTIVES:** Human papillomavirus (HPV) is the general sexually transmitted disease. This study is to predict the infected cases after HPV vaccination policy implemented in Taiwan. **METHODS:** The 5 years epidemiologic consequences of HPV vaccination was estimated via a transmission dynamic approach based on a Susceptible-Infectious-Recovered (SIR) model. The required epidemiological parameters were obtained from the database in Taiwan’s Health and Welfare Data Science Center and available public sources. The moderate-term epidemiologic consequences of non-vaccinated and vaccinated were estimated and compared. The differential equations were solved with the fourth-order Runge-Kutta method that is implemented in R Statistical Software. **RESULTS:** Compare to those non-vaccinated, 9-valent vaccine will decrease incidence of HPV infections in different age groups (15-19, 20-29, 30-39, and 40-59 years old) among high sexual active female population. The trend is more obvious in the lower aged group. The cumulative reduction incidence over 5-year horizon is 54.5, 64.2, 60.7, and 56.6 per 100,000 female respectively. There will be more female in non-vaccinated group suffer cervical intraepithelial neoplasia 1 (CIN1) in different age groups among high sexual active female population than in vaccinated group. However, the incidence increases moderately along year. The incidence of CIN1 decreases in vaccinated group in each aged groups. However, for CIN2/3 the incidence increases in 30-60 years old high sexual active female population by year not matter HPV vaccine is given or not. The incidences at the 5th-year increase 2.2 times to 22.0 times from the 1st-year in all aged group. There is no different incidence between non-vaccinated and vaccinated for cervical cancer in each age group. **CONCLUSIONS:** The result from this model suggests that HPV vaccination can protect female avoid suffering HPV infection and CIN1 in Taiwan.

**PRM87: BAYESIAN METHODOLOGY CONSIDERING HISTORICAL DATA TO PREDICT OVERALL SURVIVAL FROM IMMATURE TRIAL DATA IN ONCOLOGY**

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OBJECTIVES: At time of health technology assessment, overall survival (OS) data can be immature. This results in higher uncertainty over long-term extrapolations, and consequently in decision-making. The aim was to assess whether Bayesian methods using historical data could be used to predict long-term survival from immature trial data. METHODS: First, two reports on different data cuts (30 and 50 months) of the VISTA trial were retrieved. In that trial, bortezomib (V) combined with melphalan and prednisone (MP) was compared to MP in patients with multiple myeloma (MM), first-line setting. Additionally, we retrieved another report where mature OS data for MP in first-line setting was reported (historical trial). Second, individual participant data was extracted from reported Kaplan-Meier curves. Third, we fitted parametric survival models in WinBUGS over the MP arm of the historical trial. The resulting shape coefficient was used as an informative prior for the shape coefficient of the combined parametric fit over OS data from the VISTA trial. Non-informative to very informative priors were assessed. The analysis was based on the 30-months follow-up data and best fit was assessed using the 50-months follow-up data. The best fit was based on minimizing the area under the curve (AUC) between the observed and fitted curves. RESULTS: Compared to extrapolations with non-informative priors, extrapolations with the informative priors resulted in 13% and 14% decrease in the AUC for the MP and the VMP arms, respectively. With the very informative priors, compared to extrapolations with non-informative priors, an 18% and 16% decrease in the AUC for the MP and the VMP arms was observed, respectively. CONCLUSIONS: The Bayesian approach with the use of historical trial data can be used to more accurately predict overall survival on immature survival data. In future, the findings need to be confirmed by other datasets.

PRM88: PROBABILISTIC SENSITIVITY ANALYSIS IN HEALTH ECONOMIC MODELS; HOW MANY SIMULATIONS SHOULD WE RUN?

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OBJECTIVES: Probabilistic sensitivity analysis (PSA) addresses parameter uncertainty inherent in a decision problem, and provides the most accurate incremental cost-effectiveness ratio (ICER) for non-linear models. Literature on the number of simulations required suggests a "sufficient number", or until "convergence" which is seldom defined. Some methods to assess convergence of the mean ICER (such as "jackknifing") exist, but are rarely used. In this study, we aim to define convergence and use empirical data to propose simulation numbers for different outcomes. METHODS: 250,000 individual simulations were drawn from a variety of cohort models (n=30) constructed in different disease areas. Random samples were drawn to simulate 1,000 PSAs using up to 25,000 simulations per PSA. We identified the numbers of simulations required for the mean values of the PSAs to be reasonably close to the ‘true’ results, defined as the mean results of the 250,000 individual simulations. Convergence to the edges of the distribution was also analysed. The results considered were the costs, quality-adjusted life years (QALYs), incremental net monetary benefit (INMB) and ICER. RESULTS: Costs, QALYs and INMB were within 1% of the mean by 1,000 simulations in over 98% of scenarios. For the ICER at 1,000 simulations the ICER was within ±£500 of the ICER in 94.7% of scenarios, which increased to 98.6% at 5,000 simulations, and to 99.3% at 10,000 simulations. The edges of the distributions took longer to stabilise in all cases, not stabilising within 1% until over 10,000 simulations for nearly 90% of scenarios. CONCLUSIONS: Health economic models have sufficient complexity that low numbers of samples cannot guarantee accurate results. We recommend 10,000 simulations be used for decision making, which gives suitably stable mean results without excessive computational burden, unless convergence before this point has been demonstrated either via repeated sampling, or jackknifing.

PRM89: APPROACHES TO MODELLING THE COST-EFFECTIVENESS OF INTERVENTIONS FOR HEART FAILURE: A SYSTEMATIC REVIEW

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OBJECTIVES: To review modelling methods used to assess the cost-effectiveness of interventions for heart failure (HF). METHODS: A systematic search of the literature up to September 2016 across Medline, Embase, Cochrane Library, EconLit and CINAHL databases. We included studies that reported a model-based evaluation, including both costs and health impacts, of a HF intervention. Studies reporting only cost-effectiveness analyses alongside a clinical trial were excluded. RESULTS: We identified 54 publications describing 52 economic models associated with HF interventions. The model-based evaluations comprised surgical (n=20), medical (n=16), service-level (e.g. telehealth, specialist clinics) (n=9) or screening/monitoring-type interventions (n=4), or assessed disease management (n=2). One study compared multiple interventions. The most common modelling framework was a Markov cohort method (n=41); with models predominantly modelling disease progression via New York Heart Association grade or using a simple two-state (alive/dead) model. Several studies additionally included transition states for hospitalisation events. Two studies adapted the Markov cohort approach for sub-group analyses using risk equations. Eight studies reported a patient-level discrete event simulation approach, and four studies were decision trees. Key structural inputs to
OBJECTIVES: Organizations that submit systematic reviews (SR) and network meta analyses (NMA) to regulatory agencies, health technology assessment bodies, and guideline groups often employ manual methods and technologies that obscure decisions made and limit replicability. This research assessed the transparency of manual methods with comparison to software assisted replication and representation of SRs. METHODS: We considered four SRs, three non-governmental and one governmental agencies in the US and Europe, for multiple myeloma (MM), plaque psoriasis (PPs), Type 2 diabetes mellitus (T2DM) and multiple sclerosis (MS). Text descriptions of inclusion criteria (patients, interventions, comparators, outcomes) and meta-analysis methods were used to recreate each SR with software-assisted extraction and analysis tools to record and store decisions made at each step of the analyses. We then compared our results to that of each SR. RESULTS: Seventy-seven studies were included in the original SR: MM=9, MS=33, PPs=28, T2DM=7. The replication SR analysis identified 80 studies: MM=11, MS=34, PPs=28, T2DM=7. Efficacy rankings, point estimates and number of studies differed between the published and recreated SRs. For example, in the PPs NMA, the PASI 75 ranking for infliximab was #3 in the original analysis and #1 in the replication. Other factors that hindered replication included lack of reported search strategy, incorrect inclusion or exclusion of studies (MM and MS), insufficient details on analytical methods (MM), data extraction errors (PPs), and unclear grouping of outcomes (T2DM). CONCLUSIONS: Traditional manual methods of performing SRs make it difficult to replicate SRs and analyses due to lack of transparency and traceability of methods; these can impact conclusions drawn. Use of digital platforms with artificial intelligence technology overseen by expert methodologists may improve quality and improve replicability. The use of such technological advancements may also facilitate dialogue with payers and reimbursement agencies by allowing more transparency in submissions.

OBJECTIVES: A recently conducted systematic review including 76 type-2-diabetes (T2D) cost-effectiveness studies utilizing 10 different simulation models, reported a consistent relationship between initial HbA1c intervention effect-size (HbA1c-IES) and simulated, undiscounted health-benefits (0.642 and 0.371 increase in life-expectancy (LE) and quality-adjusted-life-expectancy (QALE) per 1%-point HbA1c decrease, respectively). Beyond HbA1c-IES, other aspects of the model configuration such as employed cardiovascular-risk-equations (CV-RE), consideration of a long-term HbA1c-treatment-effect-decay (HbA1c-TED) and study population represent important determinants of this relationship. The objective of our study was to illustrate the HbA1c/outcome relationship across a series of possible model configurations. METHODS: The QuintilesIMS-CORE-diabetes-model (CDM, version 9.0) was used to project undiscounted lifetime gain in LE and QALE per 1%-point HbA1c reduction considering the following configurations: Patient characteristics, obtained from NHANES patient-level-data, were stratified across three age groups (Young (<45yrs), intermediate (46-64yrs), old (>65yrs)); three alternative sets of CV-RE were applied (UKPDS-Outcomes-Model-1 (OM1), UKPDS-Outcomes-Model-2 (OM2), Swedish-National-Diabetes-Registry (SNDR)); HbA1c time trajectories were assessed via a random-effects-panel-equation from UKPDS (considering HbA1c-TED over 5-10 years) or a steady increase of 0.15%-points per year (considering no HbA1c-TED). RESULTS: Across all configurations explored, the CDM predicted a mean increase in LE and QALE of 0.56 and 0.49, respectively. Benefits were higher when no HbA1c-TED was considered (mean increase in LE and QALE of 0.98 and 0.83 (no- HbA1c-TED) vs. 0.15 and 0.15 (included- HbA1c-TED)). LE and QALE benefits also declined with increasing age (0.88, 0.59 and 0.22 LE gain and 0.79, 0.5 and 0.19 QALE gain for young, intermediate and old patients, respectively). Differences for alternative CV-RE were projected at 0.64, 0.54 and 0.51 LE gain and 0.57, 0.46 and 0.45 QALE gain for OM1, OM2 and SNDR, respectively. CONCLUSIONS: Patient age, HbA1c-TED, and CV-RE represent important components (beyond HbA1c-IES) for an appropriate characterization of the HbA1c/outcome relationship in T2D-simulation-models.
PRM92: CLINICAL DRIVERS OF ECONOMIC MODELS AND UTILITY MAPPING ALGORITHMS IN SCHIZOPHRENIA

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OBJECTIVES: To assess the published literature on the clinical drivers and design of health economic models in schizophrenia, as well as utility mapping algorithms, in order to support the construction of health economic models. METHODS: As part of a systematic literature review, studies describing health economic models in schizophrenia were searched in MEDLINE. A targeted literature review was also conducted regarding utility mapping algorithms in schizophrenia. Both literature searches were conducted on December 1, 2015. RESULTS: Eighty-nine studies, from 483 screened abstracts, were included in the assessment of models. Models found were published from the early 1990s. Markov models were the most prevalent modelling method, followed by decision tree models, then simulation models, though models of the last category were more frequent in more recent studies. Of the assessed models, 37.8% used quality-adjusted life years (QALYs), and an additional 8.1% used disability-adjusted life years (DALYS) as benefit drivers. The rest of the models used various clinical endpoints as value drivers, for example relapses, annual number of stable days, or percentage of patients in remission. The targeted literature review identified four main approaches for utility mapping algorithms, mainly based on Positive and Negative Syndrome Scale (PANSS) scores: the Mohr-Lenert, Chouinard, Siani, and Briggs approaches and their subtypes. These methods showed various levels of detail, for example Mohr and Lenert categorizing categorized patients into three or eight different health states, while the Chouinard approach only used three health states. CONCLUSIONS: Health economic models developed for schizophrenia showed great variability, with simulation models becoming more frequently used in the last decade. While nearly half of models used QALYs or DALYs for value drivers, the others used a great variety of clinical outcomes. Several methods to convert PANSS scores to utility values were also identified and assessed.

PRM93: MODELLING CARDIOVASCULAR OUTCOMES IN TYPE 2 DIABETES IN THE ERA OF CARDIOVASCULAR OUTCOMES TRIALS

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OBJECTIVES: Modelling cardiovascular (CV) outcomes in type 2 diabetes mellitus (T2DM) typically employs the extrapolation of short-term changes in surrogate markers and estimation of their long-term impact via predictive risk equations. The evidence base from cardiovascular outcomes trials (CVOTs) in T2DM is growing rapidly, due to FDA requirements for new treatments to demonstrate CV safety versus placebo as part of standard care. This new generation of CVOTs may require a new approach for associated cost-effectiveness models in T2DM. METHODS: A targeted literature review was conducted to identify opportunities for future modelling of CVOT evidence from approaches taken in other therapy areas. Current NICE clinical and public health guidelines for CV conditions were reviewed to identify methods employed in de novo economic models to assess the impact of comparator interventions on CV outcomes. RESULTS: Across 22 guidelines for treatment of hypertension, lipid modification, myocardial infarction (MI), stroke and other CV conditions, a total of 21 cost-effectiveness models were identified that explicitly modelled at least one CV outcome: MI, stroke, angina, revascularisation, peripheral arterial disease (PAD), heart failure and/or CV mortality. The majority of evaluations utilised lifetime (n=19) cohort-level (n=20) Markov (n=16) modelling approaches; the only patient-level evaluation utilised time-to-event simulation. Intervention-specific relative risks derived from meta-analyses were commonly applied to baseline risks of CV events, obtained from clinical trials and observational studies, including audit data. Surrogate markers were rarely modelled and the use of published risk equations limited to the estimation of baseline CV risk: Framingham (n=4), QRisk2 (n=1) and UKPDS (n=1) in the only T2DM-specific evaluation. CONCLUSIONS: When modelling the outcomes of CVOTs in T2DM patients, alternative modelling methods may be more appropriate than typical T2DM approaches; a more suitable framework, consistent with the approach taken in CV modelling, may be to assess the comparative evidence via the application of relative risks.

PRM94: THE POTENTIAL VALUE OF REAL-WORLD EVIDENCE ALONG WITH TRIAL EFFICACY TO ESTIMATE EFFECTIVENESS OF NOVEL TREATMENTS IN REAL-WORLD SETTING; AN APPLICATION WITH OVERALL SURVIVAL IN TWO ONCOLOGY INDICATIONS

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OBJECTIVES: Payers might be more interested in real-world effectiveness rather than efficacy of novel treatments. We aimed to assess the use of real-world evidence along with efficacy data reported in a clinical trial setting (CTS) to estimate effectiveness in a real-world setting (RWS). METHODS: Two RCTs in non-small cell lung cancer (NSCLC) and renal cell carcinoma (RCC) were selected. First, patient-level data (PLD) was extracted from reported Kaplan-Meier curves for overall survival (OS). Cox proportional hazard model and parametric survival models were fitted on PLD. Second, based on reported treatments in respective control arms, similar patient populations were identified from a German sickness fund dataset. Parametric survival models were fitted over the retrieved PLD. This curve was considered to represent the effectiveness of control treatments in RWS. Third, estimated HRs were applied to RWS to estimate OS in active treatment arms. Finally, we estimated mean OS in both CTS and RWS. RESULTS: In NSCLC, estimated mean OS in the CTS was 40.7 months (95% confidence interval (CI): 25.0-61.1) and 24.8 (95% CI: 17.2-35.6) for the active and control arms, respectively. In the RWS, estimated mean OS was 15.4 (95% CI: 12.2-19.8) for the control arm, and based on a HR of 0.61 (95% CI: 0.42-0.90), the mean OS for the active treatment was 23.3 (95% CI: 16.8-32.2). In RCC, estimated mean OS in the CTS was 27.8 (95% CI: 17.5-44.8) and 23.8 (95% CI: 17.1-33.8) for the active and control arms, respectively. In the RWS, estimated mean OS was 31.4 (95% CI: 23.1-43.4) for the control arm and based on the HR of 0.72 (95% CI: 0.55-0.95), the mean OS was 41.8 (95% CI: 32.9-52.5) for the active arm. CONCLUSIONS: If treatment effect is expected to be comparable in both CTS and RWS, this methodology may be used to estimate the effectiveness of novel treatments.

PRM95: THE RELATIONSHIP OF PREDICTED BENEFITS IN LIFE EXPECTANCY AND QUALITY ADJUSTED LIFE EXPECTANCY FOR IMPROVED GLUCOSE CONTROL IN TYPE 2 DIABETES SIMULATION MODELING

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OBJECTIVES: Understanding the relationship between improved glucose control and modeled gains in life-expectancy (LE) and quality-adjusted-life-expectancy (QALE) in type-2-diabetes (T2D) populations is important for health policy decision making. A recently published systematic review assessed this relationship based on 76 modeled cost-effectiveness-studies in T2D. The review quantified the relationship between changes in glucose control and gains in LE and QALE, with limited commentary on why some modeling studies project relatively higher gains of LE vs. QALE. The objective of our study was to use a T2D simulation model for a series of heterogeneous T2D-populations to identify factors associated with reduced QALE vs. LE benefit. METHODS: We used version 9.0 of the QuintilesIMS-CORE-diabetes-model (QI-CDM) to project the lifetime benefits (gains in LE and QALE) of a 1%-point HbA1c reduction. Patient characteristics were obtained from NHANES patient-level-data and stratified to three age categories: Young (30-yrs), intermediate-aged (50-yrs), elderly (70-yrs). Each age category was further subdivided into five levels of increasing degree of baseline comorbidity from level-0 (no comorbidities) to level-4 (high comorbidity level). Outcomes were discounted at 3%. RESULTS: For patients with no baseline comorbidities, the respective gains in LE and QALE associated with a 1%-point A1c lowering were 0.48 and 0.58, 0.68 and 0.64 and 0.35 and 0.34 for young, intermediate-aged and elderly, respectively. The corresponding ratio of QALE vs. LE gain (QALE/LE-ratio) was 120%, 93.2% and 95.5%. For increasing comorbidity levels, the QALE/LE-ratio declined to levels of 120.8%, 111%, 110% and 74% (young), 88.7%, 81.5%, 71.9% and 60.3% (intermediate aged) and 84.9%, 78.5%, 69.7% and 60.0% (elderly) for comorbidity levels 1 to 4, respectively. CONCLUSIONS: Assessing the functional relationship between improved glucose control and gains in LE and QALE cannot be considered in isolation from the cohort’s baseline characteristics.

PRM96: SURVIVAL OUTCOMES PREDICTED BY A DISCRETE EVENT SIMULATION MODEL FOR RENAL CELL CARCINOMA FOR USE IN A COST EFFECTIVENESS ANALYSIS: A COMPARISON WITH A TRADITIONAL PARTITIONED SURVIVAL MODEL

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OBJECTIVES: To assess long-term survival outcomes predicted by a discrete event simulation model (DES) for nivolumab in renal cell carcinoma (RCC) and to compare the results with a more traditional partitioned survival model (PSM) approach. METHODS: Two model structures were developed in Microsoft Excel and populated using data from an analysis of 24-month patient-level data from the CheckMate 025 trial. Both models comprised three key health states: progression-free (PF), progressed disease, and death. The DES models patients individually, and their journey through time is characterized as a series of events. Patient history and patient heterogeneity are incorporated by deriving a set of predictive equations to estimate the time to an event (progression, death) based on patient characteristics at baseline and progression. The PSM uses a cohort-based approach to estimate state occupancy based on an ‘area under the curve’ approach using overall survival (OS) and PF survival curves derived from the
OBJECTIVES: Previous economic evaluation of ocriplasmin for treatment of VMT used a de novo model consisting of a decision tree and nested Markov components, simulating the MIVI-TRUST trial and extrapolating long-term disease progression. Dependent on patient characteristics and disease history, patients could transition between six different vision health states (HS). Patient-level data requirements for estimating a 6x6 transition matrix poses a challenge with smaller sample sizes of new trial evidence. Learnings from survival partition models were adopted to investigate a more flexible approach to estimate patient distribution in vision HS (partitioned distribution model). METHODS: Eight vision HS and eight disease HS were used. Patient vision, for each disease HS, at each time point, is described using mean and standard deviation (SD) following (scaled) beta distribution to capture lower and upper bounds of the 0-100 Early Treatment Diabetic Retinopathy Study (ETDRS) vision scale. Mean and SD were estimated from OASIS data. Beta distribution was partitioned according to vision HS cut-offs determining the vision HS proportion of patients for each disease HS. RESULTS: Preliminary results (ETDRS letters read) indicate mean (SD) baseline best-corrected visual acuity (BCVA) for HS1 (VMT with FTMH) and HS2 (VMT without FTMH) are 57.82 (9.81) and 66.00 (8.29), respectively. For 24-month disease HS distributions using linear regression models and OASIS observed data, mean BCVA (SD) were: HS3 (unresolved FTMH) 57.69 (9.60), HS4 (surgically resolved FTMH) 68.65 (11.26), HS5 (Non-surgically resolved FTMH) 70.00 (8.23), HS6 (unresolved VMT) 67.96 (10.39), HS7 (surgically resolved VMT) 68.95 (13.24), and HS8 (non-surgically resolved VMT) 75.82 (9.00). CONCLUSIONS: Compared to previous modelling techniques, this approach offers a simpler, more clinically intuitive methodology to simulate patient vision. Patient vision over time requires only three parameters (mean, SD and change in mean over time) as opposed to a large and granular transition probability matrix.
absence of sequencing trials, modellers often applied simplifying assumptions to treatment effects obtained from trials of single treatments. These assumptions were frequently not validated, nor their impact assessed: an important limitation of these models. CONCLUSIONS: Modelling treatment sequences may require a complex model, which can be time consuming to develop and implement. Using simplistic assumptions, regarding sequencing effects, results in significant uncertainty around the effectiveness and cost-effectiveness estimates, the extent of which is generally unknown. This needs to be recognised in decision making, and further evaluated.

PRM99: IMPLEMENTATION OF A DATA MINING MODEL WITHIN A MONITORING WEB-BASED TOOL TO ASSESS HER2 BREAST CANCER STATUS USING THE HER-FRANCE REAL WORLD DATABASE

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OBJECTIVES: HER-France is a French national database focused on HER2 status in breast cancer and provided by 125 pathology laboratories (PL) since 2011. PL used to compare their HER2 positivity (HER2+) rate with the calculated national average. To provide a more sensitive monitoring tool evaluating their practices quality through indicators, a new strategy considering a predicted estimate of HER2+ rate by PL instead of national average was investigated. METHODS: Model to predict probability of HER2+ on core-needle biopsies (CNBs) was developed using penalized logistic regression on tumor characteristics. PL HER2+ rate estimations were obtained by averaging individual HER2+ probabilities. A PL having included more than 100 CNBs between January 2014 (ASCO-CAP recommendations) and April 2016 is considered as outlier when its averaging HER2+ predicted rate is outside a 99% confidence interval (CI) limits of its observed rate. Other indicators are absolute and relative percentage differences between observed and predicted HER2+ rates. RESULTS: Prediction accuracy (AUC) on 30,777 CNBs was higher than 0.77. Among the 56 PL with at least 100 CNBs (i.e. 95% of all the analysed CNBs), 6 (10.7%) were identified as outliers. Illustration with 4 PL: 2 not outliers: PL1 (n=676): observed rate: 13.6%; 99%CI: [10.2; 17.0]; predicted rate: 10.9%; absolute (relative) difference: 2.7 (20%) PL2 (n=2,062): observed rate: 9.1%; 99%CI: [7.4; 10.7]; predicted rate: 10.1%; absolute (relative) difference: 1.0 (11.8%) 2 outliers: PL3 (n=1,468): observed rate: 13.5%; 99%CI: [11.2; 15.8]; predicted rate: 10.9%; absolute (relative) difference: 2.6 (19%) PL4 (n=1,854): observed rate: 9.6%; 99%CI: [7.8; 11.4]; predicted rate: 12.0%; absolute (relative) difference: 2.4 (25%) CONCLUSIONS: PL tumor characteristics provide better accuracy in quality assessment practices than comparison to national average. Data mining models implemented in the HER-France monitoring web-based tool will help PL to assess their own rate through consistency indicators.

PRM100: A DISCRETE EVENT SIMULATION MODEL FOR RENAL CELL CARCINOMA FOR USE IN A COST-EFFECTIVENESS ANALYSIS


OBJECTIVES: To develop a flexible and comprehensive discrete event simulation model (DES) for nivolumab versus everolimus in the treatment of renal cell carcinoma (RCC) that captures differences in treatment outcomes and costs between patients with heterogeneous baseline characteristics. METHODS: A DES was developed in Microsoft Excel based on individuals experiencing three key events: disease progression, treatment discontinuation, and death. Risk prediction equations were derived from 24-month patient-level data from the CheckMate 025 trial, using a step-wise backward elimination process to identify relevant predictors of the risk of progression or death. Hypothetical patients were generated from a multivariate normal distribution based on the characteristics of patients enrolled in CheckMate 025. Times to event for individuals were estimated from the predictive equations for overall survival, progression-free survival and post-progression survival. The survival curves chosen were based on comparison of the Akaike information criterion. The model accounted for differences in survival between patients who continued on their allocated treatment beyond progression and those who did not. RESULTS: Four predictive equations were derived from the trial data. The following baseline characteristics were identified as significant predictors of survival: age, Karnofsky performance status, haemoglobin, time from diagnosis to randomisation and tumour size. Mean overall survival of 53.0 months and 34.8 months were estimated for nivolumab and everolimus, respectively, with mean post-progression survival of 43.0 and 26.3 months, respectively. CONCLUSIONS: The DES provides a flexible approach to capture patient heterogeneity and history when predicting long-term disease progression and survival outcomes for use in a cost-effectiveness analysis, and may be applied to other oncology settings. This becomes important in the context of immunotherapies with a novel mechanism of action and where extrapolation beyond trial duration requires consideration of such issues. Standard modelling approaches, such as the partitioned survival model, may not completely address these challenges.
**PRM101: EXPLORATION OF RUN-TIME REQUIREMENTS IN PROBABILISTIC SENSITIVITY ANALYSIS UTILIZING A PATIENT LEVEL BASED TYPE 2 DIABETES SIMULATION MODEL**


**OBJECTIVES:** Patient-level based simulation models utilize Monte-Carlo techniques to predict events which introduces random variability (Monte-Carlo-Error (MCE)). In probabilistic-sensitivity-analysis (PSA), MCE coincides with and cannot be distinguished from the outcome variability that is associated with parameter sampling if insufficient patient numbers (cohort-size) are simulated to reduce MCE appropriately. The objective of this study was to quantify the requirements to reduce MCE appropriately. The objective of this study was to quantify the minimum-cohort-size (MCS) requirements in PSA at which MCE is reduced to acceptable levels. **METHODS:** Version 9.0 of the QuintilesIMS-CORE-diabetes-model (CDM) was used to compare outcome-variability of PSA including 500 bootstrap repetitions and increasing number of patients ranging from 100 to 100000. The model was populated to evaluate the cost-effectiveness of two hypothetical interventions with differences in clinical effectiveness (1.0% HbA1c and a 2kg weight change in favor of the treatment- vs. control arm). Each PSA was performed in two ways where parameters were sampled around 5% and 20% of their mean values. MCS was assessed when the size of the ICER-per-QALE-95%-confidence-width (CW) stabilized, i.e., the trend of decreasing CW alongside increasing cohort-size (and declining MCE) stopped and the CW remained within a predefined tolerance interval (TI) (explored at 10%, 7.5%, 5% and 2.5%) surrounding expected-value (EV). EV was assumed at the ICER-CW from PSA including 100000 patients. **RESULTS:** When the TI was set to 10%, MCS was reached at 2500 and 1000 included patients for PSA with 5% and 20% input-parameter-variability, respectively. MRT increased to 5000 and 2500 for TI selected at 7.5% and 5% and finally to 25000 and 10000 included patients for a TI selected at 2.5%. **CONCLUSIONS:** MCS-requirements to reduce MCE are lower whenever input parameter variability is increased. Hypothesizing that a 5% TI surrounding expected ICER-CW represents acceptable standard, a minimum of 5000 and 2500 patients have to be applied in PSA simulations conducted with the CDM for input-parameter-variability of 5% and 20%, respectively.

**PRM102: THE EVALUATION OF ASSUMPTIONS IN COST-EFFECTIVENESS MODEL DEVELOPMENT – A CASE OF DABIĞATRAN**

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**OBJECTIVES:** Regularly several models are developed to estimate the cost-effectiveness of the same drug, but the models are based on different underlying assumptions. The aim of this study was to evaluate the influence of assumptions that derive the model structure and input data on the case of cost-effectiveness analysis of dabigatran compared to warfarin. **METHODS:** Different cost-effectiveness analyses based on three models were compared. One was previously developed (Janzic et al., Pharmacoeconomics, 2015, 33(4):395-408) in house and two (Freeman et al., Ann. Intern. Med., 2011, 154(1):1-11 and Sorensen et al., Thromb. Haemost., 2011, 105(5):908-19) were re-build as far as possible based on the published data. A step wise approach was used to test the assumptions, adjust the model structures and unify the input data. The models outputs (total cost and QALYs) were assessed in each step. **RESULTS:** Additional assumptions were necessary during rebuilding the two models based. Up to 6% difference in estimates of QALYs and up to 42% difference in estimated costs between published and our simulated results were observed. At the baseline the results among the three models varied significantly, the differences in QALY was almost 40%, while the differences in total costs were more than 10-fold. When unifying the input data, the highest impact had cost data, especially costs of events, and mortality tables. According to the assumptions underlying model structure, the most important were the number of health states and their definition, clinical events considered and treatment strategy after discontinuation. Other assumptions, such as age dependent adjustment for bleedings, had minor effect. **CONCLUSIONS:** The assumptions underlying model structure in addition to input data significantly affected the results. More emphasis should be focused on critical evaluation of the model assumptions.

**PRM103: REPRESENTING UNCERTAINTY IN ECONOMIC EVALUATIONS: GETTING MORE FROM PSA RESULTS**

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**OBJECTIVES:** Uncertainty surrounding the decision to adopt a new intervention is formally considered by health technology assessment bodies. Conventionally probabilistic sensitivity analysis (PSA) is conducted to assess parameter uncertainty, with results presented in the form of cost-effectiveness acceptability curves (CEAC). Nonetheless CEACs are subject to limitations, including: ambiguity in interpretation and being unhelpful in characterizing the key factors contributing to uncertainty. Robust decision making (RDM) explores how the uncertainty around parameter values would affect the decisions and helps determine what would need to be true to
discard one strategy in favour of another. We compare traditional methods in representing uncertainty with methods proposed by RDM using the decision to adopt a screening program for a cardiac disease as a case study application. METHODS: A Markov model was developed to evaluate the cost-effectiveness of a screening program for a cardiac disease as compared to no screening. Probability distributions were assigned to each parameter in the model, which were then sampled and recorded over 5,000 simulations to generate CEACs and scatterplots. Using PSA results we estimated the distribution of "regret" for each screening strategy versus no screening in terms of net monetary benefit across simulation runs. Decision-trees were then fit to the simulation data to identify the parameter values that need to hold for the screening strategy to be the optimal choice. RESULTS: The CEAC suggested that at a common willingness to pay threshold the probability of the screening program being cost-effective would be 50%. The mean % regret however was very low (0%-3%), highlighting that the likelihood of a much higher net benefit without screening would be low. Screening was found to perform particularly well in clusters where the cardiovascular event risks and the relative treatment effect were high. CONCLUSIONS: Use of RDM may improve understanding of the uncertainty surrounding decisions on health care interventions.

PRM105: A MARKOV MICROSIMULATION MODEL FOR THE ECONOMIC EVALUATION OF PARTIALLY IMPLANTABLE ACTIVE MIDDLE EAR IMPLANTS IN SENSORINEURAL HEARING LOSS

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OBJECTIVES: Partially implantable active middle ear implants (aMEIs) offer a solution to treat mild to severe sensorineural hearing loss when patients are unable to wear or benefit from conventional hearing aids. These patients are also unable to benefit from cochlear implants because their hearing loss is not severe enough. If left untreated, individuals report a reduced quality of life compared to normal hearing peers that may further decrease with increasing hearing loss. The implementation of this treatment strategy may have considerable consequences and involve significant uncertainties and trade-offs. Due to lack of long-term data, decision-analytic modeling can be used to inform decisions under conditions of uncertainty. METHODS: To represent uncertainty in patient-level outcomes a Markov model was analyzed as microsimulation. A third-party payer perspective of the Australian health-care setting was adopted and a discount rate of 5% was used for both costs and utilities. The model time frame was set to 10 years. The model cycle length was 6 months. This work contains previously unpublished analyses. RESULTS: Compared with no surgical intervention, aMEIs yielded an incremental cost-utility ratio (ICUR) of AUD 9,913.72/QALY. When changing the discount rate from 5% to 3%, the ICUR was AUD 9,396.51/QALY. To measure the impact of variations on the ICUR, the utility value of patients successfully aided with or without complications were varied by ± 0.03, which yielded an ICUR ranging from AUD 7,474.52/QALY to 14,591.44/QALY. When altering the time horizon from 5 years to lifetime, the ICUR was AUD 8,067.39/QALY and AUD 14,184.68/QALY, respectively. According to literature, the Australian willingness-to-pay (WTP) threshold is reported to be AUD 34,500. When comparing the ICUR against the WTP threshold, aMEI had a probability of 100% to be cost-effective. CONCLUSIONS: Based on these analyses, partially implantable aMEIs offer a cost-effective solution compared with no surgical intervention in the Australian health-care setting.

PRM106: REVIEW OF MODELS SUBMITTED TO NICE MEDICAL TECHNOLOGIES EVALUATION PROGRAMME TO INFORM A COST CONSEQUENCE TEMPLATE FOR USE IN MEDICAL TECHNOLOGIES GUIDANCE SUBMISSIONS

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OBJECTIVES: The Medical Technologies Advisory Committee (MTAC) makes recommendations to the National Institute for Health and Care Excellence (NICE) on medical devices after conducting an evaluation of clinical and cost-effectiveness evidence. Companies are required to submit relevant evidence including a cost model which demonstrates cost-saving compared with current care. This research reviews the cost models submitted for evaluation and was undertaken to inform the development of a model template [available for company submissions]. METHODS: Twenty-two models were analysed and categorised by type. Data were extracted by 1 reviewer, with a second reviewer checking a sample. Information was extracted for 17 categories. Information not available from the model was sourced from other documents considered by MTAC. Themes were then analysed based on type. RESULTS: Models were built using either Excel® (n=20, 91%) or TreeAge® (n=2, 9%). Ten models (46%) were developed by a health economics consultancy. The developer was the company (n=2, 9%) or unknown (n=10, 46%) for the remainder. Cost-minimisation analyses were most common, 95% (n=21), with 5% (n=1) being a cost-utility analysis. Twelve models were structured as a decision tree (48%), 9 (36%) were cost calculators and 4 (16%) were Markov models. Complexity of the model structure adopted varied substantially. Thirteen models had a time horizon of 1 year or greater (51%) of which 2 (9%) inappropriately omitted discounting. Data from the clinical evidence submission were commonly used to populate the model but adverse event data were often excluded. Most
models included sensitivity analysis (97%), commonly as univariate deterministic sensitivity analysis (n=18, 51%). Only 4 (18%) models included probabilistic sensitivity analysis. **CONCLUSIONS:** This review increased knowledge of the nature of models submitted for evaluation by MTAC. This information informed the development of a model template.

**PRM107: COMPARISON OF STANDARD PARAMETRIC SURVIVAL METHODS VERSUS MORE FLEXIBLE APPROACHES**

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**OBJECTIVES:** Several standard parametric methods for extrapolating overall survival (OS) exist. However, more flexible methods such as spline-based models and the Generalized Gamma or Generalized F models are less often applied, despite being recommended by the NICE Decision Support Unit (UK). The objective of this study is to compare standard with these more flexible models in simulated datasets. **METHODS:** Six datasets with active and comparator arms were simulated. The comparators arms were based on three published datasets in which the baseline hazard over time was (1) decreasing, (2) increasing, and (3) fluctuating, respectively. The corresponding active arms were simulated with (1) a constant hazard ratio (HR) and (2) improving HR over time. The following models were tested: standard parametric models (Weibull, Exponential, Lognormal, Loglogistic, Gamma and Gompertz), spline models with one knot (Weibull, Lognormal and Loglogistic), Generalized Gamma models, and Generalized F models. The tested models were fitted (1) with treatment as constant covariate, (2) with treatment as time varying covariate, and (3) as two individual curves over the separate arms. The models were compared based on visual fit of the Kaplan Meier curve, log cumulative hazard, Akaike's information criterion (AIC) and the Bayesian information criterion (BIC). **RESULTS:** For the decreasing hazards dataset, the Lognormal and spline models had the lowest AIC/BIC for constant and improving HRs, respectively. In case of increasing hazards, the Generalized Gamma and Gompertz had the lowest AIC/BIC for constant and improving HRs, respectively. Finally, for the fluctuating hazards dataset, the Generalized Gamma and spline models had the lowest AIC/BIC for constant and improving HRs, respectively. Visual fits confirmed these results. **CONCLUSIONS:** Flexible models had a better fit compared to standard parametric models in four out of six datasets. Thus, we recommend the use of these models as key alternative among standard options for extrapolating OS from clinical trials.

**PRM108: METHODOLOGICAL ANALYSES OF BUDGET IMPACT MODELS SUBMITTED TO THE HAUTE AUTORITÉ DE SANTÉ (HAS) (FRENCH NATIONAL AUTHORITY FOR HEALTH)**

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**OBJECTIVES:** French legal framework has imposed budget impact analyses under certain conditions since January 2016 and methodological guidelines have been available since November 2016. To assess the publicly available French health-economic opinions about those analyses, an exhaustive retrospective analysis was conducted on methodological objections delivered by the HAS. **METHODS:** Based on publicly available opinions published by the HAS/CEESP (Comité d’Évaluation Economique et Santé publique) an electronic database was built to extract and analyze all relevant health-economic information. Data were collected and sorted in the following items: structural choices, results, sensitivity analysis and methodological objections. Our analysis was performed from December 2014 – the publishing date of the first economic opinion – until June 16th, 2017. (34 health-economic opinions available) **RESULTS:** Currently, 34 health-economic opinions have been published, six of which include budget impact analyses. Evaluations took place between February 2014 and October 2015. Other evaluations took place but are not published yet. Among those analyses, the methods of four were not acceptable. Major limitations concern the choice of population, comparators, and absence of sensitivity analysis. Only two of the opinions included an overview of their limitations. **CONCLUSIONS:** The published French budget impact analyses were evaluated before the publication of the guideline, and many were of a low methodological quality (four out of six are methodologically unacceptable). The majority of analyses did not include adequate information concerning their limitations. According to these results, French health economic evaluation is focusing on cost-effectiveness analyses at the expense of the budget impact analyses. But with the evolution of the legal framework and the publication of the French guideline, improvements in the quality of budget impact analyses are expected.

**PRM109: IMPROVING DISEASE DETECTION THROUGH METHODS TO REDUCE PATIENT HETEROGENEITY**

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**OBJECTIVES:** Disease detection algorithms are used to find undiagnosed patients. These algorithms often employ
parametric classifiers such as logistic regression. Undiagnosed populations are usually highly heterogeneous, potentially undermining the accuracy of parametric classifiers. This retrospective database study assessed whether standard approaches for disease detection could be improved through methods designed to capture heterogeneity such as cluster analysis and gradient boosting. METHODS: Data were extracted from US prescription and medical claims (2010-2016). Separate analysis was carried out for hepatitis C and tardive dyskinesia (TD). Outcomes for patients with the disease were coded as 1 and otherwise set to 0. Diagnosis date was used as index date for patients with the disease, ensuring only pre-diagnosed predictors were used. The most recent activity was used as index date for non-disease patients. Covariates captured demographics, treatments, procedures and symptoms. The following methods were implemented: 1. Logistic regression; 2. Gradient boosting; 3. Cluster analysis followed by separate logistic regressions on each cluster; 4. Cluster analysis followed by separate gradient boosting classifiers on each cluster. Gradient boosting captures heterogeneity through empirically-determined non-linear and interaction terms. Cluster analysis reduces heterogeneity by grouping similar patients based on their distance in the feature space. Hierarchical and K-Means clustering were employed, with hold-out data used to select optimal parameters of the clustering. Predicted Positive Value (PPV) at 50% sensitivity was used to evaluate performance based on (different) hold-out data. RESULTS: There were 120,000 hepatitis C patients and 9,683 TD patients with ~120,000 patients without each disease. PPV was 65.2%, 72.3%, 69.6% and 72.6% respectively for methods 1-4 for hepatitis C. PPV was 18.1%, 32.3%, 25.9% and 34.0% respectively for methods 1-4 for TD. CONCLUSIONS: Accuracy of disease detection algorithms based on straightforward logistic regression can be improved substantially through pre-classification clustering and more notably, through gradient boosting.

PRM110: MODELLING PATIENT PATHWAYS OF LOW-DOSE COMPUTED TOMOGRAPHY SCREENING FOR LUNG CANCER IN HUNGARY

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OBJECTIVES: Scientific evidence confirms the efficacy of low-dose computed tomography in lung cancer screening. This study aimed at assessing the life-years gained and the disease-free life-years gained with different frequencies of low-dose computed tomography screening for lung cancer, compared to the current situation of no organized lung cancer screening in Hungary. METHODS: A health economic model consisting of a decision tree and Markov sub-models was built. Closed cohort of 10,000 smokers between the age of 50 and 74 was followed over life-time horizon. The model moves the population at risk through the screening process, follows undiagnosed and diagnosed patients, and handles individuals who underwent lung cancer operation separately. Patient pathways describing lung cancer screening and disease course were validated against empirical data. Assessment of robustness of results was performed by sensitivity analyses. RESULTS: The model resulted in an additional 0.0833 and 0.2407 estimated life-years gained per individual and an additional 0.1329 and 0.3334 estimated disease-free life-years gain per individual with biannual and annual screening frequencies, respectively. As a result of the validation process, the 5-year estimated survival rates from the model were comparable to data published in scientific literature. The input parameters were tested in sensitivity analyses that confirmed the robustness of the model outputs. CONCLUSIONS: Low-dose computed tomography lung cancer screening can provide additional health benefits in life-years and disease-free life-years gained compared to the current situation of no lung cancer screening in Hungary. In the future, the model can be populated with local cost and utility data; therefore, it is suitable for assessing the cost-effectiveness of introducing low-dose computed tomography lung cancer screening as a public health intervention and supporting formal decision-making.

PRM111: A SYSTEMATIC REVIEW OF PREDICTIVE MODELS IN ACUTE HEART FAILURE

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OBJECTIVES: Acute heart failure (AHF) is the most common cause of illness leading to hospitalisation and mortality. Since no proven AHF treatment is available to improve long-term outcome, it is becoming increasingly important to predict/stratify the risk of outcomes in AHF patients to optimise the treatment. The objective of this systematic review was to assess the published models predicting the in-hospital and post-discharge outcomes in adult AHF patients. METHODS: A systematic review was conducted through searching in Embase®, MEDLINE®, MEDLINE® In-Process, and Cochrane Library up to February 23, 2017. A double review process was followed to identify English language studies of prediction models tested with adult AHF patients, with both derivation and validation cohorts. Data were extracted on the population, setting, model characteristics, model discrimination and
calibration. **RESULTS:** Of 3,325 citations reviewed, 32 publications describing 23 unique models met the criteria. Included scoring/risk prediction models have been mainly derived and validated for post-discharge mortality (N=12), in-hospital mortality (N=6), re-hospitalizations (N=2), worsening heart failure (N=1), and composite of these outcomes (N=9). Data sets were derived from the public registries, clinical trials and retrospective databases. Predictive models included demographic, clinical, hemodynamic and laboratory variables. Commonly used variables across the scoring models were age (N=17), blood urea nitrogen (BUN) (N=15), systolic blood pressure (N=15), and BNP/NT-proBNP (N=8). Of 22 models reporting model performance, 18 have demonstrated the capacity to discriminate patients who reach major clinical endpoints, with C-statistics ≥0.7. **CONCLUSIONS:** In addition to the conventional predictors (demographics, medical history, signs and symptoms), the recent models suggest a strong ability of biomarkers/ renal function parameters (BUN, natriuretic peptides and creatinine) to predict in-hospital and post-discharge outcomes. Future studies are warranted to evaluate if therapeutic decision making and the outcome of patients with AHF can be improved with the help of these tools.

**PRM112:** EXPLORING STRUCTURAL UNCERTAINTY WITH AN OPEN-SOURCE COST-EFFECTIVENESS MODEL FOR RHEUMATOID ARTHRITIS

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**OBJECTIVES:** Cost-effectiveness analysis frequently leads to disputes in the scientific literature. The reason for these disputes often stem from disagreement or misunderstanding about the underlying model structure. At the same time, models quickly become outdated as the evidence base evolves. Our aim was to develop a transparent, flexible, and accessible cost-effectiveness model to help achieve consensus and ensure that estimates of cost-effectiveness reflect current evidence. **METHODS:** We developed an R package to run an individual patient simulation (IPS) model for evaluating the cost-effectiveness of treatments for rheumatoid arthritis. The model allows for multiple perspectives (i.e., health care sector, societal) and 280 possible model structures related to the initial treatment effect, the relationship between the initial treatment effect and treatment switching, the survival distribution used to model time to discontinuation, and the algorithm used to estimate utility. The IPS is primarily written in C++ so that probabilistic sensitivity analysis and analyses of structural uncertainty can be run in a reasonable amount of time. We also created a user-friendly R Shiny web application where users can modify parameter values or structural assumptions and run the model online. **RESULTS:** The R package, iviRA, is available on a public GitHub repository and the Shiny web application is freely available online at shinyapps.io. Documentation provides step-by-step instructions for conducting a cost-effectiveness analysis using the model with R. A description of the model is also available, which provides detailed information (i.e., mathematical formulas and algorithms) related to data sources, parameter estimation, and simulation techniques. **CONCLUSIONS:** Transparent, flexible, and maintainable models can be developed in open-source programming languages such as R and C++. The models can be made accessible to non-modellers with user-friendly web applications, which, when combined with flexible models, can help resolve disputes by improving understanding of the reasons behind varying cost-effectiveness estimates.

**PRM113:** UNCERTAINTY IN SELECTING SURVIVAL MODELS FOR COST EFFECTIVENESS ANALYSES

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**OBJECTIVES:** Survival models are often the back bone of cost-effectiveness models. Although goodness-of-fit data are increasingly used to select the most appropriate survival model, this selection is typically uncertain and a key driver of outcomes. Nevertheless, this structural uncertainty is not routinely included in cost-effectiveness models, which potentially biases the estimated cost-effectiveness. Therefore, we aimed to develop methods to incorporate uncertainty related to survival model selection in the probabilistic sensitivity analysis of cost-effectiveness models using model averaging. **METHODS:** A cost-effectiveness model with three survival models (progression-free survival (PFS), overall survival (OS), and time to treatment discontinuation (TTD)) was used. Seven different distributions were fitted to the PFS, OS, and TTD data. This resulted in (7x7x7=) 343 scenarios to use in model averaging. Three methods to obtain weights for model averaging were compared. Method 1 represents current practice (deterministic weight of 1 for the ‘best’ model), Method 2 uses Akaike weights, and in Method 3, bootstrap cross-validation is used to compute mean Akaike weights across bootstrap samples. Incremental net monetary benefit (iNMB), probability of cost-effectiveness and expected value of perfect information (EVPI) were calculated for each method using a willingness-to-pay threshold of €50,000 per quality-adjusted life year. **RESULTS:** The iNMB for Methods 1-3 were €11,191, €3,489 and €6,956 respectively. The probability of cost-effectiveness decreased by respectively 23% and 13% in Methods 2 and 3 compared to Method 1. The individual EVPI in Methods 2 and 3 were respectively 3 and 2 times higher than in Method 1. **CONCLUSIONS:** This paper provides methods to incorporate the uncertainty surrounding the selection of survival models for cost effectiveness analyses based on goodness-of-fit data. Our
results demonstrate that ignoring this structural uncertainty leads to biased iNMB estimates, and an understimation of the uncertainty surrounding cost-effectiveness results. This has important implications for decision making.

**PRM114: COMPARATIVE ANALYSIS OF HEALTH TECHNOLOGY ASSESSMENTS OF DRUGS FOR THE TREATMENT OF MULTIPLE MYELOMA**

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**OBJECTIVES:** The treatment landscape for multiple myeloma (MM) is constantly evolving. In the last number of years the National Centre for Pharmacoeconomics (NCPE) has received a number of submissions to assess the cost-effectiveness and potential budget impact of new drugs for the treatment of MM. This is of particular importance due to the high cost associated with emerging treatments. The objective of this study was to perform a critical analysis of company submissions to the NCPE for MM in order to identify their similarities and differences, and characterise the challenges associated with cost-effectiveness modelling in MM. **METHODS:** A qualitative analysis of company submissions submitted during the period 2013 to 2016 was conducted to determine the strengths and shortcomings associated with the methods and data inputs of each. Thematic analysis, incorporating an adapted version of the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement, was then employed to generate a framework upon which the submissions were critiqued. **RESULTS:** Analysis of three HTA submissions (pomalidomide, carfilzomib, daratumumab) yielded four major themes: report quality, systematic review methods, clinical data, and economic analysis. Coding/calculation errors (report quality) and failure to adequately report systematic review methods were common to all three submissions. Substantial limitations were identified within the clinical data and related to quality of studies, generalisability of studies to the Irish population, immature overall survival data, and indirect treatment comparisons. The main issues related to economic analysis included inappropriate choice of comparator, extrapolation methods, omission of appropriate parameters when characterising uncertainty, and exclusion of relevant costs and disutilities of adverse events. **CONCLUSIONS:** Despite the availability of NCPE submission guidelines universal to all HTA submissions, further guidance is required which is specific to MM submissions. This guidance should consider the paucity of clinical evidence accompanying recent regulatory approval.

**PRM115: ECONOMIC EVALUATION OF A BRIEF COUNSELLING FOR SMOKING CESSATION IN DENTISTRY – A CASE STUDY COMPARING TWO HEALTH ECONOMIC MODELS**


**OBJECTIVES:** This study aimed to compare the cost-effectiveness estimates of a brief counselling of smoking cessation in dentistry by using two different health economic models. **METHODS:** A brief, structured behavioural intervention in dental clinics in Sweden was compared with “usual care”. Participants were 205 Swedish smokers aged 20-75 years. Intervention effectiveness was estimated in a cluster randomised controlled trial. Number of quitters was estimated based on 7-day abstinence and on smoking reduction at follow-up. Health economic evaluation was performed using two models: 1) A population-based model employing potential impact fractions, and 2) a Markov model estimating the cost-effectiveness of the intervention for the actual participants. The evaluation was performed from health care and societal perspectives and health gains were expressed in quality adjusted life years (QALYs). **RESULTS:** The cost per quitter was 552 USD in the intervention and 522 USD in the “usual care” condition. The net saving estimated with the population-based model was 17.3 million USD for intervention and 49.9 million USD for “usual care”, with health gains of 1428 QALYs and 2369 QALYs, respectively, for the whole Swedish population during 10 years. The intervention was thus dominated by “usual care”. The reverse was true when using the Markov model, showing net societal savings of 71,000 USD for the intervention and 57,000 USD for “usual care”, with gains of 5.42 QALYs and 4.74 QALYs, respectively, for lifelong quitters. **CONCLUSIONS:** The comparison of intervention and “usual care” derived from small-scale studies may be highly sensitive to the choice of the model used to calculate cost-effectiveness.

**PRM116: COST-EFFECTIVENESS ANALYSIS OF INTERVENTIONS THAT HAVE NOT SHOWN CLINICAL EFFECTIVENESS**

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**OBJECTIVES:** A core element of considering cost-effectiveness is the clinical efficacy or effectiveness of an intervention relative to an appropriate comparator. In the absence of a statistically significant difference in clinical
effect, guidelines generally suggest the use of a cost-minimisation analysis. However, it is apparent that economic evaluations are carried out and published in cases where there is no statistically significant effect. This study investigated the context of a sample of such studies to identify circumstances in which they may be appropriate. **METHODS:** As part of a review of chronic disease self-management support interventions, systematic reviews of cost-effectiveness studies were carried out for a range of indications. We included studies that carried out cost-effectiveness analyses when no statistically significant effect had been demonstrated. A narrative review approach was adopted. **RESULTS:** We identified 16 published economic evaluations for inclusion. These studies were typically trial-based studies or simulation models with effectiveness data from a single small trial that was possibly under-powered to detect a treatment effect. The absence of a statistically significant effect was not always acknowledged as a limitation in the analyses or as an issue to be considered when interpreting the results. However, a cost-effectiveness analysis in the absence of a demonstrated treatment effect may help to identify potentially cost-effective treatments for which additional evidence on effect would support decision making. **CONCLUSIONS:** The point estimate of cost-effectiveness is strongly influenced by the mean estimate of clinical effect. Typical methods for conveying parameter uncertainty may not adequately highlight the fact that the intervention has not demonstrated an improvement in outcomes. Cost-effectiveness analyses carried out in the absence of a demonstrated clinical benefit should be treated purely as exploratory analyses, and only considered as a basis for seeking additional data.

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**PRM117: USING MATHEMATICAL OPTIMISATION IN MODEL-BASED COST-EFFECTIVENESS ANALYSES: A CASE STUDY OF A STRATIFIED BREAST SCREENING PROGRAMME**

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**OBJECTIVES:** Stratified national breast screening programmes (stratified-NBSPs) which offer women different screening regimens using the estimated risk of cancer have been proposed to improve cancer detection at a reasonable cost. Cost-effectiveness analysis (CEA) requires clear definition of a new intervention to compare with current practice. CEA of a possible stratified-NBSPs is problematic due to the substantial number of potential comparators. This study aimed to develop a method of to identify and evaluate the optimal stratified-NBSP. **METHODS:** A discrete event simulation (DES) using the healthcare perspective was structured to represent care pathways for alternative stratified-NBSP embedded within the optimisation algorithm. A three-stage analysis was used. Stage-one used the DES-outputs to calculate the individual expected healthcare costs and outcomes for screening in any given year. Stage-two solved the 'subproblem' of allocating the screening times for each woman using a bespoke algorithm. The optimal allocation should choose the strategy offering highest net health benefit (NHB) given a fixed number of screens set by the current cost of the NBSP. Stage-three selects the set of optimal individual screening times, maximising the NHB across the whole population within the budget constraints. **RESULTS:** Preliminary results show that for the screening programme budget fixed at the current funding level, the optimal allocation of screens was different from current practice. Women at very low risk of breast cancer should be offered just three screens over the programme but women at high risk should be offered up to 23 screens which is equivalent to annual screening. **CONCLUSIONS:** The suggested approach compares programmes using existing CEA criteria and informs the choice of optimal stratified-NBSP. This approach has advantages over current methods that consider a large number of scenario analyses within a CEA to represent the potential alternative screening programmes and can be adapted to other stratified screening programmes.

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**PRM118: MODEL TYPES SUBMITTED TO NICE: WHAT IS CONSIDERED APPROPRIATE BY EVIDENCE REVIEW GROUPS?**


**OBJECTIVES:** A review of Evidence Review Group (ERG) critiques of models in recent NICE submissions was conducted to determine any associations between model type and ERG criticisms. **METHODS:** Full NICE single technology appraisals published over the past 12 months were reviewed and data extracted on indication, model type, whether the ERG considered the model type appropriate and details of the ERG critique. When the model structure was considered appropriate for the decision problem, this was assumed to also apply to model type. **RESULTS:** The 52 submissions reviewed included 47 cohort state-transition models (Markov, partitioned survival, semi-Markov and decision tree/Markov models), 1 Markov model run at both a cohort and microsimulation level, 3 Monte Carlo individual patient simulations and 1 Discretely Integrated Condition Event (DICE) model. In 34 (65.4%) cases the ERG agreed the model type was appropriate, typically due to alignment with previous models in the same or similar indications. In 9 (17.3%) cases the ERG critique of the model type was unclear or not stated. In the remaining 9 (17.3%) submissions, the ERG was unsatisfied with the model type to some extent. In 2 cases a dynamic modelling approach was considered more appropriate than a Markov (in infectious diseases), and in 2 cases...
a cohort model was used where patient heterogeneity was believed to be important. A total of 5 models were criticised for inflexibility in capturing key evidence, or appeared overcomplicated and lacked transparency. Additionally, the DICE model was criticised for impractical implementation and lack of clear benefit over a discrete event simulation model. **CONCLUSIONS:** Cohort state-transition models are generally considered appropriate by ERGs, the justification often being that they have been previously used in the disease area. Other model types are more likely in disease areas with fewer submissions, and are generally considered appropriate if their implementation is transparent and user-friendly.

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**PRM119: ISSUES ENCOUNTERED WHEN MODELLING THE LONG TERM CLINICAL EFFECTIVENESS OF TREATMENTS FROM SHORT TERM TRIALS USING SECOND-LINE TREATMENTS FOR ADVANCED OR METASTATIC RENAL CELL CARCINOMA (AMRCC) AS AN EXAMPLE**


**OBJECTIVES:** Long term effectiveness data on progression-free survival (PFS) and overall survival (OS) are rarely available from efficacy trials. Methods to estimate the expected PFS and OS using a range of survival models were explored up to 30 years for patients receiving axitinib, cabozantinib, everolimus, nivolumab, and BSC for second-line amRCC. **METHODS:** Several parametric survival models, including cubic splines, were fitted to the everolimus and nivolumab groups of the CheckMate 025 trial to provide baseline curves for PFS and OS. Model fit was assessed using the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC), as well as clinical expert opinion to assess the plausibility of extrapolations. Hazard ratios (HRs), derived from a mixed treatment comparison (MTC), were applied to the everolimus curves to produce estimates for cabozantinib and BSC. A reliable HR could not be derived for axitinib due to a violation of proportional hazards (PH), as well as patient cross-over in the TARGET trial. Therefore, it was assumed that axitinib was equivalent to everolimus. **RESULTS:** For OS, there were slight differences in the AIC and BIC statistics across the treatment groups, but the best fitting model was considered to be the Weibull. For PFS, the best fitting model was the 2-knot spline, clearly indicated by the lowest AIC and BIC for both everolimus and nivolumab. The Weibull models produced a mean OS of 26.5, 38.1, 26.5, 30.3 and 15.0 months, for axitinib, cabozantinib, everolimus, nivolumab and BSC, respectively. The equivalent values for the 2-knot spline PFS models were 7.9, 15.9, 7.9, 10.8 and 2.8 months, respectively. **CONCLUSIONS:** The assumption of PH can be a limitation when comparing multiple treatments across different trials using an MTC. Practical solutions such as choosing the appropriate "baseline" trial and assuming clinical equivalence, where plausible, can help mitigate concerns in some cases.

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**PRM120: EVALUATING THE IMPORTANCE OF REALISTICALLY SIMULATING RISK FACTOR PROGRESSION OVER TIME: A HEALTH ECONOMIC MODELING ANALYSIS IN TYPE 1 DIABETES**

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**OBJECTIVES:** Glycated hemoglobin (HbA1c) is an important surrogate measure of glycemic control in patients with diabetes and is a key risk factor for many diabetes-related complications. As a result, HbA1c plays an important role in many long-term health economic models. The aim of the present analysis was to evaluate the importance of realistically simulating HbA1c progression over time in patients with type 1 diabetes in a health economic model. **METHODS:** The PRIME Diabetes Model, a long-term, externally audited and validated, patient-level simulation model of type 1 diabetes was used to model long-term clinical and cost outcomes. Scenarios were based on either a linear assumption for HbA1c progression, or a target-driven HbA1c model, capturing covariance, developed from patient-level data from the Diabetes Control and Complications Trial (DCCT). Parameters significantly covarying with baseline and subsequent HbA1c were incorporated into covariance matrices in the target-driven model. The model used age and recent severe hypoglycemic episodes to derive p

**RESULTS:** Simulating HbA1c progression based on patient-level data was shown to affect the projected cumulative incidence of diabetes-related complications, life expectancy, quality-adjusted life expectancy and the cost of complications versus the standard linear approach. Quality-adjusted life expectancy was 0.18 QALYs higher with simulated HbA1c progression. The reduction in diabetes-related complications projected with simulated HbA1c progression decreased overall direct costs per patient by GBP 3,062 over patient lifetimes. **CONCLUSIONS:** Long-term projections using the PRIME Diabetes Model indicate that realistically simulating the progression of important risk factors, such as HbA1c, over time can influence the outcomes of a health economic analysis compared with standard linear assumptions. Simulating risk factor progression, informed by analysis of patient-level data, may directly influence the outcomes of economic evaluations in diabetes and should be taken into consideration by modelers and decision-makers.

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**PRM121: HOW TO ADDRESS FRENCH HEALTH AUTHORITY (HAS/CEESP) SPECIFIC REQUIREMENTS IN MODELLING RELAPSING-REMITTING MULTIPLE SCLEROSIS IN HEALTH-ECONOMIC EVALUATION?**
MODELLING TREATMENT SEQUENCES

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OBJECTIVES: The objective of the study was to track and assess the impact of introducing treatment sequences in a cost-effectiveness model for Relapsing-Remitting Multiple Sclerosis (RRMS) in France considering real life treatment patterns. Two health economic assessments in multiple sclerosis were published by the HAS/CEESP since 2014. In both assessments two important methodological limitations were raised, focusing on the absence of treatment sequences as it didn’t reflect real care management of RRMS patients. The resulting uncertainty of such limitations led the authorities to reduce the Time Horizon of the analysis to 5-10 years rather than a lifetime horizon (30 years) as recommended. METHODS: Two models were developed in treatment naïve RRMS patients according to treatment sequences. For each model, two arms were considered as patients could receive a 1st disease modifying treatment (DMT) with ocrelizumab or interferon-beta-1a. The model with treatment sequences (M1) allows taking into account two treatment switches. After discontinuation of the 1st DMT, patients receive a 2nd DMT and then a 3rd DMT vs being off-treatment directly in former cost-effectiveness model (M2). Discontinuation of the 3rd DMT, achieving an EDSS score ≥7 or evolving towards SPMS state resulted in being off-treatment. RESULTS: Including treatment sequences allowed reducing the number of off-treatment patient-cycles in M1 versus M2. At 10 years, the number of patient off-treatment is: for ocrelizumab 5.5% in revised model versus 19.2% in classical model and for interferon-beta-1a 4.1% versus 23.8% respectively, either decrease patients off-treatment by 71% and 83%. At 30 years, patients off-treatment reduce by 27% and 17%. CONCLUSIONS: The CEESP pays particular attention to the uncertainty around cost-effectiveness assessment in regards of real life practice. The introduction of treatment sequences reduces dramatically the uncertainty associated with former models and brings a robust opportunity to increase the time horizon for future health economic assessment in MS.

PRM122: A COMPARISON OF MARKOV COHORT AND DISCRETE EVENT SIMULATION MODELS IN COST-EFFECTIVENESS ANALYSIS OF SORAFENIB AND EVEROLIMUS IN 3RD LINE METASTATIC RENAL-CELL CARCINOMA IN THE CZECH REPUBLIC

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OBJECTIVES: Markov cohort (MC) and discrete-event simulation (DES) models are inherently different. Therefore, they are rarely used in economic evaluation of the same disease. Sorafenib and everolimus are cornerstones of current metastatic renal-cell carcinoma (mRCC) treatment in 2nd line, however, there are limited effectiveness/efficacy and cost-effectiveness studies in 3rd line. The first objective was to compare MC and DES models in oncology, and the second to assess the cost-effectiveness of sorafenib versus everolimus in 3rd line mRCC. METHODS: We developed two mirror life-time cost-utility models using a) Markovian and b) DES approaches, which projected quality-adjusted life-years (QALYs) and costs from healthcare payers’ perspective. In MC, we used weekly life cycle length and three states, i.e. progression-free, progression, death. In DES, there were progression/death events instead of states. Transition probabilities, utilities and costs were derived from published literature/sources. Costs and outcomes were discounted by 3%. Probabilistic sensitivity analysis (PSA; 10,000 simulations) was performed with Czech willingness-to-pay threshold (WTP) equal to €45,000. RESULTS: Over a lifetime horizon, sorafenib is less costly but also slightly less effective than everolimus. In MC, sorafenib is less costly by €2,045 (€11,558 vs. €13,603) and slightly less effective by 0.0028 QALYs (0.7815 vs. 0.7843). In DES, sorafenib is less costly by €2,320 (€11,326 vs. €13,646) and slightly less effective by 0.0027 QALYs (0.7927 vs. 0.7954). The ICERs, expressed as savings per QALY lost, are equal to €792,646 (MC) and €874,585 (DES). The results of PSA showed that sorafenib is cost-effective with probability of 95% (MC) and 85% (DES) at the WTP. CONCLUSIONS: Despite their differences, MC and DES models yields almost identical results in simple oncologic model. The slight disparity might be due to computational differences, half-cycle correction or cycle length. Finally, sorafenib clearly proved that it is a cost-effective intervention in 3rd line therapy of mRCC.

PRM123: ASSESSING THE JOINT PROBABILITY OF COST-EFFECTIVENESS AND AFFORDABILITY IN DECISION MAKING

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OBJECTIVES: Decision makers are increasingly concerned about both cost-effectiveness (CE) and affordability, which has resulted in additional price negotiations being implemented by HTA bodies, such as NICE. Cost-effectiveness plane and cost-effectiveness acceptability curves have been widely used to summarize CE analysis results under uncertainty. However, these methods ignore the resources necessary to fund the intervention. Sendi and Briggs (2001) proposed to use cost-effectiveness affordability curves (CEAFCs) to capture the joint probability
that an intervention is both cost-effective and affordable. We aim to review the application of this method in the economic evaluation of healthcare technologies. METHODS: We searched MEDLINE, EconLit, EMBASE, CDR and HEED databases using the terms “cost-effectiveness” and (“affordability or “cost control”). Sub-headings were not used given the breadth of the search’s scope. Studies considering both CE and affordability using CEAFCs to evaluate healthcare technologies or programs, published in English after 2010, were included. A qualitative narrative synthesis was performed. RESULTS: Of the 1195 records screened, only eight utilized CEAFCs. Seven referred to a vaccine and one to promotion of breastfeeding; all were in developing countries and used both the societal and payer perspective. CEAFCs were used specifically to address concerns about affordability in situations where the incremental cost-effectiveness ratio for an individual healthcare technology was low but the overall budget impact was high. All used Markov models or decision trees and included probabilistic analyses by Monte Carlo simulations. The reported joint probability of cost-effectiveness and affordability ranged from 21% to 60%. Half of the studies were funded by pharmaceutical companies. CONCLUSIONS: Findings indicate that CEAFCs are a useful but underused tool, especially for investigating the cost-effectiveness and affordability of new treatments in developed countries. Increased use of CEAFCs may provide a beneficial framework to address affordability concerns alongside cost-effectiveness analysis.

PRM125: WEB APP ESTIMATING COST SAVINGS AND CLINICAL OUTCOMES OF BLOOD GLUCOSE MONITORING PROGRAM. EXAMPLE FROM THE UK

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OBJECTIVES: Design a budget model tp estimate financial impact of introduction of blood glucose monitoring program. Present economic model as communications app and inform hospital healthcare budgeting and decision making for patients under strict blood glucose monitoring. METHODS: The model is developed in MS Excel and then transformed into web application format. The model utilizes UK hospital episode statistics as a primary data source. Future healthcare budget projections and extent of savings from introduction of strict blood glucose monitoring program are estimated from a payer perspective. Model simulation time horizon is 5 years. Efficacy data was informed from published clinical study demonstrating high efficacy of early testing results of a diagnostic campaign. Sensitivity analysis was conducted to estimate parametric uncertainty around model outcomes. RESULTS: Direct medical cost savings following an introduction of a blood glucose monitoring program are estimated to be GBP 1,520 per patient. Cost savings in outpatient and inpatient settings were GBP 373 and 1,647 respectively. Sensitivity analyses indicated that efficacy and price of a testing device had the strongest magnitude of impact on model base case results. CONCLUSIONS: Model estimated that strict blood glucose monitoring program is a cost-saving intervention. A budget impact model app may effectively inform decision making and regional budget planning as it provides technical ability to modify model inputs during presentation to healthcare payers. An economic model app powered with dedicated data visualization libraries provide effective format to convey detailed economic data and results of economic model.

PRM126: COST-EFFECTIVENESS OF A MULTI-GENE PANEL IN THE CONTEXT OF REDUCING ADVERSE DRUG REACTIONS

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OBJECTIVES: Adverse drug reactions (ADRs) are a major causes of iatrogenic morbidity and mortality. Genetic variations, which can be identified through prospective genotyping may predispose a patient to ADRs. We aimed to develop an evaluation framework for assessing the cost-effectiveness of multiple-gene testing in the context of ADR reduction, taking into consideration the benefits of incidental findings. METHODS: We developed a decision-analytic framework for combining results from existing cost-effectiveness evaluations of single-gene tests. The framework is underpinned by a series of logical assumptions relating to their cost-effectiveness, both inclusive and exclusive of the cost of genotyping. Weighted combinations of costs and QALYs from existing analyses of single-gene tests provide a basis for estimating the outcomes of incidental findings, which are combined to provide an overall estimate of cost-effectiveness for the multi-gene test. We present an example based on existing studies of genotyping for HLA-A*31:01 prior to prescription of carbamazepine, and HLA-B*58:01 prior to prescription of allopurinol. Scenario analyses examine the complex relationship between the inclusion of single gene tests in the panel, the cost-effectiveness threshold, and the cost of the panel. Probabilistic sensitivity analysis explores parameter uncertainty. RESULTS: Independently, single-gene tests for HLA-A*31:01 but not HLA-B*58:01 are cost-effective. HLA-B*58:01 was cost-effective as an incidental finding. The incremental cost-effectiveness ratio for the panel was £13,464, based on a panel test cost of £50. In the sensitivity analysis, for 82% of replications, at least one test was cost-effective prospectively. As the test cost decreases, or the cost-effectiveness threshold increases, the likelihood
that both single-genes were cost-effective increases. **CONCLUSIONS:** We present a framework for assessing the cost-utility of multiple gene testing for predicting and pre-empting ADRs. For a case study of two single-gene tests, we show that a cost-ineffective test becomes cost-effective when the results are revealed as the incidental finding of a panel test result.

**PRM127: INCORPORATING DEPENDENCE BETWEEN MODEL PARAMETERS IN UNCERTAINTY ANALYSES**

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**OBJECTIVES:** Probabilistic Sensitivity Analysis (PSA) results depend on the assumptions about the marginal distributions of model parameters and their joint distribution. Although joint distribution of some parameters are accounted for (Dirichlet for transition probabilities, multivariate normal for regression parameters), in most health economic models investigation of different types of dependence structures is omitted. As a result, PSA results reflect model inputs that are assumed to be independently distributed. This can lead to inaccurate uncertainty analysis results. **METHODS:** We demonstrated how to fit copulas to data we used to populate a health economic model to construct joint distributions. We then sampled parameter values under different assumptions about their joint distribution: First we assumed they are independent, reflecting the current practices; second we assumed that the variables are jointly normally distributed, and finally we used copulas to sample from the marginal distributions. We compared various plots generated under different assumptions to the scatterplot of the original data. Using a health economic cost-effectiveness model, we analysed the PSA results under three different assumptions. **RESULTS:** Joint distributions with independence and multivariate normal assumption do not accurately represent the dependence observed in the data. PSA results indicate that the variability of model outcomes changed. This has implications on the conclusions about the uncertainty of the base case estimate of cost-effectiveness of the treatment. **CONCLUSIONS:** Ignoring the dependence structure between model parameters can lead to inaccurate results and can distort PSA conclusions. Investigation of the joint distribution of parameters should be a routine part of uncertainty analysis. The methodologies for fitting copulas and simulating random variables with different dependence structures are well documented and they should be incorporated in health economic modelling.

**PRM128: COST-EFFECTIVENESS ANALYSIS OF 10% INTRAVENOUS IMMUNOGLOBULIN COMPARED WITH PLASMA EXCHANGE IN TREATMENT OF CHILDREN WITH GUILLAIN–BARRÉ SYNDROME IN RUSSIA**

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**OBJECTIVES:** To assess the cost-effectiveness of 10% liquid intravenous immunoglobulin (IVIG) (Switzerland) compared with plasma exchange in treatment of Guillain–Barré syndrome (GBS) in children in Russia for 1-year period. **METHODS:** A decision tree was used to simulate the effects of medicinal drugs and procedures. The data on IVIG and plasma exchange efficacy (measured as ratio of patients with improvement by at least one grade on Hughes functional grading scale for GBS) was obtained from available clinical trials. The following costs were taken into account: ones for IVIG procurement, plasma exchange procedures (including procurement of 5% albumin and consumables), expenditures for SGB treatment, management of adverse events, disability pensions, costs of IVIG administration. As a result, cost-effectiveness ratios (CER) of 10% IVIG (Switzerland) and plasma exchange were calculated. **RESULTS:** According to van der Meche (the Netherlands,1992) therapy with 10% IVIG (Switzerland) leads to one grade and higher improvement in 19% more patients with SGB compared with plasma exchange procedure. According to performed cost analysis, 10% IVIG (Switzerland) therapy (339,681 rubles/5956 $) is less costly by the end of the 1st year per one patient compared with plasma exchange procedure (408,168 rubles/7157 $). The calculated CER in USD per 1 % of patients with one grade and more improvement per year was lowest for 10% IVIG (Switzerland) – 640,908 RUB/11,238 $ in comparison with plasma exchange – 1,200,495 RUB/21,050 $. Current rate taken as for 15.06.2017 is 1$ = 57,03 RUB. **CONCLUSIONS:** The treatment of primary immunodeficiencies with 10% liquid intravenous immunoglobulin (Switzerland) is considered cost-effective compared with plasma exchange in children in Russia for 1-year period.

**PRM129: RISK ADJUSTMENTS IN ECONOMIC MODELS - WHAT IS THEIR IMPACT ON PREDICTED RATES?**

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**INTRODUCTION:** State-transition models are based on the assumption of mutually exclusive health states. Transition probability estimates used in economic models, particularly when obtained from different sources, may however not reflect that feature: event risk often increases with age (e.g. cardiovascular (CV) events) and may even add up to more than 1 when independent risk inputs are used, leading to biased and illogical results. Risk adjustment (RA) methods and their impact on cost-effectiveness (CE) are largely neglected in the literature and economic
modelling practice. **OBJECTIVES:** To identify RA techniques and evaluate their effect on predicted event rates based on an example economic model. **METHODS:** Based on basic probability principles, three main categories of potential RA were identified: Arbitrary reductions; decreasing risks until the logical constrains are satisfied; Sequencing events: evaluating events in an assumed sequence; Creating combined health states: adding states which reflect multiple events occurrence; The effects of these RA were evaluated using a semi-Markov model based on Wilson 2012 CV risk equations and non-CV mortality estimates from life tables. The model includes 3 health states, where patients are at risk of non-fatal CV events, fatal CV events and fatal non-CV events. Additionally, the effect of altering cycle length was assessed. **RESULTS:** The differences in predicted CV rates between RA methods and the unadjusted rates were between -4% to +2% for the base case inputs. The impact of the RA methods increased with longer cycle length. **CONCLUSIONS:** A number of RA can be implemented and the decision on which one to use, if any, will depend on the inputs, model and resource availability in each particular case. Shortening cycle length reduces the impact of RA. Ignoring to implement RA might substantially affect rate predictions, leading to biases in CE results and ultimately erroneous HTA reimbursement decisions.

**PRM130: VACCINE EFFICACY, EFFECTIVENESS, OR IMPACT: WHICH ONE TO CHOOSE IN ECONOMIC EVALUATIONS OF VACCINES?**

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**OBJECTIVES:** At product launch we have access to vaccine efficacy data from randomized clinical trials to develop our economic evaluations. Later on we may obtain vaccine effectiveness data through case-control studies. What matters most however are vaccine impact data over time. If impact results are different from efficacy and effectiveness data, how do they affect the economic results? We take the example of the monovalent vaccine (RIX4414) against rotavirus disease to evaluate that point. **METHODS:** We developed models allowing the use of different vaccine effect data to calculate ICERs. We first calculated the ICER using vaccine efficacy data in a static cohort model with adjustment for herd-effect achieved after reaching the ICER steady state level (8 years). We then adjusted the vaccine input parameters with vaccine effectiveness instead of efficacy in a second analysis over a same evaluation period. The vaccine impact data requires the use of a population model instead. We compare the results of the impact data over a same period of assessment with the previous data. **RESULTS:** Results indicate as expected that the ICER with vaccine efficacy will be lower than with vaccine effectiveness (+7%) already achieved after 8 years of follow-up. The vaccine impact results heavily depend on the vaccine coverage and consequently on the level of herd effect achieved during the first years post-vaccine introduction. It however results in a higher ICER (+13%) with 86% coverage, and 8 years of follow-up. **CONCLUSIONS:** ICER-results will be different by vaccine effect data selected. Impact data are the closest results to what is happening in real life. It is therefore imperative to select those data as the most relevant to measure the economic value of new vaccines. Impact data will obviously not be available when the vaccine is launched. These results question the methodology of vaccine assessment.

**PRM131: QUANTITY AND QUALITY OF EXTERNAL EVENT VALIDATION PROCEDURES PERFORMED IN PUBLISHED HEALTH ECONOMIC MODELS IN OBESITY: OUTCOMES OF A SYSTEMATIC REVIEW**

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**OBJECTIVES:** For assessing the long-term health economic impact of obesity programs, modelling techniques are frequently applied to project obesity-associated events over time. To obtain information on the predictive quality of the applied event simulations, which ensures the acceptance of results from economic evaluations, published external event validation approaches were identified, reviewed and analyzed. **METHODS:** A systematic review was performed in Pubmed and NHSEED to identify decision models for full health economic assessments (HEA) in obesity. For each included study we extracted information on the external event validation approach, using the best practice recommendations of the report on “Model Transparency and Validation” issued by the ISPOR-SMDM Modeling Good Research Practices Task Force. **RESULTS:** We identified 87 papers and 83% (72 of 87) simulated obesity-associated events. Only ten models (=11%) performed an external validation and only for one the predictiveness of the event simulation was investigated in a cohort of obese subjects. Considering other ISPOR best practice criteria we have found that for none of these external validation cases a systematic identification of suitable data sources was performed, and that a justification of the data source selection, due to predefined criteria, was identified only in three cases. However an adequate result presentation (simulation results provided for each source, presentation of discrepancies, and a qualitative measure on fit) was provided for most external validation cases (= eight cases). **CONCLUSIONS:** We have found that only a limited number of published decision models for full HEAs in obesity have applied an external event validation. In addition, those who conducted external validation suffers from major limitations including the data source selection process, as only in one case, obesity cohorts were used as basis
PRM132: SELECTING SOFTWARE PACKAGES FOR CONDUCTING COST-EFFECTIVENESS MODELLING IN HEALTH CARE


**OBJECTIVES:** Microsoft Excel® is considered the essential software package for developing health economic models, and is one of four preferred by NICE for technology assessment submissions. As models become more complex and analyses become computationally expensive, the use of alternative software packages becomes a pertinent consideration. This study aimed to identify the different packages used for cost-effectiveness modelling in HTA submissions to NICE and the criticisms of the chosen software by Evidence Review Groups (ERG). Recommendations on choice of software for models of varying complexity across disease areas were then developed. **METHODS:** All cost-effectiveness models submitted to NICE by manufacturers and published between 2006 and 2016 were assessed for software used to develop the model. Data were extracted from submitted models to determine predictors of each package’s use, and likelihood of criticisms and acceptability by the ERGs. Results were then used to develop a decision algorithm to guide software choice. **RESULTS:** The search identified 181 submissions utilising 6 different software packages. Excel® was the most common, having been used in 90% of submitted models. Other commonly used programs included TreeAge, SAS, and Simul8. The principal factor identified in choosing to model in non-Excel software was for the evaluation of non-oncology drugs (43% of submissions). The number of health states, varying cycle length, or model structure (i.e. discrete event simulation) necessitated advanced software to manage these aspects. ERGs were sometimes critical of non-Excel models perceived as overcomplicated, but overall such models were well received. **CONCLUSIONS:** Microsoft Excel® is still the most widely used and accepted package for developing health economic models, however the use of different packages is justified under certain conditions. ERGs can be critical of non-conventional models developed in alternative software. The results of our analysis are presented in a decision algorithm to guide the choice of modelling software.

PRM133: CALIBRATING MODEL-CONSISTENT TRANSITION PROBABILITIES FOR FIBROSIS STAGES IN NASH


**OBJECTIVES:** Non-alcoholic Steatohepatitis (NASH) is a disease with its early progression characterized by five stages of hepatic fibrosis from F0 (no fibrosis) to F4 (compensated cirrhosis). The fibrosis progression rate (FPR) between fibrosis stages has been estimated by Singh, 2015 for each baseline stage as the total number of stages progressed divided by the total number of person years of follow up. The FPR has been used in Markov cost-effectiveness models as a proxy for transition probabilities between fibrosis stages (Tapper, 2015; ICER, 2016). This research argues that model specific transition probabilities calibrated to match detailed study data give a better model of disease progression than FPR. **METHODS:** The observed data include the number of patients for all 25 combination of initial and final fibrosis stages, and the total number of patient years for each initial stage. Our Markov-model assumed that transition is possible to the next stage in either direction that leaves 8 transition probability parameters to be calibrated. The calibration objective was to match the observed and modelled final patient number distribution at the modelled time horizon. For the calibration, the time horizon was set to the number of patient years for each initial stage. **RESULTS:** The model generated distribution of patients closely match the observed distribution from the data source. The resulting transition probabilities are also consistent with the estimated FPR. **CONCLUSIONS:** The calibration method for transition probabilities in Markov-models of NASH is recommended over the use of FPR. The method incorporates all available information from the data source instead of the FPR that is only a summary statistic of the observed progressions. Furthermore, the calibrated transition probabilities are fully consistent with the model by allowing for transitions in both directions from each stage and multiple transitions from each state over the model time horizon.

PRM134: COST-EFFECTIVENESS ANALYSIS OF VENETOCLAX FOR TREATMENT OF REFRACTORY/RELAPSED CHRONIC LYMPHOCYTIC LEUKEMIA WITH OR WITHOUT 17P DELETION IN BULGARIA

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**COST-EFFECTIVENESS ANALYSIS OF VENETOCLAX FOR TREATMENT OF REFRACTORY/RELAPSED CHRONIC LYMPHOCYTIC LEUKEMIA WITH OR WITHOUT 17P DELETION IN BULGARIA**

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, Velea N 1, Tsanova D 2, Vekov T 1 1Faculty of Pharmacy, Medical University – Pleven, Pleven, Bulgaria 2Faculty of Public Health, Medical University – Pleven, Pleven, Bulgaria OBJECTIVES: Modeling cost and health benefits of VEN for Bulgaria compared to best supporting care (BSC) for a third treatment line. An indirect comparison of therapeutic alternatives for the first therapeutic line in patients with CLL ± del 17p/TP53 mut and the second therapeutic line in patients with R/R CLL ± del17p/TP53 mut was performed. METHODS: Identification and analysis of published data from health technology assessment for treatment of relapsing/refractory CLL (R/R CLL) ± del 17p/TP53 mut in other countries. Literature search of published data on health technology assessment for treatment of R/R/CLL ± del17p/TP53 mut (January 2005-2017). Network meta-analysis, including also modeled data of health utilities and costs of VEN vs. BSC, discounted at 5%. The Markov model was applied with time horizon of 20 years. The indirect comparison includes VEN, BSC, ibrutinib (IBR), rituximab (RIT), bendamustine (BEN), idelalisib (IDE), ofatumumab (OFA). RESULTS: In the group of patients with CLL del 17p/TP53 mut VEN dominates IBR with better efficacy and lower costs: VEN vs. IDE/RIT (ICER 12 212 BGN/QALY), VEN vs. RIT/BEN (ICER 21 485 BGN/QALY). In the group of patients with R/R CLL, refractory to one previous therapy, VEN dominates IBR with better efficacy and lower costs: VEN vs. OFA/BEN (ICER 9931 BGN/QALY); VEN vs. RIT/BEN (ICER 39 085BGN/QALY) and VEN vs. IDE/RIT (ICER 12 212 BGN/QALY). CONCLUSIONS: VEN is a cost effective health technology in comparison with the therapeutic alternatives for treatment of CLL with and without the presence of del17p/TP53 mut in Bulgaria. Key words: HTA, Bulgaria, health technology assessment, venetoclax, chronic lymphocytic leukemia

PRM135: DEVELOPING A CONCEPTUAL MODELLING FRAMEWORK FOR ECONOMIC EVALUATION

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OBJECTIVES: Conceptual modelling (CM) is a key initial step in developing a mathematical model. Whilst there are established CM frameworks in other disciplines there has been little research in the field of economic evaluation, and no generic standardised frameworks exist. The objective of this research was to identify CM frameworks in non-economic evaluation fields, and to analyse these frameworks for common steps that would inform the development of a CM framework for economic evaluation. METHODS: After an initial scoping exercise using pearl growing techniques, a qualitative critical interpretive synthesis (CIS) approach was used to identify frameworks and synthesize results. CIS uses an iterative approach to search a range of sources, followed by an evolving selection and synthesis process to add to the research. Web of Science was purposefully searched to identify CM frameworks, broad inclusion criteria included CM frameworks with discrete steps, references and citations were examined. Alongside this a site-ation search was carried out to identify non-academic frameworks. An iterative data extraction process identified common steps in the frameworks, these were analysed and used to inform a framework for economic evaluation CM. RESULTS: Fifteen frameworks were identified from disciplines including ecology and engineering. Regardless of the discipline, similar steps were identified in each framework, ranging from two to nine steps. Using these steps, a CM framework for economic evaluation is proposed, split into three broad sections: understanding the problem (including; choose project team, objectives and outputs), model content (including; review previous conceptual models, scope and detail) and documenting the conceptual model (including review/refine, validation and assumptions/simplifications). CONCLUSIONS: Using steps from non-economic evaluation frameworks has informed a CM framework proposed for use in economic evaluation. The next stage in this research is to validate the framework with expert opinion and case studies.

PRM136: ECONOMIC EVALUATION OF ANAFERON® IN THE TREATMENT OF ACUTE RESPIRATORY INFECTIONS IN MEXICO

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OBJECTIVES: Respiratory tract infections are one of the society’s main health problems due to the high rate of hospitalization, morbidity and mortality. Despite the overall impact on human health, there are relatively few therapeutic options available to prevent or treat respiratory infections. Children can present between six and eight respiratory infections per year, many of which, especially those occurring during the infant period, affect the lower respiratory tract. Anaferon® (affinity-purified antibody to interferon gamma) promotes an immunomodulatory and antiviral action. Its efficacy in relation to acute viral respiratory infections has been established clinically and experimentally. The objective of this study is to conduct a cost-effectiveness analysis of Anaferon® for the treatment of acute respiratory infections in children and adults compared with standard treatment. METHODS: This study used a decision tree, in which the costs and effectiveness of two treatment strategies in patients with acute respiratory infections (children or adult) were compared: Anaferon® plus standard care vs standard care (consultation plus treatment for the symptoms). The time horizon is six months. RESULTS: Adding Anaferon® to the standard therapy is a cost-effective strategy over standard therapy; the incremental cost is $198 USD ($558 USD vs $360 USD). The administration of Anaferon® significantly reduced the duration of all the symptoms of the disease (4.68±0.08 vs
The duration in days of each symptom: fever (2.10±0.06 vs 3.37±0.19), intoxication (2.68±0.08 vs 4.63±0.19), cold symptoms (4.33±0.10 vs 6.79±0.23), gastrointestinal tract disorders (3.29±0.12 vs 4.65±0.26). For most of the children who received Anaferon® (81%) all the symptoms improved in 5 days vs 8 days for standard therapy alone. **CONCLUSIONS:** Anaferon® is a cost-effective alternative, it produces an immunomodulating effect, stimulates synthesis of IgA and IgG, exhibits cytoprotective activity, and improves local immunity of the upper airways in children and adults diagnosed with acute respiratory infections.

**PRM137: HIERARCHICAL BAYESIAN MODEL ACCOUNTS FOR HETEROGENEITY IN ONCOLOGISTS’ STATED PREFERENCE ON VARIOUS BREAST CANCER TREATMENTS**

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**OBJECTIVES:** Traditional stated-preference models with fixed effects assume that individuals behave similarly. However, empirical evidence has shown that individuals’ preferences are often diverse. Hierarchical Bayesian models that include random effects provide individual-specific utilities to account for heterogeneity. This research studies oncologists’ choices about various pharmaceutical therapies for patients who have metastatic breast cancer. **METHODS:** In this discrete choice experiment conducted in Lima, Peru, each of 113 oncologists was presented with 11 choice tasks (each consisting of four scenarios of therapies plus the NONE option) and asked to pick the best choice. The attributes included Treatment Scheme, Patient Recovery Status, Treatment Length, Cost, and Risk Factors. Hierarchical Bayesian methods were used in this multinomial logit conjoint analysis to account for heterogeneity in preferences. **RESULTS:** Treatment Scheme, Recovery Status, and Risk Factors showed impact on the choices. On average, treatments with shorter periods of follow-up medication were preferred, and these oncologists tended to choose therapies that would have a better recovery status (0.19 with a 95% HPD credible interval [0.06, 0.33]). More importantly, Risk Factors had a large influence: the utility estimates of all risk factors were all negative (cardiovascular disease −1.21 [−1.56, −0.86], thromboembolism −1.45 [−1.81, −1.11], arterial hypertension −1.44 [−1.78, −1.11]). Cost did not play a role, probably because the respondents were doctors (not patients) and the study dealt with metastatic breast cancer. Several entries in the covariance matrix of random effects were large, indicating diversity in preferences. **CONCLUSIONS:** Oncologists had diverse preferences in response to breast cancer therapies. Heterogeneity is an important aspect of the study, and ignoring its presence would lead to incorrect inferences. This finding has implications on clinical trials and research: hierarchical Bayesian models with random effects provide solutions to create individual-level utilities to account for heterogeneity.

**PRM138: MAPPING FROM THE WOMAC TO THE EQ-5D-5L QUESTIONNAIRE: COMPARISON OF DIFFERENT METHODOLOGIES**

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**OBJECTIVES:** Hip or knee osteoarthritis (OA) affects very negatively the health-related quality of life (HRQoL). Consequently, studies of treatment efficiency, typically conducted using health utilities are of great interest. One of the most widely used generic instruments to derive utilities is the EQ-5D-5L. However, in clinical practice, the use of specific HRQoL questionnaires is more frequent. Our objective was to develop mapping functions to estimate the utility index from the WOMAC questionnaire. **METHODS:** Prospective observational study, including 748 patients from Spain with hip or knee OA who completed the EQ-5D-5L and WOMAC, of whom 626 responded to the 6-months follow-up. Using the baseline data we derived the mapping functions from two WOMAC dimensions: pain (P) and function (F). GAM models and bootstrap were used to determine the optimal relationship grade and combinations of the WOMAC domains, and then, two strategies were used for the modelling: linear and beta regression. To select the best model the AIC was used. These functions were validated in the follow-up data using MAE and RMSE. **RESULTS:** The mean EQ-5D-5L index was 0.533 (SD=0.223, range=0.416 to 1). The best combination of WOMAC domains were: P3+F and P-F+F. Both linear and beta models obtained similar AIC values for both combinations, although the validation of these functions in the follow-up sample showed slightly lower MAE and RMSE for the P-F+F. Further, the results of the beta model were not better than the linear model. Based on linear model the function was: EQ-5D-5L=0.9525−0.000056·P·F−0.0051·F (R²=0.618, AIC=−453.39, MAE=0.135,
A modified TTO survey was used. Respondents (184, a convenience sample) answered demography questions, self-rated own health, and answered ten TTO tasks. Apart from a standard valuation, the respondent provided ranges of equally/somewhat plausible answers (EPAS/SPAS), which define the (dis)utility as a trapezoidal fuzzy number. The length of EPAS/SPAS was compared with the standard error of (a crisp) mean (SEM). The determinants of EPAS length were identified. I built several models to identify dimensions impact on (dis)utility: (A, as a benchmark) crisp disutility-crisp parameters; (B) fuzzy disutility-crisp parameters, based on the directed Hausdorff distance; two fuzzy-fuzzy models: using the Hausdorff distance (C1) or modelling the middles and lengths of EPAS (C2). Value sets were constructed. RESULTS: The average length of EPAS varied between 0.063 (state 21111) and 0.137 (11113), 2–6 times the length of SEM. EPAS widens with usual activities (UA) and anxiety/depression. Derived modelling variables (e.g. maximal level, misery index) improve the fit considerably, and were used in C2. When modelling disutility, models A and B produce similar results (with u(55555)=0.8), proving the impact of imprecision is little with crisp parameters assumed. In C1, the largest imprecision is associated with levels 3 of UA ([0.343;0.443]) and pain/discomfort ([0.423;0.498]). Counterintuitively, some parameters (e.g. for mobility) degenerate to zero-length intervals. C2 seems most favourable approach as the worsening in any dimension implies imprecision; e.g., u(55555)=[-0.828;-0.716]. CONCLUSIONS: In eliciting utilities of health states, the imprecision (not decreasing with sample size) surpasses the stochastic uncertainty. Fuzzy methods allow inspection of mechanism behind imprecision and extrapolation onto value set. The inherent imprecision should be handled in decision making.

Mapping from the BDI-II to the EQ-5D-5L questionnaire in patients with major depression disorder

OBJECTIVES: Depression is one of the most disabling mental disorders causing a significant decrease in health-related quality of life (HRQoL). Therefore, studies of treatment efficiency are of great interest. They are usually based on health utilities, being the EQ-5D-5L one of the most widely used instruments to derive these utilities. However, in clinical practice, the use of specific questionnaires is more frequent. Our objective was to develop mapping functions to estimate the EQ-5D-5L utility index from the specific BDI-II questionnaire. METHODS: A prospective observational study, including 418 patients from Spain with major depression, who completed the EQ-5D-5L and BDI-II questionnaires. Of these, 283 responded to 6-months follow-up. The baseline data was used to derive the mapping function from the BDI-II score. The GAM models were used to determine the optimal relationship grade between the utility index and the BDI-II score. Then, we used linear and beta regression for the modelling, and age and sex were also considered. To select the best model the AIC was used. These functions were validated with the follow-up data, and the fit was compared by the MAE and RMSE. RESULTS: The mean EQ-5D-5L index was 0.562 (SD=0.269, range=0.384 to 1). GAM models indicated no need of powers of the BDI-II score. Both linear and beta regression models obtained similar results for models with and without age and sex. However, the validation of these functions in the follow-up sample showed slightly lower MAE and RMSE values in the linear model. The function was: EQ-5D-5L=0.1590-0.0131·BDI-0.0036·Age+0.0180·Sex (Man) (R2=0.351, AIC=87.81; MAE=0.170; RMSE=0.215). CONCLUSIONS: To the best of our knowledge, this is the first mapping function from the BDI-II to the
Spanish EQ-5D-5L in patients with major depression. This function could be very useful if cost-effectiveness studies are needed and generic HRQoL questionnaires to derive utility indexes are not available.

**PRM141: USING REGRESSION MODELS TO ACCOMMODATE HETEROGENEITY AND ADDRESS COHORT IMBALANCE IN PARAMETRIC SURVIVAL MODELS FOR USE IN HTA**

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**OBJECTIVES:** To examine and provide a regression-based solution to the impact of ignoring patient heterogeneity when using parametric survival models to populate economic evaluation models. **METHODS:** I apply to theory to demonstrate the theoretical bias that occurs in using survival models to provide survival probabilities beyond the time-frame in data collection. I show that when non-linear models (as in all parametric survival models) are used, bias occurs when heterogeneity is not explicitly incorporated in producing expected survival functions – whether patients are randomised or not. I demonstrate this using observational data of 40 patients with 'hard-to-heal' diabetic foot ulcers and provide a regression correction method coupled with 'explicit population averaging' that can accommodate both observable and unobserved patient heterogeneity across potentially unbalanced cohorts. **RESULTS:** Failure to incorporate and adjust for patient heterogeneity is shown to produce biased estimates of survival probabilities both within and beyond trial timelines – in this case overestimating incremental median survival times by approximately 100%. Using regression models and population averaging across a heterogeneous population show that incremental difference in median survival across this population falls from 23 weeks to 12. **CONCLUSIONS:** Even where RCTs are used, a failure to explicitly incorporate patient heterogeneity in parametric survival analysis leads to biased estimates of survival probabilities frequently used in economic evaluations. Explicitly incorporating patient observable and unobservable characteristics in the survival regression models and then using explicit population averaging to produce survival probabilities provides a means for measuring and eliminating this bias. In addition, the methods shown here can be used to drive models where patient populations may be expected to differ from those used in trials.

**PRM142: USING A "LANDMARK" APPROACH TO ARTIFICIALLY POPULATE THE COMPARATOR ARM OF AN ECONOMIC MODEL USING DATA FROM A PHASE II, UNCONTROLLED TRIAL IN ADVANCED BASAL CELL CARCINOMA**

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**OBJECTIVES:** Vismodegib is a Hedgehog (Hh) pathway inhibitor indicated for the treatment of adults with advanced basal cell carcinoma (aBCC). Vismodegib is licensed for two distinct subgroups: symptomatic, metastatic BCC (mBCC) and locally advanced BCC (laBCC) deemed inappropriate for surgery or radiotherapy. Registration studies for vismodegib were both uncontrolled and single arm (ERIVANCE [2008-004945-27], STEVIE [NCT01367665]), which poses a significant challenge when populating the clinical aspect of the comparator arm in an economic model. The objective of this study was to estimate the comparative effectiveness of vismodegib against best supportive care (BSC) using a "Landmark" approach, and use the results to inform an economic evaluation of vismodegib in aBCC. **METHODS:** Non-responders at 6 months in STEVIE were used as a proxy group for patients receiving BSC. A 6-month landmark was selected as it exceeds the mean and median time to first confirmed response. A Cox regression model was used to estimate progression-free survival (PFS) and overall survival (OS) hazard ratios (HRs) of non-responders versus responders. Hazard ratios were estimated using both a common and separate treatment effect across the laBCC and mBCC populations with and without adjustment for age, and ECOG status. **RESULTS:** Mean [95% CIs] HRs estimated using a 6-month landmark and the common treatment effect amounted to 2.16 [1.27, 3.68] and 1.31 [0.99, 1.75] for OS and PFS, respectively. The separate treatment effect model yielded similar and clinically plausible HRs in the locally advanced population. In the metastatic population, HRs were not statistically significant because of the low number of patients and events. **CONCLUSIONS:** The landmark method removes bias that would otherwise occur in a comparison of ever-responders and never-responders over the entire observation period. Despite limitations, the landmark approach can be considered robust methodology when deriving comparative effectiveness from uncontrolled trials.

**PRM143: TACKLING NETWORK META-ANALYSIS METHODOLOGICAL CHALLENGES: A CASE STUDY ON BILOGIC TREATMENTS FOR MODERATE TO SEVERE PLAQUE PSORIASIS IN CHILDREN AND YOUNG PEOPLE**

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**OBJECTIVES:** Network meta-analysis (NMA) methods extend the pair-wise meta-analysis framework by allowing the
simultaneous statistical synthesis of evidence on more than two interventions. Often the evidence base produces networks that are disconnected, such that there is neither direct nor indirect evidence to compare all relevant treatments within the network. Even when a fully connected network exists, the evidence base may present cross-trial variation in the reference arm outcomes, which, if not controlled for, may create biased estimates of relative treatment effect. These challenges are addressed using a case study on the biologic treatments for moderate to severe plaque psoriasis in children/young people as the motivating example. **METHODS:** A series of Bayesian statistical NMA models were developed. The full set of relevant treatments could not be connected within the network of evidence such that only partial comparisons could be undertaken using conventional NMA approaches. We tackled this challenge by developing synthesis models which used external evidence from an adult population to connect the network in the children/young person population. Further model extensions were performed to adjust for population and cross-trial differences. Bayesian measures of fit and adequacy were used to compare and select models. **RESULTS:** There were only 3 trials in children/young people in psoriasis, which formed a disconnected network of four biological treatments. External evidence from an adult population was used to bridge the evidence gap. Reference arm response rates were identified as a key source of heterogeneity. The NMA models were therefore adjusted for population and cross-trial differences providing an appropriate method to estimate relative treatment effects for all relevant treatments in children/young people. **CONCLUSIONS:** Provided that valid external information can be inserted into the network, methodological approaches to NMA offer the opportunity to derive reliable estimates of relative treatment effects, while adjusting for key sources of heterogeneity.

**PRM144: A MODEL FOR ALZHEIMER’S DISEASE IN THE PREVENTION SETTING**

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**OBJECTIVES:** Shifting the focus of clinical trials testing disease-modifying interventions against Alzheimer’s disease (AD) from the dementia stages of the disease to pre-symptomatic stages may increase the likelihood of success for these trials. The aim of this research was to develop a model for the pre-symptomatic time course in the AD prevention setting to inform clinical trial design. **METHODS:** We developed a statistical model describing time to first diagnosis of mild cognitive impairment (MCI) or AD diagnosis using a Weibull parametric survival function and the progression of the Alzheimer’s Prevention Initiative Preclinical Composite (APCC, see Langbaum et al. 2014), a measure for cognitive decline, using a non-linear empirical function. We chose model covariates based on clinical relevance, goodness of model fit and statistical tests. We trained the model on databases which included healthy as well as cognitively impaired and demented subjects. **RESULTS:** We identified age, apolipoprotein E ε4 status, APCC at baseline and education level as important model covariates. Patient simulations showed a good fit between model predictions and observed values, for both time to first diagnosis and progression of APCC. Simulations also showed that an enrichment strategy focusing on elderly participants yielded a higher power for a given hazard ratio of the investigated interventions. **CONCLUSIONS:** The 2-step model linking APCC decline and time to MCI or AD diagnosis is the first AD disease progression model for pre-symptomatic stages of the disease. It exhibits good internal validity and can be used in the context of optimizing design of clinical trials in the prevention setting. Further refinements of the model, e.g. including biomarkers such as amyloid-beta and tau as covariates and covering other relevant endpoints, external validation of the model, and incorporation into a health economic model to evaluate interventions in the prevention setting, are objectives of future research.

**PRM145: METHOD OF EXTRAPOLATION: ESTIMATION OF THE IMPACT OF THE PROPORTIONAL HAZARD ASSUMPTION ON THE EFFICACY ESTIMATION**

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**OBJECTIVES:** In 2013, Nicolas R. Latimer published guidelines regarding the extrapolation of survival analysis data for cost-effectiveness models. Tremblay et al completed his work by highlighting the need to perform a statistical test for proportional hazard (PH), as visual inspection of the log-cumulative hazard curves is insufficient to determine if the PH assumption is justified. The goal of this work was to estimate the risk of error on efficacy estimation (percentage of error on AUC) by wrongly accepting the PH assumption. **METHODS:** We digitized PFS or OS Kaplan-Meier curves of 30 recently published phase III trials of innovative oncological drugs. For each trial, we generated individual patient data (IPD) using Guayot’s algorithm, and the PH assumption was tested using the Schoenfeld test. The hazard ratio published was applied directly on the comparator/placebo arm to create the treatment curve. The risk of error between the “real” treatment curve and the “created” one was calculated as the percentage of error between the areas under the curve (AUC) and plotted against the p-value of the Schoenfeld test. **RESULTS:** In 73.3% (22/30) of the trials, the PH assumption was verified at a 0.05 threshold. For these trials, the difference of the AUC was less
than 5% in 72.7% (16/22) of cases. However, for the 8/30 trials where the PH assumption fails, the difference on the AUC was greater than 5% for 100% of cases, with a maximum difference of 19.4%. CONCLUSIONS: Based on this preliminary work, extrapolation using HR method is not adapted if PH assumption failed, considering the high risk of error on efficacy estimation. We plan to incorporate more trial results in order to explore a threshold level on the Schoenfeld test which would guarantee safe extrapolation.

**PRM146: FROM EVALUATION TO OPTIMIZATION: USING A META-MODEL TO MAXIMIZE THE BENEFITS OF COLORECTAL SCREENING ACCOUNTING FOR CAPACITY CONSTRAINTS**

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OBJECTIVES: Model-based analyses are typically useful for assessing the cost-effectiveness of a few but not a vast number of alternative health care strategies. We aim to illustrate the potential advantages of using a meta-model to identify the best screening strategy for colorectal cancer accounting for colonoscopy capacity constraints. METHODS: We defined screening strategies by starting age, interval, number of screening rounds, and screening test positivity threshold (16,464 unique strategies). We evaluated a limited sample of predefined strategies with the validated ASCCA model and identified the best screening strategy therein, in terms of life-years gained (LYG), compared with no screening. Next, this limited sample was used to fit a Gaussian Process meta-model. Finally, discrete evolutionary programming was used to iteratively identify the best possible screening strategy according to the meta-model (GP-DEP approach). Colonoscopy demand was restricted to 500 per 1,000 simulated individuals. The sample size of predefined strategies was varied (n=50-200). GP-DEP performance was assessed with bootstrapping (n=200), brute force exhaustive search, and comparison with ASCCA outcomes. RESULTS: GP-DEP resulted in stable predicted best screening strategies when applied to a sample of >=100 strategies, identifying the exact same best strategy as exhaustive search in 94% of bootstrap samples. Compared with ASCCA, predicted colonoscopy demand, LYG and costs of the best strategies from GP-DEP were accurate, slightly too high and slightly too low, respectively. However, strategy ranking (in deciles) according to ASCCA and GP-DEP were similar. For sample size 100, average predicted benefit of the best strategy identified by GP-DEP compared to the best strategy identified by ASCCA equalled 0.028 LYG (95%CI 0.013-0.043) per individual. CONCLUSIONS: Extending the ASCCA model with GP-DEP enhances performance: the best screening strategy can be identified much faster, even when constraints apply, and will outperform the best screening strategy as typically identified from a limited sample of predefined strategies.

**PRM147: SINGLE ARMED OBSERVATIONAL DATA TO CLOSING THE GAP IN OTHERWISE DISCONNECTED EVIDENCE NETWORKS**

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OBJECTIVES: Bayesian network meta-analysis (NMA) allows for the estimation of relative treatment effects in a connected evidence network. We propose the use of single armed observational data to enrich the evidence base where RCT data alone does not form a connected network to allow for pairwise comparisons between treatments. The approach is presented using a case study in relapsed or refractory multiple myeloma (rrMM). METHODS: A systematic literature review of RCT evidence reveals two disconnected evidence networks. Non-comparative observational studies are matched based on study level covariates to bridge separate networks. Since such methods are prone to bias, we capture the additional uncertainty to reduce the risk of over-confident interpretation of results. Uncertainty is captured by exploring a range of possible matches to bridge the networks. RESULTS: 21 RCTs exploring 22 treatments for rrMM form two disconnected networks. 12 single armed observation studies were identified for matching to bridge between the networks. The similarity between studies was assessed based on age, treatment history, baseline stage and gender; 14% of possible matches were found to be reasonably similar and were included. A ranking analysis indicates that carfilzomib, ixazomib or elozumatab in combination with lenalidomide plus dexamethasone as well as carfilzomib in combination with dexamethasone show the highest efficacy within the network of treatments in terms of progression free survival. CONCLUSIONS: The analysis illustrates how observational evidence can be used to bridge the gaps in existing RCT evidence; allowing for the indirect comparison of a large number of treatments which cannot be achieved using standard NMA methods. We stress the importance of incorporating additional uncertainty to avoid interpretation of results as if obtained from clinical trials. Appropriate communication of uncertainty is an advantage, compared to a naive assumption of equal efficacy between certain interventions, which has been done in the past.
**PRM148: COST-EFFECTIVENESS OF MOLECULAR VERSUS CONVENTIONAL SCREENING FOR ACUTE INTESTINAL INFECTIOUS DISEASES: NOVEL APPLICATION OF AGENT-BASED MODELLING.**

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**OBJECTIVES:** To develop an economic model of the cost effectiveness of using molecular (polymerase chain reaction, PCR) compared to conventional microbiological methods to diagnose pathogens contributing to acute intestinal infectious diseases. **METHODS:** Agent-based models of population interaction, exposure to sources of infection and transmission were developed for major pathogens. Model parameters were identified from a literature review and from the Integrate project. A genetic algorithm was used to determine unknown parameters relating to infectiousness on encounter. The models considered 50,000 agents over a period of one year. Each agent could be infected by a source and infect other agents. A subset of infected agents in the community visit a general practitioner (GP), and a subset of these provide a stool sample for testing. We simulated a PCR method by representing a greater number of agents having their pathogen correctly identified. A threshold of correctly identified pathogens triggers outbreaks. Simulations determine the effect a PCR method could have in determining outbreaks and closing of infected sources. A UK NHS perspective was adopted. **RESULTS:** The combined incidence rate for Campylobacter, Clostridium difficile, E. coli O157, Salmonella and Norovirus is 35 per 1000 person years in the community. Simulations of PCR systems show a 25% drop to 26 per 1000 person years. The number of GP visit falls 33% from 3.8 to 2.6 per 1000 person years. Multiplex PCR costs £33.33 per sample including staff time but conventional methods cost £6.58. The PCR method results in a gain of 0.3 QALYs per 1000 person years, at a cost which is within acceptable limits of cost-effectiveness **CONCLUSIONS:** The model demonstrates that a multiplex PCR method is a cost-effective method of screening for acute intestinal infectious diseases.

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**PRM149: AN ALGORITHM TO DEVELOP CORRELATED MULTIVARIATE NON-NORMAL (E.G. BETA, GAMMA, LOG-NORMAL) DISTRIBUTIONS TO BE USED IN PROBABILISTIC SENSITIVITY ANALYSES (PSAS)**

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**OBJECTIVES:** Input parameters for models used in cost-effectiveness analysis (CEA) are surrounded by uncertainty and therefore probabilistic sensitivity analyses (PSAs) are recommended. In many situations, some of the input parameters (e.g. incidence by age group) are correlated. The objective of this work (GSK study identifier: HO-13-13333) was to create an algorithm to develop correlated multivariate non-normal distribution (e.g. beta, gamma, log-normal) to be used in PSAs. **METHODS:** First, we created a Cholesky factorization matrix using the correlation value and number of parameters correlated (N). Second, we simulated N uncorrelated normal random variables with a mean =0 and a standard deviation =1. Third, we multiplied the uncorrelated normal variables by the Cholesky matrix to generate correlated normal random variables and calculated the probability associated with each value from the cumulative distribution function from a normal distribution. In the last step, we calculated the values associated with each probability assuming a non-normal distribution. The algorithm was implemented in a model developed to assess the cost-effectiveness of a Herpes Zoster subunit (HZ/su) vaccine vs placebo in adults ≥50 years old. We ran two PSAs: (1) varying the incidence parameters only and (2) varying most parameters in the model. **RESULTS:** For the PSAs varying incidence only, 90% of simulations resulted in an incremental cost-effectiveness ratio (ICER) below $25,000, $33,000 and $38,000 using a correlation of 0, 0.5, and 0.9 respectively. For the PSAs varying most parameters in the model, 90% of simulations resulted in an ICER below $38,000, $48,000 and $58,000 using the same correlations values as above. **CONCLUSIONS:** Allowing parameters to be correlated will help explore the overall uncertainty in model inputs and consequently the impact on model outputs. The algorithm presented here can be implemented and used for other CEA.

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**PRM150: FRACTIONAL POLYNOMIAL MODELLING IN NETWORK META-ANALYSES OF CANCER IMMUNOTHERAPIES IN ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC)**

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**OBJECTIVES:** Cancer immunotherapies may have a delayed onset of treatment effect and may lead to long-term survival in a proportion of patients, something not necessarily seen with conventional therapies. Therefore, a fractional polynomial (FP) approach to network meta-analysis (NMA) a, which does not assume proportional hazards, may be more suitable than standard hazard ratio (HR) based NMA for modeling overall survival (OS) and progression-free survival (PFS). **METHODS:** For the analysis of OS and PFS, we fit first order and second order fractional polynomials with powers p1 and p2 from the set (0,1), and fixed effects and random effects with heterogeneity for the intercept. Comparisons of OS and PFS between Roche’s cancer immunotherapy drug atezolizumab (anti-PDL1 antibody) used as monotherapy with other treatments in previously treated advanced
NSCLC were made via a Bayesian FP NMA. Model fit was assessed based on Deviance Information Criterion (DIC) and visual inspection. RESULTS: Fixed effects models often provided a better fit than random effects with the lowest DICs. Second order models often provided lower DICs than first order for OS and PFS; however, visual inspection of the curves showed a survival ‘plateau’, meaning a proportion of patients did not experience the event during the time horizon. First order models were thus a better fit by visual examination. The modeled HRs were not proportional over time, supporting the use of FP NMA over standard HR based NMA in this case. CONCLUSIONS: Fractional polynomials NMA can be a suitable approach when modeling non-proportional hazards, as seen with cancer immunotherapies in advanced NSCLC. a Jansen JP. Network meta-analysis of survival data with fractional polynomials. BMC Med Res Methodol 2011;11:61.

PRM151: A PREDICTIVE TOOL FOR CHARACTERIZING AND VISUALIZING POPULATIONS UNDER COUNTERFACTUAL TREATMENT ASSIGNMENT

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OBJECTIVES: We present a novel causal tool for the characterization of sub-populations demonstrating higher affinity to one treatment over another. METHODS: The tool consists of machine learning, causal inference, and visualization modules developed by our team and tested on observational data. Using Truven MarketScan® database, we defined a cohort of patients undergoing total hip/knee arthroplasty (THA/TKA) and treated with anticoagulants – either enoxaparin or direct Xa inhibitors (“xabans”) - for prophylaxis against venous thromboembolism (VTE). The outcome was defined as either VTE or major bleeding during the three months postsurgery. RESULTS: Our tool was demonstrated on the task of identifying and characterizing a sub-population that better responds to “xabans” versus enoxaparin. The cohort comprised of 90,000 patients, randomly divided into train and test sets (63,000 and 27,000 patients, respectively). Utilizing our tool, 34 candidate variables were extracted and used in model training. Of all variables, four effect modifiers were identified by our tool (THA/TKA, previous major bleeding, number of surgical visits, previous use of “xabans”) and their weights were estimated. Using those weights, the tool calculates a score for each patient, representing their affinity to “xabans” over enoxaparin. The user may set different score thresholds, using interactive visualization, determining what is considered high affinity. That threshold impacts the benefitting population’s size and odds ratio. The high/low affinity populations are displayed in a parallel coordinates chart, where their characterizations may be compared. An additional visualization shows patients conversion potential – which patients currently on one treatment would benefit from switching to the alternative. CONCLUSIONS: Our tool enables the introduction of many candidate variables into the analysis, resulting in a small set of variables which are the causal effect modifiers. This, along with the interactive visualization, makes the model and its results easier to interpret, and the sub-populations easier to characterize.

PRM152: HOW TO SAMPLE ORDERED PARAMETERS IN PROBABILISTIC SENSITIVITY ANALYSIS

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OBJECTIVES: Probabilistic sensitivity analysis (PSA) in health technology assessment involves simulating a large number of realisations as inputs to economic models to appropriately characterise parameter uncertainty and its consequences for decision uncertainty. If two variables are believed to be related in such a manner that one is greater than another then using standard sampling approaches may result in inappropriate PSA. This research aims to propose a method, the ‘Difference Method’ (DM), for generating PSA samples where the constraint that one value is greater than another is maintained and which also satisfies both clinical and statistical validity. METHODS: The DM approach samples the target variables via a difference parameter. If the target variables are bounded, it involves transforming the variables so that they are unbounded and then sampling via the difference parameter. The DM approach was compared with two commonly applied methods (independent sampling and sampling using a common random number generator) using two examples. RESULTS: The DM-generated PSA samples have summary statistics that were similar to the given values in our examples whilst maintaining the constraint that one value was greater than another. It also implies plausible correlation between the two target variables. We have developed an Excel workbook to implement the method. CONCLUSIONS: Failure to account for constraints between parameter values may result in PSA values that do not accurately characterise the uncertainty present in a decision problem. This could result in decisions made on the allocation of scarce health care resources being sub-optimal. The proposed excel-implemented DM approach provides a solution to overcome the problem with naïve sampling methods and should be considered in PSA.

PRM153: USING NETWORK META-ANALYSIS OF INDIVIDUAL PATIENT DATA (IPD) & SUMMARY AGGREGATE DATA (SAD) TO IDENTIFY WHICH COMBINATIONS OF INTERVENTIONS WORK BEST FOR
WHICH INDIVIDUALS.

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OBJECTIVES: In many settings interventions are comprised of a number of potential components, and are sometimes therefore termed “complex”. Such a range of potential interventions means that not only do we need to consider which combination is best for a population overall, but also which combination is best for particular sub-populations. The use of Individual Patient Data (IPD) allows such a question to be answered whilst minimising the problem of ecological bias. METHODS: Using a recent Cochrane Collaboration systematic review and subsequent pairwise meta-analysis on the safe storage of medicines we undertook a Network Meta-Analysis (NMA) of both IPD and Summary Aggregate Data (SAD), adjusting for heterogeneity in study design, in order to identify which combination of interventions was the most appropriate for specific sub-populations defined by individual level covariates. RESULTS: Based on SAD from 13 Randomised Controlled Trials (RCTs) the use of any intervention led to a statistically significant increase in the safe storage of medicinal products [OR: 1.53, 95% CI: 1.27 to 1.84]. However, interventions could comprise up to 5 different separate components, and using a NMA approach, and including IPD from 9 of the 13 RCTs, we were able to explore the heterogeneity between both component combinations and their effect in specific sub-populations. CONCLUSIONS: NMA of IPD and SAD can allow identification of the optimal potential combination of individual components for specific sub-populations and when there is a high level of uncertainty be used to help identify and design appropriate further RCTs.

RESEARCH ON METHODS - Patient-Reported Outcomes Studies

PRM154: CAREGIVER BURDEN IN DAILY HUMAN GROWTH HORMONE INJECTIONS FOR CHILDREN

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OBJECTIVES: Recombinant human growth hormone (r-hGH) replacement therapy has been safely and effectively used for over 30 years in thousands of patients worldwide with growth hormone deficiency (GHD). Most commonly, r-hGH therapy is long-term and relies upon daily subcutaneous injections to achieve the goals of GHD treatment in children and adults. While caregivers commonly give or assist with injections, research documenting the burden experienced by caregivers is limited. This research explores this burden. METHODS: As part of a study to establish the content validity of new questionnaires that assess injection regimen burden, semi-structured interviews were conducted with dyads (pediatric patients from the United States taking daily r-hGH injections for GHD [n=11 children ages 4 to 11, n=4 adolescents ages 13-14], and their caregivers). During the interviews, caregivers were asked to describe their experiences relating to their child’s r-hGH injections. RESULTS: Caregivers discussed a variety of burdens, including the need to keep medication cold (particularly when away from home), negative reactions from their children (e.g., crying, resisting injections), and impacts on travel (e.g., difficulties at airport security screening and travel limitations), emotions (e.g., being anxious about or bothered by giving injections to their children), and daily activities (an extra chore to do at night, changes to work schedule, unable to be away from home without child, ensuring that medicine and supplies are delivered and available). CONCLUSIONS: Daily r-hGH injection treatments impose emotional and practical burdens upon caregivers of pediatric patients. Caregivers of younger children are more constrained by the need to administer the injections daily, deal with greater resistance and hesitation from their children, and experience greater emotional effects from administering an uncomfortable or painful treatment every day to their very young children. Further research may help determine whether these burdens might be lessened with a less frequent injection regimen.

PRM155: PSYCHOMETRIC PROPERTIES OF THE EQ-5D-5L IN PATIENTS WITH MAJOR DEPRESSION DISORDER

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OBJECTIVES: The objective was to perform the validation of the Spanish EQ-5D-5L questionnaire for patients with major depression disorder, studying the psychometric properties, such as reliability and validity, including the structural validation. METHODS: We included 433 patients with major depression, who completed the EQ-5D-5L, the BDI-II and the PHQ-9 questionnaires. The EQ-5D-5L contains five questions rated on a five-level scale, from which a utility index can be derived based on the recently developed preference-based scoring function (Ramos-Gohi et al. 2016). The BDI-II consists of 21 items conforming a global score, in addition to classifying patients according to their severity. The PHQ-9 allows to establish the diagnosis and severity of the depression. Statistical analysis: Floor and ceiling effects were examined. Reliability was assessed using Cronbach’s alpha coefficient. Structural validity was studied by confirmatory factor analysis (CFA) for categorical data. Convergent validity was studied by the Spearman correlation coefficient between EQ-5D-5L and BDI-II. We examined known-groups validity by comparing the EQ-5D-5L index among the different severity groups according to the BDI-II and PHQ-9 using the analysis of variance or Kruskal-Wallis test. RESULTS: The floor and ceiling effects in EQ-5D-5L index were 0% and 3.94%, respectively. Cronbach’s alpha coefficient was 0.77. The fit indexes of the CFA were excellent (RMSEA=0.036, CFI=0.999, TLI=0.995) and factor loadings were all statistically significant and >0.60. The correlation between the EQ-5D-5L index and BDI-II was -0.58. Patients with higher severity level, had significantly lower scores on the EQ-5D-5L (P<0.001). CONCLUSIONS: The results support the reliability and validity of the EQ-5D-5L questionnaire in patients with major depression disorder. Further, the hypothesis that the five items of the questionnaire make up a single factor (the utility index) is confirmed. Therefore, the recently derived EQ-5D-5L, could be very useful as an outcome measure, at least in patients with major depression disorder.

PRM156: CROSS-CULTURAL ADAPTATION AND VALIDATION OF THE PEDSQL CARDIAC MODULE VERSION 3.0

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OBJECTIVES: Develop a Russian version of the Pediatric Quality of Life Inventory (PedsQL) 3.0 Cardiac Module (J. Varni et al., USA). METHODS: In a prospective study a cross-cultural adaptation of the English-language questionnaire was done, the reliability of the new version (Cronbach’s alphas), constructive validity (comparison of responses of patients who had different ejection fraction), convergent validity (comparison of answers of PedsQL Cardiac Module and the PedsQL Generic Core Scale), sensitivity (retest after 4 months) were assessed. RESULTS: The study involved 99 patients aged 2-17 years with heart diseases accompanied by heart failure. Language and cultural adaptation of the questionnaire included: direct translation, reverse translation, expert evaluation, the formation of a preliminary version, approbation of the preliminary version, the formation of the final version and its validation. The reliability of the questionnaire was confirmed (Cronbach’s alphas was from 0.75 to 0.91). During the assessment of the constructive validity, it was shown that the level of quality of life was lower in children with the ejection fraction <60% than in children with higher ejection fraction values in all age groups (p <0.05). The evaluation of the convergent validity demonstrated the presence of the strong correlation between the values PedsQL Cardiac Module and the PedsQL Generic Core Scale (p<0.01). Test-retest were statistically significant for all scales (p <0.001). CONCLUSIONS: The appropriate psychometric characteristics of the Russian version of the cardiac module of the PedsQL 3.0 questionnaire recommend using it for research in the field of the quality of life in children with heart diseases.

PRM157: PREDICTING EQ-5D INDEX SCORES FROM PROMIS PROFILE 29 IN THE UNITED KINGDOM, FRANCE, AND GERMANY

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OBJECTIVES: Quality-adjusted life years (QALYs) are used for economic evaluations of clinical interventions. The EuroQoL (EQ-5D) index score is used as utility score for QALYs. It has been predicted in a US population sample from five PROMIS domain item banks: physical function, fatigue, pain impact, anxiety, and depression. The aim of this study is to validate this model in independent data from Europe and to compare it to a prediction model taking all seven PROMIS Profile domains into account. METHODS: We collected PROMIS Profile 29 and EQ-5D data in the general population of the United Kingdom (n=1,509), France (n=1,501), and Germany (n=1,502). We compared agreement using Bland-Altman analyses between observed and predicted utility scores for the US prediction model and for country specific linear regression models estimated in these samples. RESULTS: The EQ-5D predictions of
the US model underestimated health utility on average for the UK by 0.10 (95%CI 0.09-0.10; RMSE 0.18) and for France by 0.08 (95%CI 0.08-0.09; RMSE 0.17) points, but not for Germany 0.00 (95%CI -0.01-0.00; RMSE 0.11). Predictions based on regression models estimated in these samples come with smaller, but still substantial root mean squared error (RMSE UK: 0.13, France: 0.13; Germany: 0.10). We found systematic deviations from the linear prediction.

CONCLUSIONS: Keeping in mind that EQ-5D index scores range from 0 to 1, predictions from the PROMIS Profile 29 using either linear model are imprecise, regardless of taking five or seven PROMIS Profile domains into account.

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**PRM158: THE CYSTIC FIBROSIS IMPACT QUESTIONNAIRE (CF-IQ); QUALITATIVE DEVELOPMENT AND COGNITIVE EVALUATION OF A NEW PATIENT-REPORTED OUTCOME INSTRUMENT TO ASSESS THE LIFE IMPACTS OF CYSTIC FIBROSIS**

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OBJECTIVES: Patients with cystic fibrosis (CF) experience significant disease burden, including progressive pulmonary decline, reduced lifespan, treatment burden, and complex comorbidities. This multicenter study was designed to develop a patient-reported outcomes (PRO) instrument to assess the impact of disease burden on quality of life in patients with CF. METHODS: Semi-structured qualitative concept elicitation (CE) interviews were conducted with patients and caregivers for patients <18 years. CE interviews elicited qualitative reports of CF-related symptoms, impact of CF, and treatment experiences. After qualitative content analysis, data from CE interviews were considered alongside existing PROs, published literature, and expert opinion to develop a draft measure assessing key CF-related impacts. Three rounds of cognitive interviews evaluated respondent comprehension and supported refinement of the draft cystic fibrosis impact questionnaire (CF-IQ) instrument. RESULTS: Forty-two patients with CF and 22 caregivers from 8 centers in the US completed CE interviews for CF-IQ development. Patients were between 6 and 58 years and represented a broad range of disease severity (FEV1 range 22%-127% predicted); 57% were female, and 88% were white. CE interviews identified 57 unique CF-related impact concepts in domains including: activity limitations (physical, social, leisure); functional limitations (school, work); vulnerability/lack of control; emotional impact; treatment burden; and future outlook. Saturation of concept was achieved, a conceptual framework was developed, and a draft questionnaire was constructed. The findings from the 3 rounds (18 cognitive interviews) confirmed that the instructions, item content, and response scales were relevant, clear, and interpreted as intended by patients. CONCLUSIONS: The CF-IQ is a novel PRO developed as a standardized assessment reflecting domains to quantify disease impact in patients with CF. The domains and conceptual framework identified highlight the multifaceted impact of disease burden. CE and cognitive interviews support the content validity of the CF-IQ in patients with CF. Sponsored by Vertex Pharmaceuticals Incorporated

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**PRM159: NON-INTERVENTIONAL REAL-WORLD EUROPEAN STUDY QUANTIFYING THE BURDEN OF CENTRAL NERVOUS SYSTEM (CNS) METASTASES ON HEALTHCARE RESOURCE USE (HRU) IN PATIENTS WITH METASTATIC NON-SMALL-CELL LUNG CANCER (mNSCLC) – RESULTS FROM AN INTERIM ANALYSIS**

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OBJECTIVES: Limited information is available regarding CNS metastases impact on HRU and HRQoL for patients with mNSCLC in Europe. This ongoing study (MO39084) compares HRQoL and HRU in mNSCLC patients with and without CNS metastases alongside demographic/clinical characteristics and concomitant medications. METHODS: Patients ≥18 years with mNSCLC, CNS metastases documented 2–8 months before inclusion visit (V1), and a life expectancy ≥12 weeks are eligible (31 sites Germany/France). Three study visits were planned: V1, follow-up visit (6±3 weeks after V1), final visit (12±3 weeks after V1). HRU data are collected via validated patient questionnaires and clinical charts. Student’s T-test (continuous variables), chi-square test or Fisher’s exact test (categorical variables) were used for group comparisons. RESULTS: At data cut-off (29 May 2017), 123 patients were eligible: CNS metastases cohort n=49 and non-CNS metastases cohort n=74. Baseline characteristics were similar between cohorts: mean age 63 vs 67 years; 53% vs 66% male; mean BMI 23.6 vs 24.9 kg/m2; ex-smoker status 51% vs 47%; mean time since diagnosis 6.1 vs 5.4 months; ECOG PS 1 55% vs 54%, and 1-2 chronic comorbidities 51% vs 49%. At V1, 41% (CNS cohort) and 14% (non-CNS metastases cohort) had ≥3 metastatic sites (p=0.002). Dyspnoea (16% vs 31%, p=0.07), cough (14% vs 28%, p=0.07) and pain (12% vs 28%, p=0.03) were more common in the non-CNS metastases cohort. Similar HRU patterns were recorded in the cohorts before V1; no significant differences in number of hospitalizations (p=0.75), emergency room (p=0.22) or outpatient visits (p=0.22). Length of hospital stay was significantly longer in the CNS metastases cohort.
OBJECTIVES: Severe hypertriglyceridemia (sHTG) is a rare condition, complicated by episodes of acute pancreatitis (AP), which can cause variable inflammation, pain and/or life-threatening multi-organ dysfunction in acute attacks. Currently, there are no disease-specific patient reported outcome (PRO) measures evaluating signs and symptoms or dietary impact among patients who experience the effects of AP associated with sHTG. METHODS: In-depth, semi-structured interviews were conducted with 12 US-based participants with clinician confirmed AP associated with sHTG. Concepts from the literature informed the discussion guide and initial conceptual model. Individual patient experiences of AP associated with sHTG were explored to identify key symptoms and impact of dietary behavior, both during and between episodes. Transcripts were coded using thematic analysis. RESULTS: Participants’ age ranged from 28-63 years, 67% were female, 83.3% Caucasian and 16.7% Hispanic. Participants had a range of AP severity (one severe; six moderate; five mild) all with a previous triglyceride reading above 1000mg/dL, and at least one attack of AP within the last two years. All participants reported abdominal pain during and between attacks of AP and substantial changes to diet to prevent/minimise attacks of AP. Back pain, nausea, fatigue, distension/bloating, excessive sweating, and being hungry just after eating, were reported by ≥75% participants. Other symptoms that were also important and impacted quality of life included insomnia, excessive gas, vomiting and loose stools/diarrhea. Most symptoms were reported both during and between episodes. The conceptual model was refined based on patient input and used to develop two PRO measures evaluating signs and symptoms and dietary changes in AP associated with sHTG, reported during and between episodes. Items were drafted using patient-derived language. CONCLUSIONS: This research resulted in the development of two PROs with strong content validity. Psychometric properties of the measures will be explored in an upcoming study.
OBJECTIVES: Previous work examined whether preferences for hearing-related health states can be described using a sensory experience, in the form of an acoustic simulation of hearing loss, rather than using vignettes. This research examined whether utility values vary depending on how participants interact with the stimuli, and whether simulating healthy hearing as a comparator to simulations of hearing loss would increase the reliability of health valuations. METHODS: Single-sided deafness (SSD), a complete loss of hearing in one ear, was simulated. Several talkers were positioned within a virtual acoustic environment to create multi-talker conversations. 64 normal-hearing participants were asked to express their preferences for two hearing-related health states based on acoustic simulations using a time trade-off task. Participants either listened actively for a talker within the simulation and were asked to report what the talker said, or listened passively to the simulations without any further instructions. In 50% of participants, the simulations of SSD were presented with a simulation of perfect hearing health as a comparator. RESULTS: Actively listening to the simulations resulted in significantly lower utility scores compared to passively listening (mean difference -0.14, CI 0.03 to 0.25). On average, there was no effect on utility values from providing a simulation of perfect hearing health as a comparator to the simulations of SSD. However, providing a perfect hearing health comparator made utility values more reliable (ICC 0.81, CI 0.67 to 0.92) compared to when no comparator was provided (ICC 0.74, CI 0.57 to 0.88). CONCLUSIONS: The use of an active listening task together with a comparator simulation of perfect hearing health produces utility values more in line with those reported by patients. The use of a comparator simulation also increases the reliability of valuations, making the large-scale use of simulations more feasible by avoiding the need to obtain repeated valuations.

PRM163: EXPLORATORY ANALYSIS OF THE REASONS FOR CREATING WORLDWIDE TRANSLATIONS OF PATIENT REPORTED OUTCOME INSTRUMENTS

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OBJECTIVES: Key goals of translating Patient Reported Outcome questionnaires (PROs) are accuracy and comprehensibility; other important considerations are consistent terminology and translation choices within languages. One method to achieve this consistency is to create a single translation for a language, typically called a "worldwide" translation, intended for speakers across multiple countries. The reasons for creating this worldwide translation vary based on the needs of the project. The aim of this study was to quantify which stakeholders (e.g. sponsor, developer, or eCOA vendor) advocated for worldwide translations, and to begin to qualitatively delineate the reasons for those requests. METHODS: All worldwide translations produced from January 2010 to June 2017 were categorized according to the stakeholder that requested them and frequencies calculated for each category. A qualitative analysis of a randomly selected 5% of the sample was performed on project documents and communications in order to find common motivations for worldwide translations. RESULTS: 574 worldwide translations were found in the Corporate Translations project database, comprising approximately 3% of all projects. These translations, intended for use in two or more countries, were prompted by either the sponsor (70%), developer (29%), or eCOA vendor (1%). A review of project documents and communications showed that the most common sponsor reasons for creating a worldwide translation were to limit costs and satisfy logistical concerns dictated by the study sites, while developers frequently communicated a desire to increase consistency in key terms across multiple countries and easier updating in case of source text revision. CONCLUSIONS: Overall, worldwide translations constituted a small percentage of translation projects. In most cases, worldwide translations are created at the behest of the sponsor due to constraints on costs or time. There are deeper questions as to the underlying procedural distinctions between different worldwide translations that will be the topic of further investigation.

PRM164: ASSESSING METHODOLOGIES FOR HEALTH STATE UTILITIES IN PAEDIATRIC INDICATIONS FOR COST-UTILITY ANALYSES: REVIEW OF NICE TECHNOLOGY APPRAISALS FOR PAEDIATRIC INDICATIONS

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OBJECTIVES: Choosing an appropriate methodology for health state utilities is imperative when conducting a cost-utility analysis (CUA). This remains a challenge particularly in paediatric populations where direct utilities (from trials) are often not available. The objective of this review was to assess the methods used for obtaining utilities in prior National Institute for Health and Care Excellence (NICE), UK technology appraisals (TAs) submitted for paediatric indications. METHODS: A search was conducted on the NICE website in December 2016 to identify the TAs for paediatric indications. TAs which included patients aged <18 years, irrespective of the indication, were included in the
review. Revised TAs for which full information was not available were excluded. Data pertaining to basic information about the TA (e.g. intervention, indication), age, and methodology used for measuring utilities, and comments given by Evidence Review Group (ERG) were extracted in a pre-designed extraction grid. **RESULTS:** Out of a total of 405 TAs, data from 24 TAs for paediatric indications were identified. EQ-5D was used in 11 out of 24 submissions for measuring utilities and mapping from other non-preference based measures to EQ-5D was done in two submissions. ERG did not criticize the use of EQ-5D even though it is not recommended for use in paediatric populations. For submission of CUA to Health Technology Appraisal bodies like NICE, utility values derived from clinical trials is preferred over values obtained from literature as commented by ERG in one of the submissions. Mapping data to EQ-5D from a non-preference based measure using data collected from patients experiencing the treatment of interest is accepted as an alternative within the NICE reference case. **CONCLUSIONS:** In the absence of direct utility data from trials, mapping data from other measures to EQ-5D for obtaining utilities for CUA may be an appropriate methodology particularly for paediatric indications.

**PRM165: VALIDATION OF THE EQ-5D-5L IN PATIENTS WITH HIP OR KNEE OSTEOARTHRITIS**

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**OBJECTIVES:** The objective of the present work was to study the psychometric properties of the Spanish EQ-5D-5L questionnaire for patients with hip or knee osteoarthrits (OA), such as reliability and validity, including the structural validity. **METHODS:** We included 758 patients with hip or knee OA, who completed the EQ-5D-5L and WOMAC questionnaires. The EQ-5D-5L contains five questions rated on a five-level scale, from which a utility index can be derived based on the recently developed preference-based scoring function (Ramos-Goñi et al. 2016). The WOMAC consists of three dimensions (pain, stiffness, physical function). Statistical analysis: Floor and ceiling effects were examined. Reliability was assessed using Cronbach’s alpha coefficient. Structural validity was studied by confirmatory factor analysis (CFA) for categorical data. Convergent validity was studied by Spearman correlation coefficient between EQ-5D-5L and WOMAC domains. We examined known-groups validity by comparing the EQ-5D-5L index among the different groups according to WOMAC pain and function domains using the analysis of variance or Kruskal-Wallis test. **RESULTS:** The floor and ceiling effects in EQ-5D-5L index were minimal (<3%). Cronbach’s alpha coefficient was 0.86. Regarding the results of the CFA, fit indexes were excellent (RMSEA=0.073, CFI=0.995, TLI=0.990) and factor loadings were all statistically significant (P<0.001) and >0.50. The correlation between EQ-5D-5L index with pain or function WOMAC domains were very high (-0.688 and -0.782). Patients with a higher level of WOMAC pain or functional limitation, had significantly (P<0.0001) lower scores on the EQ-5D-5L. **CONCLUSIONS:** The results support the reliability and validity of the EQ-5D-5L questionnaire in patients with hip or knee OA, in addition to confirming the hypothesis that the five items of the questionnaire make up a single factor, that is, the utility index. Therefore, the recently derived EQ-5D-5L, could be very useful as an outcome measure, at least in patients with hip or knee OA.

**PRM166: THE SHORT TERM HEALTH RELATED QUALITY OF LIFE (HRQOL) IMPACT ON PATIENT AT THE INTERNAL MEDICINE CLINIC.**

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**OBJECTIVES:** Health related quality of life (HRQOL) of patients at internal medicine clinic is important because it adds depth to our understanding of how a disease, and its diagnosis and treatment affect them. No previous study has addressed the impact of them. The aim of our study is to assess the short term HRQOL outcomes of patients at internal medicine clinic using the Japanese version of EuroQol 5 Dimension (EQ-5D). **METHODS:** 70 undiagnosed patients who visited to our hospital from January 2017 to May 2017 were enrolled. All patients were visited our hospital without any diagnosis. This is a prospective study and data were collected by interview at the clinic. Patient evaluated their health status using five dimensions. The EQ-5D score were calculated based on the Japanese version of the value set. Primary outcome is the the norm of EQ-5D score at the first visit and at one month after diagnosis. **RESULTS:** There were 26 male (37.1 %) and 44 female (62.9 %). The median age was 45 (95% confidence interval [CI] 40.1-49.9). The median EQ-5D score at the first visit was 0.656 (95%CI 0.590-0.768) and it is lower than Japanese norm (0.853 in male and 0.808 in female). The median EQ-5D score at one month after diagnosis was 0.880 (95% CI 0.768-1.000) and it is higher than Japanese norm. **CONCLUSIONS:** This study focused...
on undiagnosed patients who visited our internal medicine clinic. It showed that EQ-5D score was decreased compared with the Japanese norm at the first visit but it improved after diagnosis. This finding suggest the value of measuring health status in undiagnosed patients by EQ-5D, because it would allow comprehensive evaluation of the patient’s health condition and add another dimension to the subjective symptoms and laboratory data.

PRM167: ACCURATE REPRESENTATION OF PATIENTS’ OPINIONS FOR DECISION-MAKING: ARE ONLINE HEALTH COMMUNITIES GOOD CANDIDATES?

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OBJECTIVES: The development of online patient communities worldwide has prompted questions about their ability to collect reliable information for a deeper understanding of patients’ health experiences and unmet needs. The goal of this research is (1) to analyse the key socio-economic characteristics of patient communities’ users and (2) examine their correspondence with national patients’ demographics. METHODS: A nationally representative sample of patients was extracted from the French Health Insurance Information System (SNIIRAM), which compiles information about long-term illnesses’ requests for exemption (ALD: affection longue durée). Patient-reported data from a patient platform (carenity.com) were collected and matched at disease-level with SNIIRAM sample for patients with multiple sclerosis, Parkinson’s disease, diabetes, and inflammatory bowel diseases. We produce bivariate descriptive statistics on the patient-reported data sample from Carenity (19,855 observations) and SNIIRAM sample (2,826,445 observations) for the following set of socio-demographic variables: gender, age distribution and residence area. Using one-tailed and two-tailed tests, we test for equality of proportions for those variables. RESULTS: Results suggest an over-representation of females for all pathologies in the patients’ community sample (p<0.001). Geographical distribution of patients’ community users is significantly equivalent to patients from SNIIRAM database (p<0.001) for all pathologies, with the exception of diabetes. Regarding age distribution, we observe an over-representation of young people and adults (from 25 to 54 years old, p<0.001), with a corresponding under-representation of seniors (>65 years old, p<0.001) for all pathologies. CONCLUSIONS: Carenity communities, compared with SNIIRAM database, reflect the main characteristics of online users willing to share experiences related to their disease, with an over-representation of female patients, aged from 25 to 54 years old. Health communities provide a new service for a swift collection and analysis of patient-reported outcomes in a real-world setting.

PRM168: DEVELOPMENT AND PSYCHOMETRIC EVALUATION OF AN OWNER-COMPLETED MEASURE OF FELINE HEALTH AND QUALITY OF LIFE

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OBJECTIVES: As pet healthcare and longevity continues to improve, assessing health-related quality of life (HRQoL) in companion animals becomes increasingly important. This study aimed to develop and evaluate the content validity and psychometric properties of an owner-completed measure of feline HRQoL in the US. METHODS: A 23-item, owner-completed, feline HRQoL measure was developed based on findings from an online survey completed by 45 pet-owners, and revised following qualitative interviews with 10 pet-owners of healthy cats which included both concept elicitation and cognitive debriefing activities. The psychometric properties of the resulting 22-item measure were evaluated in an observational study with 199 pet-owners of healthy cats who completed the instrument at baseline and two-week follow-up. Analyses performed included: assessment of missing data, response distributions, inter-item correlations, factor analysis, internal consistency (Cronbach’s alpha >0.70), test-retest reliability (Intraclass correlation coefficients [ICC] >0.70), multi-trait analysis (correlations >0.40), known-groups analysis and distribution-based estimation of clinically important differences (CIDs). RESULTS: There were no missing data. Item response distributions were heavily skewed, due to the sample being owners of healthy cats. Six items were deleted based on item-level analyses, qualitative findings and clinical relevance. Factor analysis supported a two-factor solution (healthy behaviours, clinical signs) with adequate model fit (Root Mean Square Error of Approximation: 0.09, Comparative Fit Index: 0.89). The resulting 16-item measure demonstrated good internal consistency and test-retest reliability (>0.70 for both). All but three items correlated strongest with their respective domains, supporting item-convergent validity. Significant differences in total scores across different feline health groups (p<0.001) provided evidence of known-groups validity. Distribution-based CID analyses indicated that a 4.63 point change in the total score is likely to be clinically important on a 0-100 scale. CONCLUSIONS: Findings provide evidence to support the reliability and validity of the feline HRQoL measure in pet-owners of healthy cats.

**OBJECTIVES:** To assess the suitability for use within economic evaluation of services targeted at older people of a commonly applied functional-status measure (the Barthel Index) by examining its convergent and discriminant validity when compared with a widely used generic preference-based instrument, the EuroQoL 5 dimensions 3 levels (EQ-5D-3L). **METHODS:** Data from a cross-section of 1,690 British older people were analysed. Convergent validity was investigated using spearman’s correlation, exploratory factor analysis (EFA), scatter plots, Krippendorff’s alpha, and modified Bland-Altman plots. Discriminant validity was examined using Kruskall Wallis tests, examination of ceiling effects and EFA. **RESULTS:** There was strong convergence between the BI total and EQ-5D-3L utility scores (spearman’s correlation = 0.51; Krippendorff’s alpha = 0.52 and only 6% of scores were outside the 95% limits of agreement in the Bland-Altman plots). Correlations between BI items and EQ-5D-3L dimensions measuring the same construct were weak to strong (0.05 ≤ absolute spearman’s correlation ≤ 0.57) and all in the hypothesised directions. In the exploratory factor analysis, some Barthel Index items cross-loaded onto the same factors as the EQ-5D-3L dimensions providing further evidence that the instruments were interrelated. Both instruments showed good discriminant validity and were able to discriminate between respondent characteristics and between underlying latent health constructs represented by the extracted factors from the EFA. **CONCLUSIONS:** The lack of perfect convergent validity between the instruments shows that the Barthel Index focuses more on physical functioning while the EQ-5D-3L measures much broader wellbeing concepts. The Barthel Index however demonstrated good discriminant validity comparable to that of the EQ-5D-3L and would therefore be equally useful for measuring subgroup differences within economic evaluation. In order to capture more physical-functioning-specific constructs not measured by the EQ-5D-3L, therefore, the Barthel Index can be used as complement to the former within cost-effectiveness analysis.

**PRM170: CLINICAL OUTCOME ASSESSMENTS FOR PATIENTS WITH HEMOPHILIA**

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**OBJECTIVES:** To identify the use of patient-focused clinical outcome assessments (COAs) in hemophilia A and B, and to explore regulatory-approved product labelling to understand the use and acceptance of such measures in hemophilia trials. **METHODS:** A structured review was performed of the literature, clinical trials, and regulatory labels to identify COAs used in hemophilia, focusing on patient reported outcome (PRO) measures. A critical review of relevant measures was conducted to identify any gaps in the evidence supporting these measures, guided by the requirements outlined in the FDA PRO Guidance. **RESULTS:** Over 150 COA measures had been identified from over 500 clinical studies and over 1000 publications. The identified measures can be grouped into global efficacy measures, symptom measures, Health-Related Quality of Life (HRQoL) measures, and activity limitations measures. Annualized bleeding rates and clinician reported measures of hemostatic efficacy were almost universally included in hemophilia studies and were the only measures to have demonstrated regulatory acceptance through inclusion in hemophilia product labels. Within both clotting factor and joint repair studies in hemophilia, the pain VAS was the most frequently used PRO, followed by the Haem-A-QoL, SF-36, EQ-5D, Haemo-QoL, and patient-reported efficacy scales. Over half of these studies did not report the Haem-A-QoL, SF-36, Hemofilia-QoL, PedsQL, a physical activity checklist, WOMAC, and Patient Global Assessment all captured at least one statistically significant result in the studies identified. **CONCLUSIONS:** Hemophilia symptoms, HRQoL, and functional limitations were all identified as salient patient focused concepts in hemophilia, but only annualized bleed rate and 4-point hemostatic efficacy scale have demonstrated regulatory acceptance. Hemophilia-specific PRO measures with strong psychometric properties should be evaluated in future clinical studies to help drive comprehensive OA measure strategy.

**PRM171: QUALITATIVE INTERVIEWS TO INFORM DEVELOPMENT OF A PATIENT REPORTED OUTCOME (PRO) STRATEGY IN RLBP1 RETINITIS PIGMENTOSA (RLBP1 RP)**

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**OBJECTIVES:** RLBP1 RP is a rare autosomal recessive form of retinitis pigmentosa (RP), characterized by night
blindness, prolonged dark adaptation, constricted visual fields and reduced macular function. This study aimed to better understand the patient experience of RLBP1 RP and to evaluate the content validity of existing patient reported outcome (PRO) instruments in this condition. METHODS: This qualitative study involved 90 minute, semi-structured, concept elicitation and cognitive debriefing interviews with patients with RLBP1 RP in Canada (n=10) and Sweden (n=11). Qualitative analysis of anonymized, verbatim transcripts was performed using Atlas.Ti software and thematic analysis methods. Participants were cognitively debriefed on The National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25), Low Luminance Questionnaire (LLQ) and four items of the Visual Activities Questionnaire (VAQ). RESULTS: Fourteen visual symptoms were reported. The symptoms most frequently reported were night blindness (n=21), difficulty adapting to changes in lighting (n=21) and difficulties seeing in bright lighting (n=18). Impacts on daily activities (n=21) and physical functioning (n=17) were important to participants. Other domains of quality of life affected included social functioning (n=21), emotional functioning (n=19), work and education (n=18), and psychological functioning (n=17). Participant understanding and interpretation of the NEI VFQ-25 and LLQ was mixed. Patients reported that examples in single items represented different levels of functional impairment. In addition, some items did not specify what lighting conditions should be considered when responding. LLQ items were more relevant to RLBP1 RP than NEI VFQ-25 items. The four VAQ items assessing light/dark adaptation were well understood and relevant to participants. There were both gaps and overlaps in conceptual coverage of the instruments. CONCLUSIONS: The symptoms of RLBP1 RP have a substantial impact on patients’ daily lives and physical functioning. Issues have been identified with conceptual coverage, relevance and patient understanding of the NEI VFQ-25, LLQ and VAQ in RLBP1 RP.

PRM172: CAN WE USE DEMQOL-PROXY WITH CONFIDENCE? ROBUST SOLUTIONS TO PRACTICAL PROBLEMS

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OBJECTIVES: For over a decade, DEMQOL/DEM-QOL-Proxy have provided a practical way of reporting health-related quality of life (HRQL) in dementia clinical research. When people with dementia are no longer able to self-report, DEMQOL-Proxy provides an alternative, though this is independent of the person with dementia’s own view. We aimed to provide: a practical way of using DEMQOL-Proxy on a large scale, psychometric justification for linking DEMQOL-Proxy scores to the person with dementia’s own self-report and a way of understanding what a person’s score means. METHODS: We conducted four analyses (n=1434 dementia patients; n=1030 carers attending a first appointment at Memory Assessment Services): 1) Classical Test Theory to evaluate a self-administered version of DEMQOL-Proxy; 2) Rasch Measurement Methods (RMT) to investigate whether DEMQOL/DEM-QOL-Proxy could be placed on a common metric to develop an equated score for DEMQOL-Proxy; 3) anchor and distribution based methods to determine estimates of minimal important difference (MID); and 4) RMT to identify the item descriptions related to this clinical difference. RESULTS: 1) Self-administered version of DEMQOL-Proxy met established criteria for reliability (internal consistency) and validity (convergent, discriminant and known groups); 2) RMT findings supported equating DEMQOL/DEM-QOL-Proxy (overall fit to the model; no mis-fitting items) after addressing specific issues (eight disordered items requiring re-scoring, four pairs locally dependent items, and five items showing DIF); 3) MID statistics ranged between 2 and 6 points (100 point scale); 4) Items characterising different levels of HRQL on the DEMQOL/DEM-QOL-Proxy include: low negative emotion (high-end scale); worry about cognitive decline (mid-range scale); and worry about social situations (low-end scale). The most conservative 6-point MID reflected a one-response category difference. CONCLUSIONS: We recommend that DEMQOL and DEMQOL-Proxy continue to be used together when possible. We have determined methods of administering and scoring DEMQOL-Proxy that mean it can now be interpreted with confidence.

PRM173: RELIABILITY AND VALIDITY OF THE MOBILITY SECTION OF THE PROSTHESIS EVALUATION QUESTIONNAIRE AND ITS MODIFIED VERSION. DO THEY MEASURE THE SAME CONSTRUCT?

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OBJECTIVES: The Prosthesis evaluation questionnaire (PEQ) is used to assess patient-reported prosthesis-related quality of life. PEQ mobility section consists of 12 items. This study assessed the properties of the original mobility section of the Finnish version of the PEQ instrument on a visual analog scale (VAS) and its modified version with five response categories. METHODS: Patients having undergone major lower extremity amputation for various reasons were recruited for this cross-sectional study and completed the PEQ instrument (scale, 0-100 points) and its modified mobility section, the Locomotor Capabilities Index (LCI-S) (scale, 0-48 points), the Houghton scale, the 1SD health-
related quality of life instrument, and answered general health and pain questions on a VAS. Participants who completed the mobility sections twice (n=117) in a 2-week interval were included. The two versions of the PEQ mobility section were compared with each other and with the other instruments. **RESULTS:** Mean (SD) scores of the original and the modified mobility section were 58 (25) and 31 (13) and coefficients of variation 0.42 and 0.43, respectively. Reproducibility (intraclass correlation coefficient) was consistent between the measures (0.87 and 0.85, respectively). Even though Spearman’s correlation coefficient was high (r=0.83) and Kendal coefficient of concordance excellent (0.91), considerable differences were noted between the two measures. Significant correlation (p<0.001) was found for both measures with the PEQ scales of Utility, Well-being, and Social burden. The original section had significant correlation with the scales of Frustration and Perceived Responses (p<0.01 and <0.001, respectively). There were differences in correlations with all other patient-reported instruments. **CONCLUSIONS:** The original and the modified mobility section of the PEQ have moderate measurement differences. Thus their results are not directly comparable. Nonetheless, both measures are reliable and valid, but the modified version with five response categories is easier to complete and analyze in clinical work.

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**PRM174: ELECTRONIC PATIENT-REPORTED OUTCOMES: ARE THERE GAPS BETWEEN GUIDANCE AND ISSUES ENCOUNTERED IN PRACTICE?**

**OBJECTIVES:** Electronically captured patient-reported outcomes (ePRO) have become essential in clinical research and are a welcome platform to promote the patients’ perspective on how they feel function and survive. Regulatory agencies and working groups have published guidance; yet between the various stakeholders involved in the process, issues and ambiguities are readily encountered in practice. The aim of this research was to summarize current guidance and make comparisons to issues identified in practice. **METHODS:** A pragmatic literature search was conducted in PubMed from January 2007 to April 2017 to identify key articles reporting methodology or recommendations for ePRO development or migration. In addition, the authors identified additional publically available documents based on their experience and by searching websites of key working groups and organizations in the ePRO field. Issues encountered in practice were identified from various stakeholders including a panel of PRO experts (including the study authors) working in the field and from a survey sent to corresponding authors/publishers of questionnaires (n=28). **RESULTS:** From the PubMed search, a total of 25 articles or conference abstracts, with a primary focus on ePRO methods, good practices and recommendations, were selected. In addition, the authors identified over 16 regulatory documents or presentations/guidance from key working groups or organizations in the ePRO field. Content mainly addressed migration from paper to ePRO systems: general implementation considerations and migration study methodology to document adequacy. The identification of issues encountered in practice is on-going (April-June 2017). Results from the panel discussion and the questionnaires’ author/publisher survey are currently analyzed. A comparison of these results with the content of the documents retrieved during the literature search will be undertaken to identify gaps and unanswered questions. **CONCLUSIONS:** Publically available guidance provides a useful starting point for the general process of ePRO development/migration with probable room for improvement from a practical perspective.

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**PRM175: THE NEED FOR DEVELOPING A DECISION AID TOOL ABOUT FEEDING OPTIONS**

**OBJECTIVES:** To identify the characteristics of feeding options that may influence the decision-making process of switching from oral to enteral tube feeding (ETF) and that should be included in a Patient Decision Aid to achieve shared decision making. **METHODS:** A systematic search regarding to studies of patients’ and surrogate decision-makers’ perceptions for ETF nutrition was performed in Medline, Cochrane Library and ISI-WOK. European and North-American studies including original articles, reviews, and congress communications, published in English or Spanish between January 1st 2005 and June 6th 2016, were selected. The quality of these studies was assessed using Oxford Centre for Evidence-based Medicine levels of evidence. **RESULTS:** Of the 742 publications identified in the literature search, 7 were included (1 systematic review, 5 original articles and 1 congress communication). Thirteen items which may potentially influence the decision-making process of switching to ETF were identified. Eight characteristics: loss of food tasting, loss of life normality, loss of independence, loss of social role, feeling of blame and concerning about permanent loss of ability to eat, perceived loss of dignity and loss of quality of life, are
perceived by the decision makers as disadvantages of ETF and could hamper the decision to start ETF. Three items: less time needed for feeding, best caloric control and longer overall survival are perceived as benefits of ETF and could promote its implantation. Two additional items have an unclear outcome in the decision-making process: potential feeding complications and patient-caregiver relationship during feeding, that represents an emotional connection between them but as well a stressful situation. **CONCLUSIONS:** Most of the potential factors identified are perceived as disadvantages, which may contribute to delay the switch to ETF. These results highlight the need to develop a decision aid tool aimed to clarify these aspects and facilitate the decision-making process.

**PRM176: REDUCING COGNITIVE BURDEN IN DISCRETE CHOICE EXPERIMENTS**

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**OBJECTIVES:** Challenges arise when discrete choice experiments (DCEs) involve many attributes. Two methods to deal with many attributes are Partial Profiling and Hierarchical Information Integration, but they require additional assumptions and pose practical difficulties. We present a new approach, fold-in-fold-out (FiFo), which makes it possible to retain all necessary attributes while reducing the cognitive burden. **METHODS:** A DCE was conducted to quantify contributions of various aspects of COPD to its burden of disease. Choice sets consisted of 15 attributes with three levels. In order to make the choice task feasible, 13 attributes were grouped into three dimensions. In some choice sets, all dimensions were folded-in: all attributes in that dimension were set at the same level. In most sets, one dimension was folded-out, so attribute levels varied. In the Bayesian mixed logit analysis extra parameters were added: (1) \(\phi\) for additional complexity in fold-out choices, and (2) \(\lambda_1, \lambda_2, \lambda_3\) for differences in choice behaviour due to each dimension being fold-out or in. Raw regression coefficients represented attributes’ fold-in states. Folded-out could be represented by coefficient \((1 + \lambda)\). A burden of disease Index on a 0-100 scale was developed by extrapolating coefficients, without and with partial adjustment to fold-out status. The latter was considered the best representation of the choice context. **RESULTS:** The \(\phi\) parameter indicated that folding out led to more complexity and to less consistency. The \(\lambda\) parameters showed that attributes got more weight when fold-out. When no \(\lambda\) adjustment was made in the extrapolation, the fatigue attribute made the largest highest contribution to the Index (maximally 14 points). With adjustment, limitations at daily activities became equally important (11 pt for both), while these limitations seemed considerably less important without adjustment (8 pt). **CONCLUSIONS:** FiFo makes DCEs with many attributes feasible, but requires more complex statistical models with additional parameters.

**PRM177: THE PATIENT-REPORTED APNEA QUESTIONNAIRE (PRAQ): A PROM OPTIMIZED FOR USE ON BOTH INDIVIDUAL PATIENT AND AGGREGATE LEVEL**

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**OBJECTIVES:** We aimed to create a patient-reported outcome measure (PROM) for patients with obstructive sleep apnea (OSA) that is optimized for use on an individual patient level to improve patient care and on an aggregate level for outcome measurement. **METHODS:** 35 patients with OSA and 30 healthcare professionals reflected on the importance of different topics and items from existing OSA-related quality of life PROMs. They also gave their opinion on which topics they would like to discuss in clinical practice. Based on the collected information, a working group consisting of two researchers, a patient and a physician selected topics and items, that together formed the Patient-Reported Apnea Questionnaire (PRAQ). Subsequently, a validation study led us to identify a subset of items of the PRAQ that can together be optimally used for outcome measurement. **RESULTS:** The PRAQ consists of 40 items distributed over 10 topics, including topics that are directly related to OSA (sleepiness, tiredness) and less directly related to OSA (emotions, social interactions). The validation study identified a subset of 32 items and 6 domains of the PRAQ that can together be optimally used for outcome measurement. **CONCLUSIONS:** The PRAQ can be employed in the following way: patients complete all items of the PRAQ before their consultation, the results of which will be discussed with a healthcare professional; and the aggregate outcomes of groups of patients can then be studied by making use of a subset of the completed items. This is beneficial for patients, who get feedback from clinicians on their results, for physicians, who quickly gain insight into their patients’ main problems, and for sleep centers that wish to collect outcome data, because it ensures a steady stream of data due to integration into clinical practice. This aggregate data can be used as management information and for continuous quality improvement.
**PRM178: EVALUATION AND VALIDATION OF THE PROACT MEASURES FOR CANCER PATIENTS AND INFORMAL CAREGIVERS**

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**OBJECTIVES:** In the PROACT study we developed two scales to enable a broader evaluation of the impact of cancer and cancer treatment, measuring ‘real world’ roles and responsibilities such as caring for others and financial and employment responsibilities. Here, we report the initial evaluation and validation. **METHODS:** The PROACT measures have 29 items for patients (intended to be administered alongside FACT-G), 60 for caregivers (standalone). Participants completed the PROACT measure alongside FACT-G, WHOQOL-BREF and SDI (patients) and WHOQOL-BREF and CQOLC (caregivers) at baseline and PROACT measure alone after 7 days. Recruitment was from 11 UK sites, stratified by age and tumour site. **RESULTS:** Patients: 135 patients with stage III/IV lung, melanoma, gynaecological or breast cancer completed baseline questionnaires; 128 completed test-retest. Age ranged from 33-85, median 61 years. The PROACT questionnaire showed good internal consistency (Chronbach’s α = .901) and test-retest reliability (ICC=.859). Correlations with validation measures were strong (FACT-G r=.653; SDI r= -.759; WHOQOL-BREF r=.653). There was no evidence of floor/ceiling effects (total score). Rate of missing data was low (.006% baseline; .005% retest). Caregivers: 110 informal caregivers completed baseline; 103 completed test-retest. Age ranged from 18-88, median 60 years. Relationship to patient was partner/spouse 83 (75.5%), child 14 (12.7%), friend 5 (4.5%), sibling 4 (3.6%), parent 2 (1.8%), other 2 (1.8%). The PROACT questionnaire showed good internal consistency (Chronbach’s α = .92) and test-retest reliability (ICC=.894). Correlations with validation measures were strong (CQOLC r=.837; WHOQOL-BREF r=.710). There was no evidence of floor/ceiling effects (total score). Rate of missing data was low (.0025% baseline; .001% retest). **CONCLUSIONS:** We developed two scales to measure broad life impacts of cancer for patients and informal caregivers. These performed well in initial evaluation and will be validated in a large study with broader tumour sites/stage to test they are sufficiently generic and appropriate for use in clinical trials and real world studies.

**PRM179: TOO BROAD TO BE SENSITIVE? EXPLORING THE RESPONSIVENESS OF THE ICECAP-O CAPABILITY WELLBEING MEASURE COMPARED TO THE EQ-5D-3L TO THE CHANGE OF CLINICAL AND QOL ASPECTS IN PEOPLE WITH PARKINSON’S**

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**OBJECTIVES:** The vision of the ICECAP-O measure is to enable economic evaluations to incorporate capability wellbeing. This broader wellbeing scope, however, may generate concerns over the measure’s sensitivity to capture specific changes in a narrower health-focused context. This study aims to assess the responsiveness of the ICECAP-O to the clinical and quality of life (QoL) changes in people with Parkinson’s. **METHODS:** The ICECAP-O, EQ-5D-3L, PDQ-39 (a Parkinson’s specific QoL), demographics and clinical characteristics were collected from 1,023 participants with varying severity of Parkinson’s at intervals two years apart in the PD MED trials. The Hoehn and Yahr (H&Y) motor symptom clinical measure, PDQ-39 summary index (PDQ-39-SI) and its eight dimension scores were used as external indicators to classify participants to five change groups: largely/slightly improved/deteriorated, and no change. Correlation coefficients, standardized response mean (SRM), and effect size (ES) statistics of the change were used to evaluate the responsiveness of ICECAP-O and EQ-5D-3L. **RESULTS:** The mean age of participants was approximately 74 years, with a mean duration since Parkinson’s diagnosis of 6.54 years. The ICECAP-O change score was slightly more strongly correlated with PDQ-39 (r = 0.526) than the EQ-5D-3L (with PDQ-39: r = 0.483). Consistent with this was that the ICECAP-O was associated with a larger magnitude of SRM in all of the four change groups to the change of PDQ-39-SI than EQ-5D-3L. Moreover, it was shown to be slightly less responsive to the change of H&Y than EQ-5D-3L. Overall, there was no statistically significant difference in the SRM and ES statistics between ICECAP-O and EQ-5D to any of the external indicators. **CONCLUSIONS:** The broad scope of ICECAP-O could provide rich information on the capability wellbeing of patients without compromising its sensitivity to the clinical and specific QoL change in the Parkinson’s population.

**PRM180: TERMS REQUIRING MULTIPLE TRANSLATIONS OR A DESCRIPTIVE TRANSLATION IN THE TARGET LANGUAGE AND VICE VERSA**

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**OBJECTIVES:** Clinical Outcomes Assessments (COAs) often contain terms that have no equivalent one-word translations in the target language. They can also contain terms or expressions that may be seen as including redundancies if they were literally translated. The aim of this study is to investigate why certain terms do not have a succinct equivalent translation and how the linguistic validation (LV) process enables their identification and
resolution. **METHODS:** Looking back through 8 COAs that underwent linguistic validation, examples from 10 language pairs were analysed of key terms which had no direct equivalent in the target language or for which there was only one equivalent where the English source used several synonyms. The translations of the terms were collated from the back translation review stage where the differences with the source were most apparent, and analysed. **RESULTS:** Issues and resolutions were found in 100% of the projects reviewed. One example is the term ‘downhearted’, translated into Hiligaynon (Philippines) descriptively as ‘dismay on mood’. Such emotive terms can be interpreted differently across cultures, meaning a more elaborate translation may be required. Various technical terms materialized as being problematic because they weren’t widely used or known in the target country. For example, it was necessary in an Afrikaans translation to provide the name ‘MEM caps’ in English as well as an explanation in brackets (‘cap that can count pills’). **CONCLUSIONS:** Where a term does not possess a direct equivalent translation, it may be necessary to introduce several terms or a description to the translation to fully convey the meaning. Alternatively, translations might benefit from being more concise. Within the LV process, it is possible to identify areas lacking succinct equivalent translations and to avoid accidently conveying more specific, less specific or alternative meanings in order to achieve conceptual equivalence.

**PRM181: ASSESSING HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH PSORIASIS COMPARED WITH THE PORTUGUESE POPULATION**

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**OBJECTIVES:** To assess the health-related quality of life (HRQoL) in patients with psoriasis (PsO) and to compare with the Portuguese general population. It also aims to explore the associations between HRQoL and sociodemographic variables. **METHODS:** Data came from a cross-sectional study in patients with psoriasis (PsO) in Portugal, the PeSSoA study (recruitment period: Jun-Jul 2016). Patients with PsO aged 18 or more (n=564) filled-in a questionnaire that included HRQoL measured by the EQ-5D-3L, medical history, health behaviors, PsO related social impact, healthcare resources use, sociodemographic characteristics, among others. Descriptive statistics were used to describe the EQ-5D-3L scores of psoriatic patients and parametric tests were used to compare these scores in different types of PsO patients. Comparisons with normative data HRQoL from the Portuguese population were also carried out. Regression analyses were used to identify factors associated with HRQoL. **RESULTS:** The burden of PsO was observed mainly in the EQ-5D-3L pain/discomfort (PD) and anxiety/depression (AD) domains. The intensity of these problems was significantly higher in respondents with psoriatic arthritis and plaque PsO. HRQoL of respondents with PsO was related to sociodemographic variables and was lower (MeanEQ-5D-3L=0.75; ranging from -0.11 to 1.00) when compared with the Portuguese population (MeanEQ-5D-3L=0.76; ranging from -0.50 to 1.00). Psoriatic arthritic patients had a lower HRQoL (MeanEQ-5D-3L=0.62; ranging from -0.11 to 1.00) than other psoriatic patients. **CONCLUSIONS:** Suffering from PsO has a significant impact on self-perceived HRQoL, with more impact on PD and AD. These results show the importance of using HRQoL instruments as routine in population surveys or in clinical settings.

**PRM182: THE INFLUENCE OF AGE ON PATIENT ATTITUDES AND ACCEPTABILITY TOWARDS USING THEIR OWN MOBILE DEVICE TO RECORD PATIENT-REPORTED OUTCOMES DATA IN CLINICAL TRIALS**

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**OBJECTIVES:** To evaluate the influence of age on attitudes towards the use of “bring your own device” (BYOD) to record patient-reported outcomes data in clinical trials. **METHODS:** Subjects entering a health questionnaire study using BYOD and a provisioned device were asked to complete a questionnaire assessing their attitudes towards BYOD use in clinical trials. **RESULTS:** 155 subjects (72 male, 83 female) aged 19-69 years [mean 48.6 ± 13.1; 19-40: 43 (28%), 41-60: 80 (52%), >60: 32 (21%)] with a range of conditions resulting in chronic pain entered the single-center study. Proportionately more >60 year olds presented with tablet devices compared to the other age groups (9%, 10% and 38%, respectively). 16 subjects (10%) encountered difficulties downloading the study app (2%, 14% and 13% of the three age categories, respectively). More subjects >60 years were unfamiliar downloading apps (0%, 2.5% and 12.5% respectively), and fewer felt definitely/probably able to download a study app without assistance (95%, 94% and 81% respectively). Over 90% of subjects in each age category would definitely or probably be willing to download an app on their own device for a forthcoming trial, with 135 (87%) reporting no concerns in doing so. Of those identifying a concern, a higher proportion were >60 years old (12%, 10% and 22%, respectively). A lower proportion of the youngest age group identified that a provisioned device would be more convenient (7%, 15% and 13%, respectively). **CONCLUSIONS:** Amongst our sample there was good acceptance for the use of BYOD in clinical
trials including subjects >60 years old, though those over 60 were more likely to identify concerns about downloading the app. Concerns cited could be mitigated by assistance downloading, training, information and good app design. This study required subjects to use their own mobile device, and attitudes in the wider population may differ.

**PRM183: COMPARING THE METHODS OF INCORPORATING THE HEALTH RELATED QUALITY OF LIFE OF ADVANCED CANCER PATIENTS IN ECONOMIC MODELS**

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**OBJECTIVES:** Considering quality of life in oncology is particularly important, given that extension of life provided by treatments are often associated with large disutilities. There are currently several methods and opinions on the best predictor of health-related quality of life (HRQL) for patients with advanced cancers. We describe and assess the methods being used in recently published economic models, the predictors of HRQL chosen (if available) and the pros and cons associated with these methods. **METHODS:** Recently published NICE Technology Appraisal Guidance reports relating to advanced cancer were chosen as a sample of recently undertaken economic models. The following information was extracted for each of these models from the available reports: how HRQL was modelled and what information and data the HRQL estimates were based. **RESULTS:** 9 economic models of advanced cancer patients were assessed and their chosen method for HRQL prediction extracted. The majority derived their HRQL estimates from trial-based standardised instruments to elicit preferences. These were both generic (e.g. EQ-5D-5L) and disease specific instruments (e.g. EORTC QLC-C30). However, some models simply used utility estimates derived from published literature. Some of the submissions provided detail on the approaches used to estimate the best predictor of utility within their models. Two submissions linked disease progression to HRQL: another included both time to death and disease progression. Finally, another included fixed covariates for progression status, treatment arm and an interaction variable. **CONCLUSIONS:** The results showed no clearly recognised best practice for incorporating HRQL in the oncology economic modelling literature reviewed. There are several methods being used and there are advantages and disadvantages associated with each technique. These include data limitations, small samples and lack of the correct data being collected. There are also statistical issues with HRQL associated with time to death in models that use Markov model framework.

**PRM184: EVALUATING PATIENT REPORTED OUTCOMES COMMONLY USED IN CURRENT LUNG CANCER CLINICAL TRIALS**

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**OBJECTIVES:** Lung cancer continues to be the most prevalent cancer worldwide. As new treatments are developed there is a greater need for incorporating the patient perspective and a number of patient reported outcomes (PROs) have been developed specifically for lung cancer. This study aimed to conduct a brief review of PROs used in lung cancer clinical trials. **METHODS:** A search was conducted using clinicaltrials.gov, to identify lung cancer clinical trials and the primary, secondary and exploratory PRO measures used in these trials. The search was restricted to interventional clinical trials that were currently recruiting and without results. **RESULTS:** The search yielded 186 current trials. The PROs most frequently used in these clinical trials were the EORTC-QLC C30 (n=56), the EORTC-QLC LC13 (n=32), the FACT-L (n=16), the EQ-5D (n=15) and the MDASI-LC (n=6). In a majority of cases (88%), these were secondary endpoints. The EORTC-QLC LC13, FACT-L and MDASI-LC were all developed specifically as lung cancer measures, but were not the most frequently used. Each of the PROs was reviewed in accordance with regulatory guidelines, evaluating the advantages and drawbacks of each with respect to context of use. For example, although the EORTC-QLC LC13 is the most commonly used symptom PRO, it is an additional module to the EORTC-QLC C30 and used together, there have a total of 43-items. Time to complete this measure and associated patient burden must be considered. **CONCLUSIONS:** Selecting the most appropriate PRO measure as an endpoint during cancer clinical trials is important to provide full insight into the condition and treatment benefits. There are multiple existing validated measures developed for lung cancer and a number of comparisons can be made between them. The differences between the most commonly used measures have been summarised in this study and should be considerations when selecting a suitable measure for use in clinical trials.

**PRM185: FUNCTIONAL ASSESSMENT AFTER TREATMENT OF UPPER EXTREMITY SOFT TISSUE SARCOMAS USING STRUCTURED OUTCOME MEASURES: A SYSTEMATIC REVIEW**

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**OBJECTIVES:** Treatment of soft tissue sarcomas (STS) of the upper extremity can have an impact on extremity function. The authors conducted a systematic literature review to identify which structured outcome measures have
been used to evaluate the upper extremity function after treatment of STS. METHODS: The authors searched the PubMed database to identify relevant articles using predefined search terms. Two independent reviewers assessed article eligibility. Articles written in English using a defined system to assess upper extremity function after treatment of STS were included. The reference lists of eligible articles were reviewed to identify relevant articles. RESULTS: The search yielded a total of 1448 studies of which 83 articles met the inclusion criteria. Three most commonly used outcome measures were the Musculoskeletal Tumour Society Score (MSTS) -93 (n = 56), Toronto Extremitv Salvage Score (TESS) (n = 19) and MSTS -87 (n = 16). Most articles had less than ten upper extremity STS patients (66.3%), or did not report STS patients' function independently from other tumours (41.0%) or from lower extremity tumours (13.3%). CONCLUSIONS: Few studies have specifically assessed the functional outcome after treatment of upper extremity STS. There was much variance in how findings had been reported making comparison of functional outcome among different treatment centres challenging. Further investigations are needed to clarify what would be the optimal instrument for assessing upper extremity functional outcome in the treatment of soft tissue sarcoma.

PRM186: QUALITATIVE RESEARCH METHODS FOR COLLECTING, ANALYZING, AND PRESENTING PATIENT-REPORTED DATA ON NOTICEABLE AND IMPORTANT CHANGE IN DISEASE-RELATED SIGNS AND SYMPTOMS

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OBJECTIVES: This study demonstrates how qualitative research methods can help assign meaning to change observed in patient reported outcome (PRO) data. METHODS: In an anonymized PRO instrument development study, data were collected to inform noticeable and important change in signs/symptoms from the patient perspective. During concept elicitation interviews (CEIs), participants rated severity of signs/symptoms on a ‘0’ to ‘10’ numeric rating scale and indicated the minimal change needed in that sign/symptom to be (i) noticeable and (ii) important. During cognitive debriefing interviews (CDIs), participants completed the developed PRO questionnaire on a five-point verbal rating scale and indicated which alternate response would represent a (i) noticeable and (ii) important change. Qualitative data were coded using Atlas.ti and numeric responses were characterized via descriptive statistics. Noticeability and importance ratings were generated by subtracting those values from the severity ratings for each sign/symptom. RESULTS: Twenty subjects participated (mean age=42.7 years, 55.0% male) in CEIs. For the two most frequently reported concepts (fatigue/tiredness, n=15 and impaired vision, n=12), a mean change of 2.64 (SD=1.12) and 2.22 (SD=1.62) was “noticeable,” and a mean change of 2.82 (SD=1.54) and 2.63 (SD=1.58) was “important,” respectively. Twelve subjects participated (mean age=36.9 years, 17.7% male) in CDIs and fatigue/tiredness was evaluated in two items and impaired vision in one item. Mean noticeable ratings were 1.38 (SD=0.52), 1.44 (SD=0.53), and 1.14 (SD=0.38). Mean importance ratings were 2.00 (SD=0.63), 1.75 (SD=0.71), and 1.29 (SD=0.49). CONCLUSIONS: As expected, subject reported “noticeable” change was less than what was reported as “important” change. On average, for the developed questionnaire, subject responses indicated that a 26% to 40% improvement on the sign/symptom scale could characterize a clinically important response. The methods discussed here can be used to inform treatment responder definitions and, more broadly, as supportive evidence for interpreting efficacy results in clinical trials.

PRM187: THE RISKS IN TRANSLATING SMARTPHONE STRINGS FOR MEDICAL STUDY SMARTPHONES APPS & SMARTWATCHES

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OBJECTIVES: Recently there has been an increase in the ‘Bring Your Own Device’ approach to clinical studies as a means of participants carrying out Patient Reported Outcomes (PROs) on their own smartphones or smartwatches. The aim of this study is to evaluate the risks in translating smartphone strings used in such apps and to highlight solutions in conveying the context of individual strings. We will focus on a study related to mobility being translated into France-French. METHODS: This Linguistic Validation project underwent the following steps outlined by the ISPOR Principles of Good Practice: Preparation (including concept elaboration); Dual Forward Translation; Reconciliation; Editing; Dual Back Translation; Back Translation Review and Proofreading. During Back Translation Review, the risks in translating smartphone strings were analysed, establishing which translations needed further clarification and updates. RESULTS: When reviewing the Back Translations, 7% of items required updates. Of these; 82% were misinterpretations of the source due to lack of context and 18% were formatting updates to ensure the translations were short enough to fit within a smartphone screen. Without being able to refer to the English source in screenshot form, translating these smartphone strings into French presented two specific areas of risks. 1) Many translations were too long due to additional clarifications being required in French. 2) French occasionally required several translations depending on the specific context of each source string (e.g. ‘skip’ was both ‘ignoré’ and ‘non
CONCLUSIONS: To provide clear and accurate text for the app, it is important to provide linguists with screenshots and concept elaborations from project initiation. This aids the linguist to retain the appropriate character length for the smart-device displays. French texts often require elaboration so developers should consider flexibility and precision of language when developing the app. Both elements ensure accurate Linguistic Validation of smartphone strings and a reduced need for edits.

PRM188: “IT’S ALL RELATIVE” – EXPLORING THE CHALLENGES DURING CULTURAL ADAPTATION OF FAMILY NAMES IN PRO (PATIENT REPORTED OUTCOMES) QUESTIONNAIRES

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OBJECTIVES: Some PRO questionnaires list family members to establish genetic links in illnesses, or when referring to a guardian. The aim of this study is to investigate challenges in linguistically validating common family titles in the context of PRO questionnaires. METHODS: 18 common family titles were selected for use in this research. Native linguists of 31 languages worldwide, experienced in translating PRO questionnaires, provided translations for the titles as well as explanations regarding family culture in their respective countries. The results were compiled and analysed to identify variations. RESULTS: Not a single language studied has a direct equivalent of all 18 titles. For “brother” and “sister”, there are variations required in 10% of the languages. For example, in Vietnamese, the language distinguishes between older and younger brother/sister. There is no distinction between “Half-brother/sister” and “step-brother/sister” in Hindi whilst in Sesotho there is no distinction between a half, a step and a full sibling. In Arabic for Egypt and Israel, “step-brother/sister” are not considered as relatives and have no specific equivalents. Instead, they would be described in the translation as “son of father’s wife/mother’s husband”. In some cultures, “Aunt/uncle” can also be a term of respect for an older man/woman regardless of genetic connection. These differences in language and culture can bring up many issues and could potentially cause confusion for participants. It may also require changes to the format, number of response options, or required space especially in ePRO instruments. CONCLUSIONS: Where a title does not have an equivalent translation, it may be necessary to provide the closest alternative/s or a description to fully render the meaning and cultural intricacies in the context of the questionnaire. Through back translation and use of a Concept Elaboration as part of the Linguistic validation process, this can be identified and investigated to ensure objective pooling of data.

PRM189: FINDING THE PATIENT IN CLINICAL MEANINGFULNESS THROUGH RIGOROUS COGNITIVE INTERVIEWS

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OBJECTIVES: Since the late 1980s, several methods have been introduced and used to interpret health-related quality of life (HRQoL) and patient-reported outcome measures (PROs) results. The objective of all of them is to devise a way to determine meaningful change in HRQoL and PRO domain or instrument scores. Although there are examples of including patient input into what constitutes a meaningful change that is important to patients and clinically relevant, very limited work has been done. The objective of this study was to document the ways in which patients evaluate scales and think about the meaning of moving up or down on that scale. METHODS: Using a semi-structured interview guide to debrief several validated and reliable PROs with MID estimates, trained qualitative interviewers explored patients’ meaning of movement on a scale in several projects. These varied projects produced audiotapes and transcripts of patients’ verbatim reports, which were analyzed using Atlas.ti and synthesized to document how patients think when faced with a scale and what would make them choose an alternative response. RESULTS: Results indicate that not all patients understand scales as they are intended to be used and that this may be influenced by sociodemographic and cultural factors; that patients give relatively consistent, sensible reasons for what constitutes meaningful change when the scale is comprehensible to them, and clinician and patient definitions of meaningful change differ. CONCLUSIONS: There is a gap in the clinical meaningfulness research that often excludes the input of patients entirely or uses it in ways that are often too late to make a difference. This research points to methods that can be used to better understand what changes in health status patients want to see from an intervention as a starting point, not to be determined post hoc.

PRM190: COGNITIVE DEBRIEFING OF THE DMD-SPECIFIC MEASURES OF PHYSICAL FUNCTIONING – CAREGIVER QUESTIONNAIRE

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OBJECTIVES: Duchenne muscular dystrophy (DMD) is a rare, fatal, X-linked recessive disease that causes
progressive muscular degeneration. The DMD-Specific Measures of Physical Functioning – Caregiver Questionnaire (DMD-CQ) is an observer-reported outcome developed to assess changes in physical function in ambulatory patients with DMD. The objective of this cognitive debriefing study was to evaluate the content validity of the DMD-CQ. METHODS: The DMD-CQ was cognitively debriefed in ten in-person interviews with caregivers of ambulatory patients with DMD, recruited through a patient advocacy group. The think-aloud method was used, which includes having caregivers state their thoughts while reading the questionnaire aloud. After the think-aloud exercise, the interviewer probed for additional feedback on areas that seemed confusing, and asked questions from an interview guide to elicit feedback on the instructions, recall period, items, and response choices. The interviews were audio-recorded, transcribed, coded, and analyzed. RESULTS: Caregivers came from a range of educational backgrounds, clinical trial experience, and demographics. Caregivers’ children with DMD represented a range of ages and disease severity. Caregivers found the DMD-CQ content to be appropriate and important for understanding disease progression in patients with DMD. The instructions were easy to understand, as were most of the items and their corresponding response choices. Caregivers found the response choices well-suited to their corresponding items. Seven of ten caregivers recommended making the recall period one month instead of one week. Feedback from the interviews also informed revisions to several items and responses to improve clarity. CONCLUSIONS: Interviews with caregivers confirmed the relevance of concepts covered by the DMD-CQ, and the comprehensiveness and comprehensibility of most of the items and their response choices. Feedback from caregivers was used to refine the recall period and improve several items and response choices for clarity. Future work includes psychometric validation.

PRM191: COGNITIVE INTERVIEWING DURING LINGUISTIC VALIDATION OF CLINICAL OUTCOMES ASSESSMENTS (COAS): IN-PERSON OR VIDEO CHAT – AN ANALYSIS OF RESPONDENT PREFERENCE

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OBJECTIVES: As an integral step of the linguistic validation of COAs, cognitive interviews are conducted to test a translation on a representative sample of respondents. Frequently, interviews are conducted in-person or, when necessary, over the telephone. The use of video chat applications may aid in recruitment of individuals not located in major cities as it would eliminate travel for the interviewer and respondents. This research examines respondents’ preferences regarding interview methodology. METHODS: Ninety-six cognitive interview participants in 15 countries were asked to indicate access to video chat technology as well as preferred interview method, along with their rationale. Questions were asked before and after each in-person interview. Respondents were asked: Do you have access to Skype/Facetime or a similar video chat application? Would you prefer an interview that is conducted in-person or via video chat? Now that you have completed the interview, would you have preferred that this interview took place via video chat? RESULTS: During initial questioning, 50 respondents indicated access to video chat applications. Of those respondents, 27 indicated that they would prefer in-person interviews with varying rationale including: “face-to-face conversations are always better in terms of understanding” and “video is OK for overseas relatives, but not for something like this.” After completion of the cognitive interview, 7 of the 27 respondents changed their opinion with one respondent explaining, “It makes the whole process quicker and more convenient.” CONCLUSIONS: Access to video chat applications is a limiting factor as indicated by 48% of respondents, but other factors have an impact as well. While 52% of respondents had access, over half expressed hesitation to participate in video chat interviews which must also be considered. Additional research is needed to evaluate other potential factors, including the nature of the interviews (topic), methodologies such as telephone interviews, as well as surveying following video interviewing.

PRM192: COST-EFFECTIVENESS ANALYSIS OF INSULIN DEGLUDEC U100 COMPARED WITH INSULIN GLARGINE U100 IN GREECE

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OBJECTIVES: To evaluate the cost-effectiveness of insulin degludec U100 (IDeg) versus insulin glargine U100 (IGlar) in patients with: type 1 diabetes using a basal bolus regimen (T1DMB/B), and type 2 diabetes receiving basal oral treatment (T2DMBOT) or basal-bolus therapy (T2DMB/B) in Greece. METHODS: Meta-analysis data from phase 3a clinical studies were used in a simple and transparent short-term cost-utility model. The costs and effects of treatment with IDeg versus IGlar were calculated annually. Quality-adjusted life-year (QALYs) were estimated by applying a disutility representing a reduction in quality of life per hypoglycaemic event, and an estimate of the utility benefit of the flexible dosing time option with IDeg. The analysis was conducted from the healthcare payer perspective, and costs were based on the respective reimbursement prices of EOPYY (June 2016). One-way and probabilistic sensitivity analyses were performed to examine the robustness of the results. RESULTS: Base case incremental cost-effectiveness ratios (ICERs) were calculated at 8,883 € per QALY in the T1DMB/B, at 5,379 € per QALY in the T2DMBOT and at 16,269 € per QALY in the T2DMB/B treatment groups. Sensitivity analyses indicated
that the results were quite robust to reasonable changes in model parameters, with almost all of the calculated ICERs falling below a commonly accepted willingness-to-pay (WTP) threshold (33,000 € per QALY gained) in all therapy regimens. The probability that IDeg was cost-effective compared with IGlar was 68.5%, 98%, and 88.5% in the T1DMB/B, T2DMBOT and T2DMB/B therapy regimens, respectively. CONCLUSIONS: IDeg was found to be a highly cost-effective alternative therapy option compared with IGlar in T1DMB/B, T2DMBOT and T2DMB/B treatment groups in Greece from the healthcare payer perspective over a 1-year time horizon.

PRM193: WHAT TIME DO WE DINE?™- A CULTURAL STUDY TO EVALUATE PEOPLE’S VIEWS OF SET MEAL TIMES ACROSS COUNTRIES

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OBJECTIVES: Clinical Outcome Assessments (COAs) use names of mealtimes to refer to specific periods of the day, without specifying a given hour(s); this could lead to the intended timeframe being interpreted differently depending on country of origin. This study aims to assess how national differences in eating habits impact on respondent interpretation of these time periods. METHODS: 49 participants across 22 countries were asked to identify when they typically eat their morning, midday and evening meal. The responses were assessed to ascertain similarities and differences between countries, and whether an indication of a set time is preferable alongside the meal name in COAs to ensure more consistent interpretations and responses. RESULTS: The responses indicate the variance in timings: Morning meal: range 0600 – 1200. 42% of these responses indicated it would be eaten between 0800 and 0900; 12% of all responses indicating 0600, and <1% indicating 1200. Midday meal: range 1100 – 1700. 83% of these responses indicated it would be eaten between 1200 and 1400; 3% of all responses indicating 1100, and 2% indicating 1400 – 1500. Evening meal: range 1700 – 2300. 25% of these responses indicated it would be eaten at 1900; 10% of all responses indicating 1700, and 5% indicating 2300. Meal times vary greatly across countries, indicating trends due to national and cultural differences. Participants from hotter climes, e.g. Greece, Italy and India typically stated the evening meal would take place between 2000 and 2200; whereas colder countries e.g. Denmark, the UK and Canada stated typically the same meal would be between 1700 and 1900. CONCLUSIONS: Respondents interpret meals to occur at different times, spanning a range of 6 hours per meal, depending on country of origin. To enable accurate data pooling, it is optimal to include a reference to the meal alongside a specific time range in COAs.

PRM194: USING RASCH MEASUREMENT TO QUANTIFY THE PERCEIVED RISKS ASSOCIATED WITH THE USE OF TOBACCO AND NICOTINE-CONTAINING PRODUCTS

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OBJECTIVES: The policy of tobacco harm reduction – making less harmful products available to smokers who would otherwise continue smoking – is recognized as an important strategy for reducing smoking-related harm. Predicting use behavior is an important component of product risk assessment, risk perception being a possible factor driving tobacco product uptake and use. The objective of this study was to develop a new self-report measure that quantifies perceived risks of tobacco and nicotine-containing products using Rasch Measurement Methods (RMMs). METHODS: The Perceived Risk Instrument (PRI) was constructed from focus groups in three countries, literature review and expert opinion. Cognitive debriefing interviews were conducted in four countries to inform the content of the instrument and to support the cultural adaptation. The pilot PRI was then field-tested in two stages based on large cross-national web-surveys. Subsequently, The PRI was implemented in cross-sectional studies to get an understanding of the perceived risk profile of different tobacco products for both adult smokers as well as never and former smokers. RESULTS: RMMs supported the formation of an 18-item Perceived Health Risk scale and a 7-item Perceived Addiction Risk scale. Both scales showed small measurement error, correct functioning of the rating scale, and measurement invariance across types of tobacco products, populations with different smoking status and different countries, providing thus the basis for valid comparisons. Construct validity was further supported by significant differences in perceived risks between adult smokers and never smokers. Products (i.e., cigarettes, electronic cigarettes, heat-not-burn product, and nicotine replacement therapy) could also be discriminated on the perceived risk continuum. CONCLUSIONS: The PRI is a psychometrically robust instrument that may be used in clinical and population-based studies; for different types of tobacco and nicotine-containing products; and for different smoking status groups.

PRM195: THE DEVELOPMENT AND USE OF A PRELIMINARY CONCEPTUAL MODEL OF INFLAMMATORY BOWEL DISEASE (IBD) TO FACILITATE PATIENT REPORTED OUTCOME (PRO) INSTRUMENT SELECTION
FOR A UK REAL-WORLD EVIDENCE STUDY

**OBJECTIVES:** Inflammatory bowel disease (IBD) is chronic in its nature and impacts patients' health-related quality of life (HRQoL). This work aimed to develop a preliminary conceptual model of IBD to guide the measurement and selection of PROs to be included in a real-world study of vedolizumab. **METHODS:** The preliminary conceptual model of IBD was developed via a detailed review of empirical qualitative literature focusing on the biological and psychological aspects of health outcomes in IBD. The model content was structured according to the Wilson and Cleary (1995) HRQoL model and concepts were extracted from the literature. This model was then used to guide PRO measurement strategy, first by examining the content of PROs for their use in IBD and then by mapping the concepts on the model with the identified PROs to identify the most appropriate PROs to include in a real-world study. **RESULTS:** The preliminary model consisted of a physiological factor level labelled, ‘IBD symptoms’, including two sub-levels, ‘Bowel’ and ‘Systemic’. All other concepts were categorised under levels of functional health and overall quality of life, and labelled according to ‘impact of symptoms on daily life’. This encompassed six sub-levels of impact: ‘activities of daily living’, ‘interpersonal functioning’, ‘emotional’, ‘society and economics’, ‘social’ and ‘treatment’. The model will next be presented to a panel of gastroenterologists and/or patients for verbal ratification to ensure that it covers the concepts described by patients in a clinical setting, and to validate the key domains important to patients. **CONCLUSIONS:** The preliminary version of the model will be used to give context to and support interpretation of the real-world study findings. This work provides an example of how the patient perspective from existing literature can be used to guide the strategy for measuring and selecting PROs in IBD.

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**PRM196: TRANSLATION AND CULTURAL ADAPTATION OF THE BODY-Q CHEST MODULE INTO FINNISH FOR USE IN GYNECOMASTIA, WEIGHT LOSS AND FTM CHEST SURGERY**

**OBJECTIVES:** The BODY-Q is a patient-reported outcome (PRO) instrument developed for weight loss and/or body contouring that measures appearance, health-related quality of life and experience of care. The aim of this study was to translate and culturally adapt a new module of the BODY-Q for chest surgery into Finnish and to establish a local branch for data collection for the international field-test. **METHODS:** The field-test version of the BODY-Q Chest Module includes a 14-item chest and 8-item nipple scale. Translation and cross-cultural adaptation processes adhered to the ISPOR guidelines. Two native Finnish translators produced separate forward-translations into Finnish and then met to create a consensus version. An English language-expert who was fluent in Finnish produced a back-translation into English. A back-translation panel and a multidisciplinary committee reviewed the translation processes. The revised version was pilot-tested among five individuals who were thereafter cognitive debriefed. The multidisciplinary committee reviewed the findings to finalize a version of the Finnish BODY-Q Chest Module for field-testing. **RESULTS:** Minor differences were encountered between the two forward translations. The translators discussed these differences to form Finnish version 1. This version was translated back to English. The panel noted that the words “breast” and “chest” needed changing as in Finnish these words are similar. The multidisciplinary review committee decided that the original word “flat” in question 4 in the Nipple scale had lost its meaning in the translation process being translated to “even” or “smooth”. Pre-testing and cognitive debriefing of the refined scales did not reveal any further problems. The committee accepted the translation process and found no need for further adjustments. **CONCLUSIONS:** The Finnish version of the BODY-Q chest can now be used for data collection in the international field-test study of this new PRO instrument. After field-testing and validation it can be used to assess treatment effectiveness of chest operations.

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**PRM197: WHEN AND WHERE TO USE FURIGANA? THE APPLICATION OF PHONETIC NOTATION IN JAPANESE TRANSLATIONS OF CLINICAL OUTCOMES ASSESSMENTS (COAS) FOR CHILDREN**

**OBJECTIVES:** Furigana (used for Japanese) is a phonetic notation which accompanies the traditional Japanese Kanji characters in the form of small symbols alongside or above the original character. These symbols aid the reader to pronounce characters out phonetically to understand the meaning of the text, principally employed in texts for children and language learners. This study concentrates on its application and importance of use in COAs intended for children. **METHODS:** To understand the relevance and application of furigana within COAs, research was conducted into its cultural use to assess the necessity of its presence in the final translation. Academic studies and feedback from 32 native speakers/developers were collated. This data was analysed to verify if the use of the
phonic notations is applicable in COAs for children. The results were set into 3 items of preference for learners of kanji, ‘text with furigana’, ‘no furigana’ or ‘other (descriptions)’. RESULTS: Considering furigana usage for respondents, 65.6% reported that if there was no furigana to assist in reading, a page with a high density of kanji was considered daunting. When asked if they preferred ‘text with furigana’, ‘no furigana’ or ‘other’, 63.3% of respondents opted for text with furigana. CONCLUSIONS: The results highlight that the safer option is to apply furigana to the translations; ensuring children can easily understand each character and reduce the risk of misinterpretation. Expert feedback showed that furigana is seldom used in most texts for adults and is usually used for clarification and pronunciation. However, it is frequently used in books for children or non-native speakers learning the language and therefore should always be considered when translating COAs aimed at children into Japanese.

PRM198: VALUE HEALTH WITH A MOBILE APP: THE INFANT HEALTH-RELATED QUALITY OF LIFE INSTRUMENT

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OBJECTIVES: The lack of preference-based HRQOL instruments for infants and adolescents precludes evaluating overall HRQOL and calculating quality-adjusted life years (QALYs) for this population. We introduce and explain the development of the Infant health-related Quality of life Instrument (IQI), which is the first preference-based HRQOL instrument developed by a novel methodology worked out under item response theory (IRT). IQI provides values for health states relevant in the first year of life. We also explain the principles of the IRT approach and how it is implemented in a mobile application consisting of two distinct tasks (classification, valuation) for the administration of the IQI. METHODS: A multistep development process began with extracting candidate health concepts from relevant measures identified by two literature searches. Next, three expert panels and two surveys with primary caregivers in New Zealand, Singapore, and the United Kingdom evaluated the relevance of the candidate health concepts, organized them into attributes based on their similarities, explored alternative attributes and generated response scales. Additional interviews assessed the cross-cultural interpretability and parents’ understanding of health attributes and usability of the mobile application. RESULTS: The final list of 8 health attributes included in the IQI consisted of sleeping, feeding, breathing, stooling/poo, mood, skin, interaction and other health problems. All attributes were assigned 4 levels, ranging from ‘no problems’ to ‘severe problems’. The users’ experiences with the mobile application were generally positive. CONCLUSIONS: The IQI is the first generic instrument designed to assess overall HRQOL in 0-1-year old infants providing a value for infant health status. It is short and easy to administer with a mobile application. Close attention was paid to the opinions of the infants’ primary caregivers during the instrument and mobile application development process.

PRM199: VALUE OF A PILOT STUDY IN A RETROSPECTIVE CHART REVIEW: FINAL PROTOCOL DESIGN SHOULD BASE ON PILOT RESULTS

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OBJECTIVES: This is a mandated Retrospective Chart Review (RCR) collecting drug utilization data for a blood disorder treatment, with the primary objective to assess the level of off-label use. Prior to launching the RCR, a pilot study was conducted to confirm the approach of utilizing pharmacies for data abstraction and to evaluate data variability and usefulness of a questionnaire as instrument for off-label ascertainment. METHODS: The pilot included a survey among European hospital pharmacies collecting information on access to prescription data, format of the pharmacy records, relevant variables documented and accessible for data abstraction. A questionnaire was utilized to support consistent data abstraction and to establish uniform criteria for determining off-label use. Each patient file was abstracted by two separate abstractors. Agreement between the two abstractors was assessed using the κ statistic. RESULTS: Drug usage information was available at 85% of all pharmacies that responded to the survey (n=27) of which 9% did not have access to prescription data. 15% still utilize paper records at their department, with the majority using electronic records or both. Access to all critical variables through their records was available for 40% of the pharmacies. For the pilot study data was abstracted for 54 patients. Despite high agreement on off/in-label use between the two abstractors, kappa’s varied from 0.00 to 1.00 for the subgroups analysed. CONCLUSIONS: These results helped to select the right countries, type of clinical setting best suited to collect the data, as well as validated the usefulness of the tools for data abstraction. This pilot was of large value for the proper planning and execution of the main study. Adjustments to the main study design and operational approach were reported back to the Regulatory Authority for approval prior to implementation.

PRM200: STUDY OF POLYPHARMACY AT A TERTIARY CARE TEACHING HOSPITAL BANGALORE
OBJECTIVES: The study was designed to study the extent of polypharmacy among the prescriptions received at Out Patient pharmacy in St.Philomena’s Hospital, Bangalore, to identify the most common class of drugs prescribed in polypharmacy prescription, to identify the drug interactions among the prescribed drugs, to identify the various therapeutic classes involved in major drug interactions. METHODS: A prospective hospital based observational study was carried out in the outpatient department of St.Philomena’s hospital. The research student collected all the prescriptions received at OP pharmacy. All the prescriptions were carefully analyzed for polypharmacy and the data were pooled and analyzed. RESULTS: A total number of 200 polyphonic prescriptions were found in the out-patient pharmacy of St.Philomena’s Hospital. During the study period of 6 months, it was found that the majority of the prescriptions were prescribed to female 101(50.50%) and 99(49.50%) were prescribed to male. Among 200 prescriptions it was found that 134(67%) contain 5 drugs followed by 42(21%) contain 6 drugs, 15(7.50%) contain 7 drugs and 9(4.50%) contain more than drugs. The most common therapeutic class was found to be Analgesics pertaining to 122(61%) drugs followed by antibiotics, which were 65(32.50%) drugs and 55(27.50%) drugs were Vitamins. It was found that the majority of polypharmacies have been occurred in the age group of adults 113(56.50%) patients followed by neonates and infants 52(26%) patients and geriatrics 19(9.50%) patients. Among 200 prescriptions, 82 drug interactions were observed which were found to be 43(52.43%) major followed by 36 (43.90%) moderate and 3 (3.65%) minor. Among the Major interactions, anti-inflammatory drugs were found to be the most commonly participating therapeutic class of drug in interactions. CONCLUSIONS: only 10% of prescriptions were found to have polypharmacy which was commonly observed in female patients. Among polypharmacy prescriptions less than 50% had drug interactions, majority of which were major drug interactions.

RESEARCH ON METHODS - Statistical Methods

PRM201: RESULTS OF INDIVIDUAL PARTICIPANT DATA META-ANALYSIS VS AGGREGATE DATA META-ANALYSIS OF RCTS OF EXERCISE REHABILITATION IN CHRONIC HEART FAILURE

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OBJECTIVES: Traditional meta-analyses synthesise aggregate data obtained from study publications or study authors, such as a treatment effect estimate and its associated uncertainty. An increasingly popular approach is the meta-analysis of individual participant data (IPD) where the raw individual-level data are obtained for each study and used for synthesis. This study compares and discusses results from an IPD meta-analysis versus standard meta-analysis of randomized controlled trials of exercise cardiac rehabilitation in chronic heart failure (CHF). METHODS: Based on a previous systematic review, the Exercise Training Meta-Analysis of Trials for Chronic Heart Failure (ExTraMATCH II) identified and collected IPD from RCTs that compared exercise rehabilitation with a non-exercise control and a minimum follow-up of 6 months. Outcomes of interest were mortality, hospitalization, exercise capacity and health-related quality of life. Original IPD were checked for consistency and compiled in a master dataset. Standard meta-analytic models were used for aggregate data whilst one-step approaches accounting for the clustering of participants within studies were planned for statistical analyses of IPD. RESULTS: Overall 33 RCTs were included in the original systematic review, whereas within the ExTraMatch II project, IPD were obtained from 19 RCTs in approximately 4,000 patients. From aggregate data there was no significant difference in pooled mortality (RR 0.92, 95% CI 0.67 to 1.26), whereas there was an effect of exercise rehabilitation on hospitalization (RR 0.75, 95% CI 0.62 to 0.92) and health-related quality of life (SMD −0.46, 95% CI −0.66 to −0.26). IPD analysis is currently underway; the results will allow examining how patients’ characteristics modify treatment benefit. CONCLUSIONS: Given the limitations of current evidence in CHF, access to individual data from several RCTs offers a timely and important opportunity to revisit the question of which CHF patient subgroups benefit most from exercise-based rehabilitation.

PRM202: SECOND-LINE TREATMENTS FOR ADVANCED GASTRIC CANCER: A NETWORK META-ANALYSIS OF OVERALL SURVIVAL USING PARAMETRIC MODELLING METHODS

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OBJECTIVES: Advanced gastric cancer (AGC) is one of the most common forms of cancer and remains difficult to cure. There is currently no recommended therapy for second-line AGC in the UK despite the availability of various interventions. This work aims to compare interventions for treatment of second-line AGC using more complex methods to estimate relative efficacy, exploring various parametric survival models and to compare results to those published adopting conventional methods of synthesis, including network meta-analysis (NMA) of median survival data and hazard ratios. METHODS: Seven studies were identified in an existing literature review evaluating seven
comparators which formed a connected network of evidence. Citations were limited to randomised controlled trials in previously-treated AGC patients. Studies were assessed for the availability of Kaplan-Meier curves for overall survival. Individual patient data (IPD) were recreated using digitisation software along with a published algorithm in R. The data were analysed using multi-dimensional NMA methods. A series of parametric survival models were fitted to the pseudo-IPD. Both fixed and random-effects models were fitted to explore long-term survival prospects using extrapolation methods, and to estimate mean survival for each comparator. RESULTS: Relative efficacy estimates were compared to those previously reported which utilised conventional NMA methods. Results and trends were consistent with findings from other publications and identified ramucirumab plus paclitaxel as the best treatment, however all the treatments were associated with poor survival prospects, with mean survival estimates ranging from 5.0-12.7 months. CONCLUSIONS: Whilst the approach adopted does not adjust for differences in trial patient populations and is particularly data-intensive, use of such sophisticated methods of evidence synthesis may be more informative for subsequent cost-effectiveness modelling and may have greater impact when considering an indication where observed data is particularly immature or survival prospects are more positive, which may then lead to more informative decision-making for drug reimbursement.

PRM203: ASSESSING THE ROBUSTNESS OF NETWORK META-ANALYSIS OF ATYPICAL ANTPSYCHOTICS IN THE PRESENCE OF HETEROGENEITY

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OBJECTIVES: Network meta-analysis (NMA) is a valuable tool for synthesis of results from different studies, allowing an understanding of the relative efficacy of multiple interventions. However, between-study heterogeneity and reporting bias can limit the validity of results obtained. This research extends recent proposed methods of addressing the difficulties presented by heterogeneity in meta-analysis, to assess robustness of findings in NMA. METHODS: Data came from recently published Cochrane systematic reviews investigating the effect of atypical antipsychotics in schizophrenia patients. Positive and Negative Syndrome Scale (PANSS) total score endpoint data for trials included in seven direct treatment comparisons (aripiprazole vs. clozapine, quetiapine, risperidone, olanzapine, and ziprasidone; risperidone vs. quetiapine, and olanzapine) were extracted and synthesized using Bayesian random-effects NMA. Relative efficacy was measured using mean difference (MD) in average PANSS total score. NMA results of all trials were compared to NMA results when (1) the single most precise trial was used for each direct comparison, (2) analyses were restricted to the largest trials, (3) a meta-regression model was used to allow effect size to depend on its standard error, and (4) analyses were restricted to trials at a low risk of attrition bias. RESULTS: Pair-wise effect sizes between antipsychotics, probabilities of being the best antipsychotic, and ranking of antipsychotics differed between analysis strategies. Differences in results for comparisons with strategies (1) and (2) favored clozapine; however, MDs were not statistically significant. Furthermore, differences were small, with all differences in MD (∆MD) less than 4, which is unlikely to correspond to a clinically significant difference. No meaningful differences in effect sizes were observed in the comparison with strategies (3) and (4) (∆MD < 1). CONCLUSIONS: Relative efficacy estimates differ depending on the strategy used; however, in this example such differences were small. The study illustrates how confirmatory sensitivity techniques can be used to help validate NMA conclusions.

PRM204: ESTIMATION OF HEALTH-RELATED QUALITY OF LIFE (HRQoL) IN CANCER PATIENTS UTILISING A TIME-TO-DEATH ANALYSIS

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OBJECTIVES: This research involved analysis of EQ-5D data according to 'time-to-death' (TTD) as an alternative approach to using markers of response and disease progression for health-related quality of life (HRQoL) estimation in cancer patients. In clinical trials, EQ-5D measurements are not sufficiently captured after disease progression and therefore may not accurately reflect HRQoL over time; analysis of utilities according to TTD better take into account HRQoL changes over time as a patient ‘progresses’ towards death. METHODS: A mixed-effects statistical model was fitted to longitudinal data, adjusting for predictors believed to impact HRQoL. Predictors were informed by clinical experts. TTD was categorised into four time periods (>12, 6-12, 3-6 and <3 months to death). A stepwise selection algorithm was applied to yield the most parsimonious model, identifying the final list of predictors. RESULTS: Results from the TTD analysis identified similar trends and statistically significant explanatory variables as those observed when adopting a conventional approach (based on overall response); adverse events, gender, race, hospitalisations and TTD were found to be associated with a statistically significant effect on HRQoL. The TTD variable showed that utility scores decline over time as a patient approaches death; statistically significant differences were observed between both 3-6 months and <3 months versus >12 months prior to death (p-values: 0.023, <0.001 respectively). CONCLUSIONS: The TTD analysis indicated patients experience a reasonably stable HRQoL up to 12 months prior to death (frequently patients continue to receive treatments that relieve symptoms and maintain
HRQoL), remaining stable to slightly declining between 3-12 months prior to death, with a larger decrease observed in the final 3 months of life. These findings support clinicians’ feedback that in cancer HRQoL can reduce substantially in the last few months of life. Future economic evaluations of anti-cancer therapies should consider the role of TTD in the analysis of utility outcomes.

**PRM205: CHALLENGES IN DEMONSTRATING DISEASE-MODIFYING EFFECTS: EVIDENCE-BASED TESTING OF A NOVEL STATISTICAL APPROACH IN ALZHEIMER’S DISEASE**

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**OBJECTIVES:** Several methodological issues arise when demonstrating disease modifying effects. The results of studies with delayed-start treatment can often be confounded by non-robust data analysis mechanisms, discontinuation rates and mixed drug effects. Accurate comparison of treatment differences using non-inferiority hypothesis testing methods largely depends on assumptions applied in the simulation testing procedure. Liu-Siefert and colleagues tested the validity of the non-inferiority test comparing disease modifying effects and estimated Alzheimer’s disease (AD) progression scenarios without real world data (RWD) informing their extrapolation parameters. Consulting at McCann Health (CMH) replicated their simulations using parameters informed by RWD to characterise the extrapolation of AD progression, expected to further validate the robustness of the non-inferiority tests performed. METHODS: Patient transitions throughout the treatment stages of AD were modelled using multicentre RWD. The natural history of AD and the delayed-start treatment effects for the placebo and treatment arm, respectively, were parameterised using data extracted from Consortium to Establish A Registry for Alzheimer’s Disease (CERAD). CMH used applied parametric sampling distribution technique to enable the re-creation of 2000 samples that were then used to evaluate five non-inferiority test margins reported in the study. Nominal type I error rates of 0.1, estimated with a multivariate normal distribution, were extrapolated and reported for five test margins. Through this CMH identified the optimal non-inferiority test that generated minimal bias when determining the disease modifying effects, exploring the lower bound of the 1-sided 90% confidence interval and assuming the 50% threshold for the treatment effect. RESULTS: Based on the 2000 simulations using the RWD, CMH identified the optimal test threshold (Δ2 – 0.5 Δ1) > 0 that produced minimal bias, thus validating the findings by Liu-Siefert et al.

**CONCLUSIONS:** The applied evidence-based extrapolation method allowed us to model realistic disease progression trends for AD and to test the non-inferiority margins suggested by Liu-Siefert and colleagues, with minimal bias.

**PRM206: HOW BENEFICIAL IS INDIVIDUAL PATIENT DATA IN A MIXED TREATMENT COMPARISON?**

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**OBJECTIVES:** Individual Patient Data (IPD) from Randomised Control Trials (RCTs) are considered the gold standard for evaluating treatment regimens in a Mixed Treatment Comparison (MTC). However, as the majority of studies do not report IPD, most MTCs are carried out using aggregate data (AD) for at least some, if not all, of the studies. We investigate the benefits of including varying proportions of IPD studies in an MTC. METHODS: Donegan et al (2013) developed a number of models for including both AD and IPD in the same MTC. We carried out a simulation study of RCTs based on these models to check the effect of additional IPD studies on the accuracy of the estimate of both the treatment effect and the covariate effect. We also compared the Deviance Information Criteria (DIC) between different models to assess model fit. We then applied this to a Hepatitis C network including both RCTs and observational studies. RESULTS: Our estimate of the covariate effect becomes more accurate as we increase the proportion of IPD studies in the network. However, the estimate of the treatment effect is unaffected, as a well conducted RCT will account for differences in covariates in the study design. The DIC distinguishes between models more often when there is a high proportion of IPD studies. In the Hepatitis C network even one IPD observational study decreases the standard deviation of both covariate effect and treatment effect estimates. CONCLUSIONS: Inclusion of IPD reduces uncertainty surrounding the covariate effect. As RCTs are considered the gold standard of evidence, including IPD does not improve the accuracy of the treatment effect. However, IPD may be most useful in observational studies where the covariates may not be well balanced between individual treatment arms.

**PRM207: MINIMIZING BIAS IN PARAMETRIC SURVIVAL ANALYSES OF PUBLISHED KAPLAN-MEIER CURVES**

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OBJECTIVES: Health economic models often rely on published outcomes such as Kaplan-Meier (KM) curves. Virtual patient-level data (VPLD) can be generated from these curves on which parametric fitting analyses or treatment effects can be evaluated. We evaluated the accuracy of parameters of curves fit to VPLD derived using the Guyot et al. method in a simulation study. METHODS: We simulated one hundred trials comparing active and reference treatments with Weibull survival times and normal censoring times. The KM curves for both arms were "digitized" under multiple scenarios, varying the number of curve coordinates extracted, and the intervals at which ns at risk are available. The Guyot method was used to generate VPLD from the extracted values. Parameter estimates for Weibull models fit to individual patient-level data (IPD) and VPLD were compared. RESULTS: The shape and scale, but not the treatment effect, were found to be systematically biased. In a digitization scenario with 15 extracted coordinates the median ratio of the VPLD scale to IPD scale was 0.968 (IQR:0.952-0.974) and the median shape ratio was 1.176 (IQR:1.166-1.206). Increasing the number of coordinates extracted reduced, but did not eliminate the bias. The interval at which the ns at risk were reported had no apparent effect on the bias. Moving virtual events to interval midpoints from interval endpoints changed the sign of and markedly reduced the bias, in the example digitization the median scale ratio became 1.002 (IQR:1.001-1.004) and the median shape ratio became 0.979 (IQR:0.965-0.996). To eliminate bias, it was necessary to both increase the number of extracted coordinates and place events at interval midpoints. CONCLUSIONS: Placing events at the end of time intervals in VPLD may bias survival projections. The bias can be minimized by extracting the greatest number of KM coordinates feasible and by placing events at interval midpoints.

PRM208: THE USE OF INTRA-CLASS CORRELATION COEFFICIENTS TO ASSESS TEST-RETEST RELIABILITIES IN PSYCHOMETRIC EVALUATIONS OF PATIENT REPORTED OUTCOME MEASURES

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OBJECTIVES: Considerable confusion exists around the nomenclature, interpretation, and calculation of intra-class correlation coefficients (ICCs) for measuring test-retest reliability (TRT) of patient-reported outcome assessments (PROs). This literature review describes the most common ICC forms used in computing TRTs. METHODS: A systematic search using OvidSP (Embase, MEDLINE®, PsycINFO®) identified publications that reported use of ICCs in their various forms in psychometric evaluation studies. Articles were included for full-text review if they reported on TRT as determined by one of 6 ICC forms by Shrout and Fleiss or 10 versions by McGraw and Wong and excluded if they reported data without TRT or ICC results. Full-text articles that met inclusion criteria were reviewed, and data (e.g., ICC type and rationale, study design/model) were extracted and summarized. RESULTS: A total of 216 abstracts from the initial literature search were reviewed, and eight publications spanning therapeutic areas were selected for full-text review. Five full-text articles were identified by Google search. A majority of the studies employed two-way random or mixed-effects model with absolute agreement definition (i.e., use of ICC[2,1], ICC[2,2] and ICC[3,1]). Two articles employed a one-way random effects model to compute ICC(1,1). One article compared results for ICC(1,1) versus ICC(3,1) and found minimal differences, thereby showing no systematic error in measurement errors associated with patient ratings. The most commonly cited rationale for employing the two-way mixed-effects model was the assumption of patients being random and the raters (i.e., items) being fixed. CONCLUSIONS: Given that there are several forms of ICCs, psychometric evaluation studies should identify ICC type and justify its use in establishing TRT of PROs, a practice that has not been consistently implemented. This literature search aims to bridge that gap by focusing on the few recent articles that do provide rationales, helping inform specific ICC types for use in future studies.

PRM209: VALUE OF INFORMATION ANALYSIS USING GENERALIZED ADDITIVE MODEL REGRESSION: A CASE STUDY IN HEART FAILURE DISEASE MANAGEMENT

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OBJECTIVES: Recently, value of information (VOI) analysis is more popular in health economics to investigate the added value of conducting future research to reduce parameter uncertainty in decision-analytic models. Such analysis generally calculate a bounded value (i.e., expected value of (partial) perfect information (EV(P)PI)) in a compute intensive way. We applied in this study an efficient approach to calculate EV(P)PI based on a previously conducted model-based economic evaluation on heart failure disease management. METHODS: The comparators considered were a conventional nurse-led management program and an alternative strategy using a novel point-of-care testing device. A continuous-time three-state Markov model was developed to describe the disease progression with the uncertainty of the transition rate of the novel device arm being captured probabilistically from two cardiologists. The Markov model was simulated in five years. Generalized additive model (GAM) regression was used to model the incremental net monetary benefit (averaging between cardiologists) with the experts' elicited transition
rate. The EV(P)PI was then calculated based on the predicted value of the GAM. The base-case EV(P)PI was calculated with an €20,000 willingness-to-pay (WTP) threshold. The elicited transition rates were assumed to be independent in base case. We subsequently altered the WTP threshold and relaxed the assumption of independence to see how the results were influenced. RESULTS: In base case, the EVPI per patient was €401 and the EVPPI for the elicited rate from the second cardiologist was €340. The EVPI value ranges between €337 and €1131 when altering the WTP threshold from €10,000 to €80,000. Both values hardly changed when the independent assumption was relaxed. CONCLUSIONS: GAM can be successfully applied in our case to efficiently calculate EV(P)PI. There is a profound difference between the two cardiologists regarding the added value of conducting future research to reduce parameter uncertainty existed in the current decision-analytic model.

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**PRM201: DIFFERENCES IN LABOUR PARTICIPATION BETWEEN PEOPLE LIVING WITH HIV AND THE GENERAL POPULATION: RESULTS FROM SPAIN ALONG THE BUSINESS CYCLE**

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**OBJECTIVES:** HIV/AIDS (Human immunodeficiency virus/Acquired immune deficiency syndrome) not only has a strong impact on the health of the worldwide population but also affects the labour status of HIV-positive people. The primary aim of this paper is to compare the labour participation of people living with HIV (PlwHIV) with the labour participation of the general population along the last business cycle in Spain. METHODS: The data used are from the Hospital Survey on HIV-AIDS and the Labour Force Survey from 2001 to 2010. A statistical matching method was used to analyse the differences between the labour participation of PlwHIV and the general population. Additionally, several specific models categorised into different subgroups (gender, education, source of infection and level of defences) were also performed. RESULTS: We identified a convergence in labour participation across the period in the two populations considered: PlwHIV was 23% less likely to have a job than the general population during 2001-2002 and 14% less likely during 2009-2010. CONCLUSIONS: Immunological status, source of infection and level of education play a relevant role among the PlwHIV population when comparing their labour participation with the general population. Is spite of this positive result, the likelihood of being employed in HIV-positive people continues to be different from that of non-carriers. Our study shows that institutional features of labour markets are relevant and should be considered in comparison between countries.

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**PRM211: CHANGES IN PRIVATE FINANCING OF THE GREEK HEALTH SYSTEM DURING THE ECONOMIC CRISIS**

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**OBJECTIVES:** Several reforms have been implemented during the recent years to curtail public health spending in Greece. The aim of this study was to explore the impact of the recent reforms and economic crisis on out-of-pocket (OOP) payments. METHODS: Data for 26,941 households were derived from the Household Budget Surveys for the period 2008-2014. Expenditure data were deflated (2008=100) with the price index and were also equivalised with respect to the economy scale of household consumption. Households were disaggregated into five consumption expenditure quantiles. RESULTS: Both mean annual equivalised total consumption and OOP payments demonstrated a downward trend during 2008-2014, albeit for consumption the relative change was larger at the end of the period of observation, i.e. -32.3% (from 18402.00 € to 12459.73 €) vs. -21.7% (from 1016.00 € to 795.76 €), respectively; the share of OOP outlays to total consumption increased from 5.5% to 6.4% between 2008 and 2014. In the lowest expenditure quintile, although the share of OOP was reduced from 6.6% to 5.8%, an ascending trend is recorded following 2012. Spending for medical products and inpatient care increased by 25.8% (from 248.60 € to 312.85 €) and 48.45% (from 149.51 € to 222.08 €) respectively, while for outpatient care it decreased by -57.80% (from 617.89 € to 260.84 €). The poorest quintile devoted the chunk of their health spending to medical products and inpatient care increased by 25.8% (from 248.60 € to 312.85 €) and 48.45% (from 149.51 € to 222.08 €) respectively, while for outpatient care it decreased by -57.80% (from 617.89 € to 260.84 €). The poorest quintile devoted the chunk of their health spending to medical products and inpatient care increased by 25.8% (from 248.60 € to 312.85 €) and 48.45% (from 149.51 € to 222.08 €) respectively, while for outpatient care it decreased by -57.80% (from 617.89 € to 260.84 €). The poorest quintile devoted the chunk of their health spending to medical products and inpatient care increased by 25.8% (from 248.60 € to 312.85 €) and 48.45% (from 149.51 € to 222.08 €) respectively, while for outpatient care it decreased by -57.80% (from 617.89 € to 260.84 €). CONCLUSIONS: The recent reforms have shifted part of the Greek health system’s financing to health consumers, for pharmaceutical and hospital care in particular. However, the increase in OOP inpatient spending is mainly driven by the higher socioeconomic strata. Promotion of the prescription and dispense of generic medicines may lessen the financial burden related to co-payments for poorer citizens.

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**PRM212: IMPACT OF NON-RANDOMISED DROP-OUT ON TREATMENT SWITCHING ADJUSTMENT IN THE RELAPSING-REMITTING MULTIPLE SCLEROSIS CLARITY TRIAL AND THE CLARITY EXTENSION STUDY**


OBJECTIVES: Several designs were used to analyse the differences between the labour participation of PlwHIV and the general population. Additionally, several specific models categorised into different subgroups (gender, education, source of infection and level of defences) were also performed. RESULTS: We identified a convergence in labour participation across the period in the two populations considered: PlwHIV was 23% less likely to have a job than the general population during 2001-2002 and 14% less likely during 2009-2010. CONCLUSIONS: Immunological status, source of infection and level of education play a relevant role among the PlwHIV population when comparing their labour participation with the general population. Is spite of this positive result, the likelihood of being employed in HIV-positive people continues to be different from that of non-carriers. Our study shows that institutional features of labour markets are relevant and should be considered in comparison between countries.

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OBJECTIVES: Several designs were used to analyse the differences between the labour participation of PlwHIV and the general population. Additionally, several specific models categorised into different subgroups (gender, education, source of infection and level of defences) were also performed. RESULTS: We identified a convergence in labour participation across the period in the two populations considered: PlwHIV was 23% less likely to have a job than the general population during 2001-2002 and 14% less likely during 2009-2010. CONCLUSIONS: Immunological status, source of infection and level of education play a relevant role among the PlwHIV population when comparing their labour participation with the general population. Is spite of this positive result, the likelihood of being employed in HIV-positive people continues to be different from that of non-carriers. Our study shows that institutional features of labour markets are relevant and should be considered in comparison between countries.

CONCLUSIONS: The recent reforms have shifted part of the Greek health system’s financing to health consumers, for pharmaceutical and hospital care in particular. However, the increase in OOP inpatient spending is mainly driven by the higher socioeconomic strata. Promotion of the prescription and dispense of generic medicines may lessen the financial burden related to co-payments for poorer citizens.
OBJECTIVES: The rank preserving structural failure time model (RPSFTM) can be used to adjust time-to-event efficacy estimates for treatment switching. The RPSFTM relies on two key assumptions (1) common treatment effect (CTE) assumption, which assumes that the effect of treatment was equal regardless of when it is received and (2) randomisation assumption, which can be violated if non-random drop out occurs during follow-up. The aim of this analysis was to assess the sensitivity of the RPSFTM results to these assumptions when applied to time to 6-month confirmed disability progression in the CLARITY and CLARITY Extension study. METHODS: We applied the rank preserving structural failure time model (RPSFTM) to adjust for treatment switching from placebo to low-dose cladribine. A propensity score matching (PSM) method was used to test the sensitivity of the RPSFTM to the CTE assumption. The PSM method does not rely on the CTE, however estimation of an unbiased HR still requires that the randomization assumption holds. To overcome this issue, the PSM method was combined with inverse probability of censoring weights (IPCW) to adjust for potential selection bias from non-enrolment into the extension study. The PSM method and IPCW require all relevant confounders are included in the estimation procedure. RESULTS: During CLARITY, the cladribine tablets (3.5 mg/kg) vs placebo HR was 0.58 (95% CI 0.40-0.83). During CLARITY+ CLARITY Extension, the unadjusted HR was 0.67 (95% CI 0.50-0.90), the RPSFTM HR was 0.62 (95% CI 0.44-0.88), the PSM was 0.62 (95% CI 0.40-0.84), and the PSM+IPCW HR was 0.63 (95% CI 0.40-0.87). CONCLUSIONS: The adjustment methods produced consistent results. The addition of IPCW to the PSM made little difference. Provided the assumption of no unmeasured confounders holds, these results indicate no significant bias in the RPSFTM cladribine efficacy outcomes due to participant non-enrolment into the extension study or violation of the CTE assumption.

PRM213: QUALITY OF REPORTING AND ANALYSIS OF TRIAL-BASED COST EFFECTIVENESS EVALUATIONS IN OBSTETRICS AND GYNAECOLOGY; A SYSTEMATIC REVIEW

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OBJECTIVES: This systematic review aimed to assess whether the reporting and analysis of trial-based economic evaluations in obstetrics and gynaecology comply with existing guidelines and recommendations, and whether this has improved over time. METHODS: A literature search was performed in MEDLINE, NHS Economic Evaluation Database and Health Technology Assessment to identify trial-based economic evaluations in obstetrics and gynaecology published between January, 2000 and May, 2017. Studies performed in middle and low income countries, and studies related to prevention, midwifery and reproduction were excluded. Reporting quality was assessed using the Consolidated Health Economic Evaluation Reporting Standard statement and the statistical quality using a literature-based list of criteria. Exploratory regression analyses were performed to assess the association between reporting and statistical quality and publication year. RESULTS: The electronic search resulted in 5,482 potentially eligible studies. Forty-five studies fulfilled the inclusion criteria, 22 in obstetrics and 23 in gynaecology. Twenty-seven (60%) studies adhered to less than 50% (n=10) of the reporting quality items and 32 studies (76%) met less than 50% (n=4) of the statistical quality items. As for the statistical quality, none of the studies used appropriate methods to evaluate cost differences, to deal with missing data, and clustering of data. No significant improvements over time were found in reporting or statistical quality in gynaecology, whereas in obstetrics a significant improvement in reporting and statistical quality was found over time. CONCLUSIONS: The reporting and analysis of trial-based economic evaluations in obstetrics and gynaecology is generally poor. Poor reporting and analysis of trial-based economic evaluations can result in biased results, leading to incorrect conclusions, and inappropriate healthcare decisions. Therefore, there is an urgent need to improve in the methods of economic evaluations in this field. Further research is needed to explore whether results from this review are generalizable to other medical disciplines than obstetrics and gynaecology.

PRM214: COMPARATIVE EFFECTIVENESS STUDY OF A NEW BAYESIAN'S CAUSAL INFERENCE METHOD

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OBJECTIVES: We present a Bayesian's semi-parametric causal inference method using Gaussian Process (GP) Prior that is designed to evaluate the averaged causal treatment effect. The method is compared with other commonly used causal inference methods under simulation studies where the true functional form of the model is unknown. The case study applied the method to a comparative effectiveness research (CER) to evaluate the effectiveness of early initiation of biologic treatment for children with newly diagnosed Juvenile idiopathic arthritis (JIA). METHODS: The proposed Bayesian GP model can incorporate prior information about covariate matching, thus offers a natural way for Bayesian causal inference to address the treatment selection bias as part of the outcome modeling. Simulation studies compared the performances of different statistics causal inference methods, including propensity score sub-classification, inverse treatment probability weighting (IPTW), regression adjustment, Bayesian...
additive regression tree (BART) and the newly proposed Bayesian GP causal inference method. Finally, we applied
the methods to a prospective inception cohort CER study that followed 98 children with JIA and treated on DMARDs
at baseline. The study endpoint was Juvenile Arthritis Disease Activity Score (JADAS) at the 6 months of follow up
visit. RESULTS: Our simulation study demonstrates the proposed method clearly outperform the existing methods in
terms of bias, coverage rate and root mean square error, and is well calibrated in Frequentist properties. Bayesian
GP method find children treated with early aggressive biologic DMARDs show 3.83 points improvement (95%
confidence interval of 0.14-7.53) in JADAS than those treated with non-biologic DMARDs at 6 month. Other causal
inference methods suggested improved JADAS but varying in estimated averaged treatment effect and with wider
confidence intervals. CONCLUSIONS: The proposed method offers more efficient and robust Bayesian’s approach to
causal inference, and is particularly useful for CER with rare disease and/or small sample size.

PRM215: MAXIMUM DIFFERENCE SCALING TO ENHANCE INSIGHT IN QUALITATIVE PAYER RESEARCH

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OBJECTIVES: Multiple-Criteria Decision Analysis (MCDA) considers multiple criteria in complex decision-making
environments, helping to understand needs and preferences in healthcare. Here we assess the benefits of MCDA vs
Likert preference scales to understand payer preferences. METHODS: Multiple MCDA methods can be applied.
Qualitative payer research often has restricted sample sizes and interview duration does not permit using lengthy
assessments. Maximum Difference scaling has been validated for small sample sizes. From an online platform,
respondents select and weight attributes and criteria relevant to their decision-making context. Payers from national,
regional and local levels from France, Germany, Spain, Sweden the UK (n=5 per country) and US (n=15) underwent
in-depth interviews to understand their opinions on the attributes of a novel product profile. Likert (7-point scale) and
Maximum Difference exercises were completed. Median Likert scores were calculated, and hierarchical Bayesian
analyses were performed on the Maximum Difference data. RESULTS: Likert scale results show that respondents
tended to avoid extreme scores, known as ‘central tendency bias’, resulting in a restricted score range of 3-6. Thus,
although interview findings provided more granularity, isolated scores were not sufficiently spread to confidently state
any one attribute was preferred over another. With Maximum Difference, total score differentiation was more
pronounced, with a 12 point spread between maximum and minimum values. CONCLUSIONS: Payer research is a
key pre-market step to understand opportunities for pricing, reimbursement and market access. Unlike market
research, the aim for market access research is robust insight. While Likert scales are frequently used, easy to
construct and implement, validity and reproducibility are among their weaknesses. In our comparison of approaches
to capturing payer preferences for product attributes, we have demonstrated that a short, well designed Maximum
Difference exercise can produce clearer and less biased preference data than a Likert scale, even with a small
sample size.

PRM216: THE USE OF MATCHING ADJUSTED INDIRECT COMPARISON (MAIC) AND SIMULATED
TREATMENT COMPARISON (STC) IN HTA SUBMISSIONS; LEARNINGS FROM RECENT SUBMISSIONS


OBJECTIVES: It is increasingly common for health technology assessment (HTA) submissions to be prepared based
on evidence from single arm trials or in situations where comparisons cannot be made between randomised
controlled trials (RCTs). Manufacturers are using increasingly complex statistical approaches to fulfil the requests of
HTA bodies for robust comparisons between drugs of interest in these situations of data paucity. In this study we
evaluate the use of two of the main approaches used in recent oncology HTA submissions, “Matching Adjusted
Treatment Comparison” (MAIC) and “Simulated Treatment Comparison” (STC). METHODS: HTA websites for
England, France, Germany and Scotland were searched to identify oncology drug submissions that relied on the use of
either MAIC or STC to compare between single arm trials or individual arms of RCTs. The methods, criticisms and
response of the HTA agencies to both MAICs and STCs were assessed and summarised. RESULTS: Four oncology
interventions for which HTA submissions have been submitted were selected as relevant: ibrutinib, axitinib,
panobinostat and osimertinib. All of these interventions were assessed by NICE between 2015 and 2017. The use of
both MAIC and STC was criticised in all cases due to their underlying assumptions. However, in all cases the
treatments have been recommended by at least one HTA body. CONCLUSIONS: The use of MAIC and STC in the
HTA submission process is still in its early stages and is still subject to some criticism. The different assessment
criteria and data requirements of HTA bodies across these countries leads to differences in their willingness to accept
MAIC and STC data. It is possible to receive positive recommendations based upon MAIC and STC data, this is
especially the case in situations of high unmet need.
OBJECTIVES: Machine Learning (ML) is becoming an increasingly important approach for the analysis of real-world data and there is a lively debate about which approach is best among experts. However, for non-statisticians there is a general lack of clarity around appropriate use of ML versus a traditional statistical approach (TSA). Through a practical example, we set out to examine the similarities and differences between the two approaches in an unbiased exploration.

METHODS: We used both approaches to examine the possible predictors being diagnosed with Non-Valvular Atrial Fibrillation (NVAF) before or after a stroke using a large US Health Insurance Claims dataset (Pharmetrics). Analysts were blinded and asked only to address the study objective using either a TSA or a ML approach. RESULTS: Logistic regression was used for the TSA, the most important predictor of after stroke diagnosis was aortic plaque (OR=1.4 [95% CI 1.2-1.6]) and the TSA had an area under the curve (AUC) of 0.67. For the ML random forest was used and the most important predictor of after stroke diagnosis was a healthcare cost (mean decrease in accuracy=4.3%) with an overall AUC of 0.80. Comparing the analyses we found that machine learning approach considered more variables in the analysis, without the variable preselection steps present in the TSA. It was therefore stronger in identifying potentially new predictive relationships. Addressing data quality issues was considerably more complex for the TSA. The TSA provided a more interpretable assessment of the influence of discovered predictor variables in the form of an odds ratio, highlighting the fact that this approach is stronger in making inference. CONCLUSIONS: This work discusses the strengths and weakness of ML versus TSA and helps to clarify the similarities and potential use cases for each approach.

PRM218: MINIMIZING BIAS IN INDIRECT COMPARISONS UTILIZING VIRTUAL PATIENT LEVEL DATA

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OBJECTIVES: When individual patient-level data (IPD) are unavailable, virtual patient-level data (VPLD) can be derived from published Kaplan-Meier (KM) curves for use in various analyses. A particular use-case is in MAIC or STC, where VPLD for comparators are analyzed with IPD for an index treatment to derive adjusted effect estimates. Several VPLD derivation techniques exist, but the method of Guyot et al. is regarded as the most robust. We evaluated the accuracy of this method in the MAIC setting in a simulation study. METHODS: We simulated one hundred populations each of index and comparator treatment patients using Weibull survival times and normal censoring times. The comparator KM curves were “digitized” under multiple scenarios, varying the number of curve coordinates extracted, and the intervals at which ns at risk are available. The Guyot method was used to generate VPLD from the extracted values. IPD vs VPLD and IPD vs VPLD Cox HRs were compared. RESULTS: The median ratio between the IPD vs VPLD and IPD vs IPD HRs was 1.108 (IQR:1.097-1.117) under a digitization scenario with 15 extracted coordinates. Varying the spacing of the reported n at risk had no effect. Investigation attributed the bias to the placement of virtual events at the ends of time intervals defined by the extracted coordinates. Moving virtual events to the interval midpoints removed the bias: the median ratio between HRs was 1.002 (IQR:0.994-1.009). CONCLUSIONS: Placing events at the end of time intervals in VPLD may produce biased HRs in MAIC analyses when few KM curve coordinates are extracted. The bias can be avoided by extracting the greatest number of coordinates feasible and by placing events in the middle of intervals.

PRM219: REPORTING QUALITY & TRANSPARENCY OF PUBLISHED NETWORK META-ANALYSIS. IS IT SATISFACTORY?

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OBJECTIVES: Network Meta-Analysis (NMA) is becoming more commonly used method comparing several treatments at one time. Since the methodology applied in such approach is not straightforward (includes Bayesian statistics and random sampling) it essential to keep the highest methodological standard on each step to ensure credibility of such analyses. Nowadays the related methodology is developed and grounded in number of guidelines. But is it really commonly applied in published journal articles? In this research aimed to assess reporting quality and transparency using related subdomain of the ISPOR checklist. METHODS: A systematic PubMed search of NMAs published in 1st quarter of 2017 were performed. We restricted to NMAs based on randomized controlled trials, containing at least four treatments. The information on reporting quality and transparency including reporting of individual study results (necessary to re-conduct the calculations), presentation of all pairwise contrasts between interventions as obtained with the NMA reported along with measures of uncertainty and ranking of interventions provided by outcome (essential to fully understand the results) were extracted. RESULTS: 108 NMAs satisfying the including criteria were identified over screened 249 items which identified by the search strategy. The general impression is that results of the NMAs tend to be presented clearly. The majority of publications (but not all) include
all pairwise results and some kind of ranking of treatments (e.g. based on probability of being best or SU
cRa). On the other hand the presentation of the input is not that clear. Although the network plots are usually included in
the articles, but individual study results are not. CONCLUSIONS: Nowadays there are tools, such as the ISPOR one,
facilitating the review process of NMA journal submissions. Their role should be increased since there are still some
typical gaps made by the authors decreasing credibility of that kind of analyses.

PRM20: EVIDENCE SYNTHESIS FOR HEALTH TECHNOLOGY ASSESSMENT WITH LIMITED STUDIES

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OBJECTIVES: Pairwise and network meta-analyses using fixed effect and random effects models are commonly
applied to synthesise evidence from randomised controlled trials in health technology assessment. Fixed effect
models are often used because there are too few studies with which to estimate the between-study standard
deviation from the data alone. When heterogeneity is expected and inferences are required beyond the sample of
studies available, then an analysis using a fixed effect model will underestimate uncertainty about the treatment
effect. This research aims to provide a Bayesian approach to overcome the problem of too few studies to use a
random effects model, by proposing a framework for eliciting an informative prior distribution for the between-study
standard deviation in a random effects model to genuinely represent heterogeneity. METHODS: We developed an
elicitation method using external information such as empirical evidence and experts’ beliefs on the “range” of
treatment effects in order to infer the prior distribution for the between-study standard deviation. We also developed
the method to be implemented in R using the SHELF package. RESULTS: The three-stage elicitation approach
allows uncertainty to be represented by a genuine prior distribution to avoid making misleading inferences. It is
flexible to what judgments an expert can provide, and is applicable to all types of outcome measure for which we can
construct a treatment effect on an additive scale. CONCLUSIONS: The choice between using a fixed effect or
random effects meta-analysis model depends on the objective of the analysis and knowledge of the included studies,
but not on the number of available studies. Our elicitation framework captures external evidence about heterogeneity
and overcomes the often implausible assumption that studies are estimating the same treatment effect, thereby
improving the quality of inferences in decision making.

PRM21: GENERIC REIMBURSED MARKET SHARES IN GREECE FROM 2012-2016. A STUDY BASED ON
AGE GROUP PREFERENCES.

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OBJECTIVES: A generic drug shares the same active and inactive ingredients as the branded though it is marketed
under a different trade name, trademark, packaging than the branded. Increased penetration of prescribed generics
has been primary goal during the memorandum years (since 2010) in Greece. We assessed trends in the
prescriptions of authorized generics in the public reimbursed market from EOPYY in Greece during the years 2012-
2016. METHODS: Medicines Data were derived from the EOF (Greek Medicines Organization) databases, the Greek
Positive list of prescribed medicines and published reimbursement data by EOPYY (Greek Public Reimbursement
Organization). Time trends in generic market were described and compared with chi-square tests in each semester
from 2012 to 2016. RESULTS: In 2012 generics market share was 22% both in values and volume of the public
reimbursed market. In 2016 Gx value and volume shares were approximately 25%. Generic value share increased
linearly from 72% in S2 2012 to 80% in S2 2015 in patients age group >60 years old. In S1&S2 2016 Generic value
share decreased significantly to 72% in patient group >60 years old but increased in almost all other age groups. In
the same period older patients switched from generics to Off patent medicines in a rate 10% per semester and to On
patent medicines in a rate 20% per semester. Chronic deseases patients count for over 70% volume in public
reimbursed market shares. CONCLUSIONS: Generic medicines are preferred by older patients. The use of generics
in reimbursed market is increased overtime. The effect of increased generic penetration on the reimbursed market
and the incentives for generic preference should be assessed.

PRM22: FRACTIONAL POLYNOMIAL NMA MODELS FOR SURVIVAL ANALYSES: RESULTS FROM A
SIMULATION STUDY


OBJECTIVES: When conducting a Network Meta-Analysis (NMA) of survival data, the proportional hazard
assumption has been increasingly challenged, especially in oncology. The fractional polynomial NMA model has
been proposed to tackle this issue and has been used in HTA submissions. However, using this type of model in
practice raises several methodological and computational issues. Our aim was to assess the behaviour of the
fractional polynomial NMA based on number of included data points and time windows for corresponding
hazards. METHODS: Simulation studies were conducted to investigate the behaviour of the fractional polynomial model. First, the influence of the number of data-points from the Kaplan-Meier curves was investigated, aiming to provide guidance on the number of data points to optimise model convergence while minimising computation time. In a second step, model robustness to different time windows selected for the corresponding hazards was assessed. RESULTS: Simulation results showed a decreasing marginal benefit of adding further data points, whereas computation time increased exponentially and the local hazard rate estimation noise increased. Optimal number of points should be selected based on available running time and sample size of included trials. A sample of ten to fifteen data points provided a good trade-off between computation time, uncertainty reduction and local hazard rate estimations across most simulations. The model was robust to time window specification, which should be selected based on each study and not across studies. CONCLUSIONS: In conclusion, the fractional polynomial NMA model has proven to be a valuable method allowing incorporation of a fully flexible time-dependent hazard function, addressing an important source of structural uncertainty in NMA for survival outcomes. This study provides an overview of the model behaviour in various scenarios. However, additional research is needed to provide guidance on how to integrate such models into cost-effectiveness model.

PRM223: ASSESSING THE ROBUSTNESS OF DIRECT META-ANALYSIS IN THE PRESENCE OF HETEROGENEITY

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OBJECTIVES: Systematic reviews and meta-analyses are valuable tools when researchers require a synthesis of the results of different studies. However, between-study heterogeneity (e.g., differences in population, methodology, or results) can limit the reliability of results from meta-analyses. This study applied current methods which have been proposed to address the difficulties presented by heterogeneity to recent systematic reviews, to assess robustness of the reviews’ findings. METHODS: Recently published Cochrane systematic reviews that contained five or more trials investigating the effects of atypical antipsychotics in schizophrenia patients were identified. Positive and Negative Syndrome Scale (PANSS) total score endpoint data up to week 12 was extracted for seven direct treatment comparisons (aripiprazole vs. clozapine, quetiapine, risperidone, olanzapine, or ziprasidone; risperidone vs. quetiapine or olanzapine). Relative efficacy was measured using mean difference (MD) in average PANSS total score. For each direct treatment comparison, the results from the original, conventional meta-analysis were compared to that for (1) the single most precise trial in the comparison, (2) a meta-analysis restricted to the largest trials, (3) a limit meta-analysis, and (4) a meta-analysis restricted to trials at a low risk of attrition bias, using the difference in mean difference (ΔMD). RESULTS: Where considerable differences were observed, MD in PANSS total score was smaller in the conventional meta-analyses than that for three of the four analytic strategies. Such differences were notably small, with all ΔMD less than 4, which is unlikely to correspond to a clinically significant difference. No considerable differences in effect size were observed in the comparison with a limit meta-analysis (|ΔMD| < 1). CONCLUSIONS: The analyses validated the systematic review results and demonstrate the value of confirmatory sensitivity analysis. Routine sensitivity analyses are recommended to assess the robustness of findings and validate conclusions in the presence of between-study heterogeneity.

PRM224: MATCHING-ADJUSTED INDIRECT COMPARISON (MAIC): SENSITIVITY ANALYSES AND GRAPHICAL DIAGNOSTICS

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OBJECTIVES: MAICs have been used to compare treatment outcomes across separate clinical trials and to inform health technology assessments, especially when anchor-based or network meta-analyses are not feasible or may be biased by cross-trial differences. As in any adjusted analysis of non-randomized treatment groups, an important decision in the design of an MAIC is the set of baseline characteristics used for adjustment. We present analyses and graphical summaries that can be used to help evaluate this choice. METHODS: Given a set of baseline characteristics, univariate MAICs matching one baseline characteristic at a time, and multivariable MAICs matching all selected baseline characteristics but removing one at a time, are performed. Impacts on the estimated treatment effect, and on its estimated level of uncertainty (the standard error), are tabulated from each analysis and summarized graphically in conjunction with the baseline differences in each characteristic. RESULTS: Example applications based on simulated and real data illustrate how these analyses can be used to identify sensitivity (or lack of sensitivity) to the choice of adjustment variables in an MAIC. The analyses also help assess the face validity of the analysis (e.g., does the estimated treatment effect move in the expected direction after adjustment) and help identify baseline characteristics for which adjustment increases uncertainty without substantially impacting estimated treatment effects. CONCLUSIONS: Analytical and graphical approaches to evaluating the contribution of each baseline characteristic to an MAIC can be helpful for assessing the sensitivity and face validity of estimated treatment effects.
PRM225: APPLICATION OF BALANCING TECHNIQUES IN STUDIES UTILIZING GERMAN ADMINISTRATIVE CLAIMS DATA

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OBJECTIVES: The use of administrative claims data to estimate the effects of health related outcomes for specific diseases, treatments and interventions is surging. To avoid selection bias when comparing effects between groups and to mimic randomization, matching or weighting techniques are applied. Aim of this study was to assess the use of matching and weighting techniques in studies using German administrative claims data. METHODS: A systematic literature review via PubMed was conducted to assess the application of matching and weighting techniques in studies based on German administrative healthcare data published until May 2017. Relevant studies were identified via keywords linking the terms “matching” or “weighting” with various synonyms for claims data and Germany. Titles and abstract were screened by two independent researchers. The studies were stratified by type of used data, category of study objective (e.g. burden of disease) and applied methodology (e.g. propensity score matching or weighting). RESULTS: In total, n=363 studies were identified of which n=114 met the inclusion criteria. The most frequent study objectives included cost analyses followed by burden of disease assessments and studies on healthcare resource utilization. Direct matching approaches based on variables such as age and gender were used in almost two thirds of the studies, followed by matching on the propensity score, which was applied in roughly one third of the analyses. Weighting techniques such as inverse probability of treatment weighting or newer approaches such as entropy weighting were rarely incorporated. Claims data from health insurances were the most prominent data source followed by administrative outpatient data. CONCLUSIONS: To balance treatment and control groups in German claims data, most researchers rely on matching methods, especially direct matching and propensity score matching. The use of weighting techniques and relatively new approaches is rare in the German context but should be considered in the future.

PRM226: OVERALL SURVIVAL IN PATIENTS WITH NON-SMALL CELL LUNG CANCER: A COMPARISON OF CLINICAL TRIAL VERSUS REAL-WORLD OUTCOMES USING A PROPENSITY SCORE REWEIGHTING APPROACH

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OBJECTIVES: Overall survival (OS) is an established outcome in randomized controlled trials (RCTs) addressing new cancer treatments. However, because characteristics of patients included in RCTs typically deviate from real-world patient characteristics, it is unclear whether OS outcomes as shown in RCTs can be used to estimate the real-world OS associated with observed treatments. We aimed to compare the OS reported in a recent RCT for advanced non-small cell lung cancer (aNSCLC) patients receiving first-line chemotherapy with the real-world OS of that chemotherapy. METHODS: Using claims data from a German sickness fund, we identified patients diagnosed with aNSCLC initiating a first-line chemotherapy (minimum follow-up 18 months) OS data from the aNSCLC-RCT were extracted by digitizing the reported Kaplan-Meier curve (KMC) of the chemotherapy group. The real-world KMC was adjusted using propensity score reweights with regard to the aggregated aNSCLC-RCT patient characteristics. Survival outcomes were finally compared using Cox proportional hazards regression. RESULTS: 95 aNSCLC-patients initiating first-line chemotherapy were identified in the real-world dataset, median OS was 12.2 months (95%CI:7.2-14.8). The RCT included 151 patients in the chemotherapy group, median OS was not reached after 18 months. Once an adjusted patient sample was used (adjustment for differences in age, gender, brain metastases, smoking status), median OS of observed 95 patients decreased from 12.2 to 8.1 months (95%CI:4.3-12.0). If this KMC is compared to the RCT-KMC, patients seemed to have a better survival prognosis in the RCT in comparison to the real-world (Hazard ratio:1.89; 95%CI:1.35-2.65). CONCLUSIONS: Our analysis confirms that the real-world OS of a treatment is likely to be worse than OS of that same treatment in RCTs, even if an adjustment for differences in patient characteristics is done. Whether this is related to any unobserved differences in patient characteristics or to differences in the diagnosis/treatment framework needs to be further investigated.

PRM228: WHICH PSM METHOD TO USE? ASSOCIATION BETWEEN CHOSEN PPROPENSITY SCORE METHOD AND OUTCOMES OF RETROSPECTIVE REAL-WORLD TREATMENT COMPARISONS: EVALUATION OF 18 DIFFERENT PSM METHODS

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OBJECTIVES: Because different methods for propensity score (PS) matching (PSM) exist, the objective of this study was to assess whether different PSM methods differ in terms of matching quality or study results. METHODS: We
used an anonymized claims dataset of type-2-diabetes-mellitus patients, who were treated with Sulfonylureas (SU; n=904), or Metformin (MET; n=7,874). Associations between treatment assignment and macrovascular outcomes (MACE) and all-cause-survival were analyzed. Three different sets of baseline variables were used for PS calculation (all available 10 variables, variables significantly associated with group exposition, age/gender/CCI only). To these, we applied the optimal without replacement (O) and the nearest neighbor with replacement (NN) matching algorithm. Caliper widths were defined as fixed (0.001) or determined by PS (0.2*standard deviation of LOG(PS)). In a further scenario, PSM was done within 5-year-age/gender classes. Matching quality was assessed by comparing differences in (1) number of matched patients, (2) baseline characteristics similarity, (3) bias reduction and (4) differences in pneumonia/arm fracture/back pain rates between groups. RESULTS: In 18 different PSM calculations, between 726 and 904 matched pairs could be derived. Percentage of baseline variables/non-study-related outcomes still significantly different between PSM samples ranged from 0%-40%/0%-20%, depending on PSM method. Highest impact on matching quality showed caliper definition and whether matching was/was not done within fixed age/gender classes. Best matching quality was achieved by using an O approach with caliper 0.001 without matching within pre-defined age/gender classes. In only 10 out of the 18 comparisons, all-cause mortality showed a significant difference between SU/MET exposition (MACE: 4 out of 18 comparisons). CONCLUSIONS: Because different PSM methods are associated with different matching quality and strongly affect the outcomes of retrospective comparative analyses, we recommend to (1) carefully choose the used PSM method, and (2) to apply different PSM-methods in scenario analyses to test robustness of study results.

RESEARCH ON METHODS - Study Design

PRM229: CLASSIFICATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) SEVERITY ACCORDING TO THE GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE (GOLD): VARIATIONS IN THE DEFINITION OF GOLD GROUPS AND THEIR IMPACT ON STAGE ASSIGNMENT

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OBJECTIVES: The aim of this investigation was to examine the impact of (1) different criteria for definition of GOLD groups, and (2) use of information from different German data sources on GOLD classification of a COPD patient. METHODS: In this non-interventional data linkage study, primary data (PD) of COPD patients provided by treating physicians were linked to claims data (CD) of a German sickness fund (AOK Nordost). PD included all information relevant for GOLD classification (exacerbations, airflow (FEV1), COPD assessment test (CAT) and modified Medical Research Council (mMRC) scale). Additionally, exacerbation frequency was obtained from CD. Based on all available data, four different methods were simulated for assessment of GOLD groups (guideline update 2014): (1) CAT+FEV1/exacerbations (PD); (2) CAT+FEV1/exacerbations (CD); (3) mMRC+FEV1/exacerbations (PD); (4) mMRC+FEV1/exacerbations (CD). RESULTS: 497 patients (mean age: 58.23 years, female: 36.0%) were included in this post-hoc analysis. 270 patients (54.5%) were uniformly assigned to one group in all 4 classification approaches. Generally, group assignment varied, ranging between: 13.8-38.4% (A), 19.1-44.9% (B), 2.4-20.7% (C) and 23.7-42.5% (D). A higher proportion of patients were assigned to the groups A and C (low symptoms) when using mMRC instead of CAT (example: 14.3% (1) vs. 38.4% (3) in stage A). The difference due to deviation of information from different data sources turned out to be smaller, assigning slightly more patients to higher risk groups (C and D) when using CD instead of PD for exacerbation frequency (example: 20.7% (4) vs. 17.1% (3) vs. in stage C). CONCLUSIONS: GOLD classification can vary as a result of the used data sources (PD/CD) and especially, according to the method used to assess symptoms (CAT/mMRC). This may have a substantial impact on COPD patients’ treatment as GOLD treatment recommendations vary across different GOLD groups.

PRM230: TRENDS IN PRAGMATIC CLINICAL TRIALS

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OBJECTIVES: Pragmatic clinical trials (PCTs) are gaining interest among decision-makers as transferability and generalisability of clinical trial results to real-world settings are increasingly scrutinised. The aim of this study was to identify how PCT design has evolved over the years. METHODS: Data on PCTs were retrieved from clinicaltrials.gov. Trials were identified using the free search term “pragmatic” and study type “interventional studies”. PCT characteristics were assessed for all identified trials (1996-2017), and for three subgroups defined according to the year of launch (2003-2007, 2008-2012, and 2013-2017). RESULTS: In total, 497 PCTs were identified. The oldest trial reported in the database was from 1996; however, the number of PCTs started to increase after 2000. The highest increase in the number of newly-launched PCTs was in 2015 (98%) and the number of newly-registered trials
was highest in 2016 (108). Most PCTs were sponsored by universities (51.1%) and medical centres (21.1%). Industry sponsored only a minor proportion of the trials (3.6%). Cardiovascular, musculoskeletal and psychiatric areas were most commonly studied (~10% each). Trials were mainly conducted for interventions classified as "other" (38.0%), "behavioural" (32.4%) and "drugs" (22.1%); 93% of PCTs were reported as randomised clinical trials (RCTs). Parallel assignment dominated (85%) in PCTs design, but an increase in crossover assignment was observed over time. There was an increasing trend for open-label design, representing 54% of all trials. On average, PCTs enrolled 5,423 patients (range: 2-933,789). The average trial duration was 2.8 years (range: 0.2-14.8), albeit more recent trials tended to be shorter. **CONCLUSIONS:** Unlike that of academics, manufacturer interest in PCTs has grown little, possibly reflecting the complexity of balancing internal and external validity in RCTs. Several initiatives are underway to assess, from a broad perspective, the challenges and potential solutions to introducing a greater degree of pragmatism in health technology development plans.

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**PRM231: APPLICATION OF MIXED-METHOD STUDY DESIGNS IN HEALTH- ECONOMIC- RELATED STUDIES. A NARRATIVE REVIEW.**

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**OBJECTIVES:** Mixed method studies aim at combining qualitative and quantitative research methods and thereby trying to offer deeper insights into a study topic. The German Institute for Quality and Efficiency in Health Care (IQWiG) recommends to combine qualitative and quantitative data to generate a wider spectrum of information for evaluation of health care services. This review aims to give an overview over mixed method designs used in health care research studies published over the last five years. **METHODS:** A narrative database search was conducted in Pubmed. According to pre-defined inclusion and exclusion criteria, titles and abstracts were screened regarding research location and mixed method designs and research methods. In a second step, full-text screening was used to extract details. **RESULTS:** In total n=236 research papers were identified. For full text screening n=82 studies remained and were included in the analysis. 25% of the evaluated studies (n=21) came from the UK; only n=3 relevant studies were conducted in Germany. The three main research fields were public health (n=27), followed by prevention & promotion (n=22) and health policy (n=16). 4 out of 82 studies focused on economic evaluations only. N=54 studies applied a data triangulation design. The majority of the studies used quantitative primary data collection as main research method (n=43). Qualitative interviews as an add-on methodology were used most frequently (n=29). Costs or socioeconomic factors were addressed in questionnaires or interviews in n=43 studies. Cost-analysis were integrated in n=12 studies as an add-on method. **CONCLUSIONS:** Of the evaluated studies, mixed method study designs are not often applied in health economic evaluations or studies with economic focus as of today. Further research is warranted for this reasons finding as it is unclear whether this is due to a lack of methodological knowledge or other influencing factors.

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**PRM232: CONSISTENCY ASSESSMENT OF INTERNATIONAL DRUG PRICE COMPARISONS**

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**OBJECTIVES:** International drug price comparisons rank countries according to the price of the available drugs. The results of these studies are often used as economic indicators and as political communication tools. The methodologies often rely on hypothesis built by the authors and involve numerous uncertainties. The main goal of this work is to evaluate the consistency of methodologies used in studies that compare drug prices in OECD countries and to assess to what extent results are reliable. The second objective is to propose a reading grid to evaluate the quality of methodologies used. **METHODS:** All full-text available studies referenced from Pubmed, Web of Science, Science Direct, Springerlink but also grey literature, published between January 2007 and March 2017 have been analyzed. The research focused on original drug price comparisons made in OECD countries. Comparisons studies involving only generic drugs were excluded. Each article has been analyzed regarding six main criteria: data sources, compared countries, drug selection, price used, economic environment and date of the data used. **RESULTS:** Thirteen studies have been retrieved. It appeared that 5 studies were based on non-official data sources; 11 studies compared countries with a diversity of socio-economic characteristics; 8 studies didn’t use any economic adjustment to compare drug markets; 9 studies were not explicit about drug selection; 4 studies didn’t use ex-factory prices and 2 studies were realized during a major event in a country that affected pharmaceutical industries. **CONCLUSIONS:** There is a crucial need for methodological guidelines that international drug price comparisons should follow in order to provide results reflecting actual pharmaceutical economy, especially in the political context surrounding high drug prices. Using the six main criteria selected, the grid developed can serve as a
support for methodology qualifications to estimate the quality of the comparisons and ensure the consistency of drug prices.

**PRM233: ADVANCED MONTE-CARLO SAMPLING SCHEMES FOR VALUE OF INFORMATION ESTIMATION**

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**OBJECTIVES:** To explore the potential of advanced Monte-Carlo sampling schemes to reduce computational cost of estimating Expected Value of Perfect Information (EVPPI). Quasi Monte-Carlo (QMC) and Multilevel Monte-Carlo (MLMC) estimation are compared with Nested Monte-Carlo (NMC) for a cost-effectiveness model in depression. **METHODS:** EVPPI provides an upper bound on the value of collecting further evidence on a set of inputs to a cost-effectiveness model. NMC estimation of EVPPI is computationally expensive as it requires a double simulation loop. QMC reduces computational effort by choosing samples systematically, optimised to reduce the variance of the estimator. MLMC reduces total computational effort by using a sequence of lower computational effort approximations. We apply NMC, QMC, and MLMC for EVPPI to a decision tree comparing cost-effectiveness of no treatment, antidepressants, and cognitive behavioural therapy (CBT) for depression. This decision tree has three outcomes: no response, response followed by relapse, and response followed by no relapse. Probabilities were based on a network meta-analysis and were correlated for each outcome. **RESULTS:** We compared number of samples required to estimate EVPPI for all probabilities (6 parameters), 1.75 for costs and utilities (6 parameters), 0.13 for treatment effect of CBT on relapse and recovery (2 parameters) and 0.78 for those of antidepressants (2 parameters). Compared with NMC, QMC required 0.37 as many samples for all probabilities, 0.39 for costs and utilities, 0.01 for CBT treatment effects, and 0.08 for antidepressant treatment effects. Similar computational reductions were found when the model was extended to 20 decision options. **CONCLUSIONS:** In some cases, MLMC and QMC demonstrated substantial computational savings over NMC. MLMC performed best for smaller number of correlated parameters while QMC was consistently superior to both NMC and MLMC.

**PRM234: ASSESSING PREFERENCES IN DISCRETE CHOICE EXPERIMENTS (DCES): EFFECTS OF THE APPLIED DESIGN ON THE STUDY RESULTS**

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**OBJECTIVES:** Discrete Choice Experiments (DCEs) are a popular method to elicit stated preferences of patients in healthcare. There exist different options how to design a DCE. However, little is known about how these options influence the outcomes of a DCE study. **METHODS:** A cross-sectional survey of 122 students at a German University was conducted, investigating preferences of students with regard to a hypothetical health insurance bonus program (fitness club, professional tooth cleaning, BMI assessment, coaching, pay-back bonus). Each respondent completed a questionnaire with three sets of choice tasks with 8 different choices each (one basic design (BD) and two further sets with design modifications). Design options tested, based on similar content, were (M1) increasing the number of levels for one attribute; (M2) changing the order of the attributes on choice cards, (M3) adding an opt-out option. Three outcome comparisons, based on a generalized multinomial logit model, were made: BD versus M1 (56 respondents), BD versus M2 (55), and BD versus M3 (43). **RESULTS:** Both the effect size and even the direction of the influence of the attributes on respondents’ utility varied between the design options. So, as an example, the most important attribute in the BD design was the mandatory tooth cleaning (relative importance: 63%-69%), but the relative importance decreased to 38% when M2 was applied. Applying M1 and M3 changed the ranking of the importance of all other attributes, e.g. fitness club membership was rated as the second most important in the BD design, but the most unimportant attribute in M3. **CONCLUSIONS:** If DCEs are used to inform health policy decision makers, it is crucial that presented results are valid and robust. Obviously, DCE design decisions may substantially influence outcomes of DCE studies. We recommend to take this aspect into account when designing a DCE study.

**PRM235: WHAT’S THE REALITY OF REAL-WORLD EVIDENCE IN HEALTH TECHNOLOGY APPRAISAL?**


**OBJECTIVES:** How real-world evidence (RWE) can contribute to assessment of product value is increasingly recognised. However, there is lack of formal guidance on using such data in health technology appraisal (HTA) for reimbursement. Against this background, we conducted two systematic literature reviews (SLRs) to explore expert opinion on using RWE in HTA (SLR 1) and on what forms of RWE could meet HTA requirements (SLR 2). **METHODS:** Following PRISMA guidelines, MEDLINE and Embase were systematically searched for English-language publications indexed between 2012 and 2017 to conduct the two SLRs, with supplementary searches of
HTA-body websites without time limits. **RESULTS:** Limited HTA guidance was found, and this focused on analytical methods for comparative individual-patient data from RWE. Of 200 references screened in SLR1, 20 were considered relevant. Most of these commented that, to date, RWE’s role in HTA has been to help address gaps in randomised-controlled-trial (RCT) evidence or to validate trial-based results (e.g., from single-arm studies in conditions with poor prognosis). Of 300 references screened for SLR2, 40 were relevant. These publications focused on statistical techniques to control for selection bias and adjust for confounder effects in RWE (e.g., adjusted survival curves, propensity modelling, inverse probability-of-censoring weighted correction, and machine-learning techniques). Additionally, a few studies suggested RWE could offer advantages in network meta-analysis, through enabling connection of networks and increasing sample size and generalizability of results. Experts’ main concerns about using RWE related to selection of the most appropriate data sources, and the validity of exchangeability assumptions where RCT data and RWE are combined. **CONCLUSIONS:** While RCTs remain the cornerstone in assessing comparative efficacy of products in HTA, RWE is increasingly acknowledged as a valuable information source. Further decision and methodological frameworks are needed to offer clear guidance on when and how RWE should be incorporated into HTA submissions.

**PRM236: ELECTRONIC CAPTURE OF CLINICAL OUTCOME ASSESSMENT DATA: WHY IS IT NOT USED MORE IN CLINICAL STUDIES?**

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**OBJECTIVES:** Electronic modes of data collection for clinical outcome assessments (i.e., eCOA) have many benefits over paper-based data collection, yet their uptake in studies is less than expected. The Patient-Reported Outcome (PRO) Consortium developed a questionnaire to elicit perceptions of and factors considered by pharmaceutical company stakeholders when choosing a COA data collection mode. **METHODS:** The 12-item questionnaire assessed preferred COA data collection mode, rationale for selection, factors considered, barriers or reasons to support eCOA adoption, and respondent background. Pilot testing of the online questionnaire was conducted and a link to the revised, final questionnaire was sent to PRO Consortium member firm representatives (n=26) for distribution within their respective firms. **RESULTS:** Respondents (n=152) represented several functional areas, including medical/clinical scientists, operations, and outcomes research groups; 52.5% had 15 or more years of pharmaceutical industry experience across multiple therapeutic areas. Electronic data collection was preferred by 90.8% of respondents while 9.2% preferred paper. The five most important factors for determining COA data collection mode were study design (58.6%), set-up lead time (46.1%), costs (44.5%), complexity of eCOA vendor management (40.6%) and respondent familiarity with eCOA (35.2%). Critical factors for successful eCOA implementation included site and patient training (80.8%), eCOA provider experience (68%), lead time for design (62.4%), help desk support (57.4%) and user acceptance testing (50.4%). Perceived barriers to adopting eCOA included set-up/lead time, funding, regulatory concerns, site and patient receptivity/burden, data integrity, device failure, internal resourcing and study team eCOA experience. A limitation of this study was that respondents were not a representative sample of pharmaceutical industry stakeholders; however, it provides insight into important issues involved with eCOA adoption. **CONCLUSIONS:** Our findings support the need for further education of stakeholders, streamlining of eCOA services, and improving partnerships between sponsor and technology providers, all of which may improve eCOA uptake.

**PRM237: EXPECTED VALUE OF INFORMATION ANALYSIS TO EVALUATE THE POTENTIAL GAINS OF AN RCT COMPARING WOUND DRESSINGS**

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**OBJECTIVES:** A variety of wound dressings are available for general surgery, categorised as Simple, Advanced, Glue and no dressing (Exposed). These differ in costs and may differ in surgical site infection (SSI) risk. This study aims to explore the use of value of information methods to assess if a new RCT is a cost-effective use of resources, to compare the value of different study designs, and compare results with standard sample size calculations. **METHODS:** We develop a simple decision tree model to compare the costs and quality of life resulting from different wound dressing types, which may differ in SSI risk. We use results from a network meta-analysis to inform the relative efficacy of the different dressing types. Expected Value of Sample Information (EVSI) is computed to evaluate the value of reducing uncertainty by running an RCT for various included interventions and sample size. Population EVSI is presented for 1,208m wounds over a 5-year time horizon. We compare the results with those from standard sample size calculations. **RESULTS:** There was considerable uncertainty as to which dressing type is the most cost-effective. Population EVSI indicates that an RCT comparing dressings is likely to be of value and that
designs that compare Simple Dressings vs Glue have much higher value than designs that do not make this comparison. Balanced designs comparing Simple Dressings vs Glue vs Exposed have population EVSI of £1515m, £2057m, and £2150m for total sample sizes of 500, 2500, 5000 resp. Standard sample size calculations suggest a much larger sample (around 25000). **CONCLUSIONS:** We discuss possible reasons for obtaining a smaller sample size with the value of information approach compared to standard sample size calculations and implications for trial design.

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**PRM238: LISTENING TO THE “PATIENT VOICE” TO IMPROVE DESIGN AND INTERPRETATION OF SECONDARY ANALYSES: AN EXAMPLE IN ATRIAL FIBRILLATION**

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**OBJECTIVES:** To elicit the perspectives of patients with atrial fibrillation (AF) and other stakeholders to improve validity and interpretation of administrative claims-based studies of AF. **METHODS:** Patient (n=5) and clinician (n=10) participants were recruited from an online AF patient community and the University of Maryland Medical System, respectively. Semi-structured interviews captured experiences with receiving or giving an AF diagnosis, variables influencing health care service utilization, treatment decision-making, and patient outcomes. A narrative analysis of the verbatim phrases identified themes that best represented stakeholder and patient perspectives and trajectories from AF diagnosis onwards. These were subsequently analyzed to provide considerations for cohort selection/assembly and relevant covariates/confounders associated with AF studies specifically. **RESULTS:** The patient participants included 3 women and 2 men with AF with a mean time since diagnosis of 3.5 years. The 10 clinicians comprised 2 from each discipline: nursing, cardiology, electrophysiology, family medicine, and pharmacy. Emerging themes included: (1) Challenges diagnosing AF due to the range of symptoms. This suggests that under-diagnosis is likely common and standard approaches used to identify patients with AF using ICD-9/10 codes may be insufficient. Sensitivity analyses to test other methods of identification may be needed; (2) Time gap between initial diagnosis and appointment with specialist suggests researchers may wish to begin follow up at the date of the patient's first eligible prescription instead of diagnosis date in order to avoid immortal time bias when evaluating treatment effects; (3) Specialist's heightened perception of stroke risk compared to generalists, indicating stratification by provider may be important in analyzing anticoagulant prescribing. **CONCLUSIONS:** Identified themes can inform methodological approaches that could improve the validity of observational research studies in AF using administrative claims data. Careful consideration and integration of patient and stakeholder experiences can inform better study designs and improve interpretation of research findings.

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**PRM239: THE IMPACT OF TRIAL DESIGN ON NETWORK META-ANALYSIS AND DECISION-MAKING: A WORKING EXAMPLE IN ULCECERATIVE COLITIS**

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**OBJECTIVES:** Network meta-analysis (NMA) is commonly used in health technology assessment (HTA), however sometimes this approach may be unsuitable because of differences in trial design. The objective of this study is to assess the impact of trial design on NMA results using NICE appraisal (TA342) considering vedolizumab in ulcerative colitis (UC). **METHODS:** The RCT data considered were extracted and assessed alongside structural elements of each trial. Impact of trial design on the NMA and its contribution to the NMA result was then assessed. **RESULTS:** The NMA inclusion criteria considered trials assessing moderate to severely active UC. There were differences between trials in duration, previous treatment with tumour necrosis factor (TNF) inhibitors and randomisation after the induction phase. Trial duration differed: 6 – 8 weeks during induction and 52 – 54 weeks during maintenance. Two trials included patients who had previously received (and in one trial failed) TNF inhibitors; the other trials did not. Two trials randomised patients based on response criteria following induction therapy, whereas other trials randomised to both induction and maintenance at baseline. Substantial trial heterogeneity was identified as an issue in this HTA, and caveats were discussed in detail. NICE highlighted that a random effects model would have been more appropriate, however a fixed effect NMA was still assessed as part of the overall evidence considered. NICE recommended vedolizumab, however this was largely based on tolerability and patient QoL considerations related to corticosteroids and invasive surgery, rather than the comparability of vedolizumab to TNF inhibitor alternatives for treating this patient group. **CONCLUSIONS:** Whilst NMA is important for HTA purposes it assumes no significant trial heterogeneity. Where trial designs differ, this may have an important influence on NMA results, and therefore should be given careful consideration alongside other factors such as tolerability during decision-making.
PRM240: IDENTIFYING ATTRIBUTES OF CANCER TREATMENTS: WHAT DO STAKEHOLDERS CONSIDER IMPORTANT?

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OBJECTIVES: Increasing cancer therapy costs have produced a recent emergence of numerous value frameworks in oncology. However, variation within frameworks and lack of clarity regarding inclusion criteria for value 'attributes' presents a need for further research. This study aims to identify such attributes based on the priorities of different stakeholder groups in order to develop a new conceptual framework for value in oncology. METHODS: January-February 2017 three focus groups (cancer patients, oncology physicians and nurses) were conducted in New York, USA. Using nominal group technique (NGT), groups were tasked to identify and prioritise cancer therapy attributes. Qualitative thematic analysis of transcripts was conducted. RESULTS: 30 attributes were identified. The focus groups highlighted that beyond a primary consideration of the health gains of the therapy (efficacy and toxicity), priorities varied. Long-term adverse effects (sequelae), alternative treatment options, quality of evidence, how well established the treatment is and reputation of the treating oncologist/centre were prioritized by patients (n=8) whilst the nurses (n=10) preferences focussed on mode of administration, quality of life, communication and treatment innovation. The physicians (n=6) prioritised the burden and inconvenience of treatments (to patients and carers), functional outcomes, the financial toxicity to patients, and the societal costs and consequences of the treatment with reference to the disease burden to be addressed. From the thematic analysis a conceptual framework was developed whereby attributes where assigned across health-related, cost-related and non-health-related categories. CONCLUSIONS: Whilst cancer therapy health-gains are prioritised, value frameworks should include considerations beyond health gains and potentially incorporate differences across stakeholders. The study outlines that the relative importance of attributes varies across stakeholder groups. Results of this study are currently informing the development of a discrete choice experiment (DCE) to elicit specific weightings of preferences across stakeholders.

PRM241: EVALUATING ROBOTREVIEWER FOR AUTOMATED RISK OF BIAS ASSESSMENT IN A SYSTEMATIC REVIEW: A CASE STUDY


OBJECTIVES: Risk of bias (RoB) assessment is an important part of a systematic review and hence the production of health technology assessment. However, it is a time consuming, subjective and labour intensive process, and disagreements on a study's RoB between reviewers are common. In response, novel software tools have emerged which aim to support this process. RobotReviewer is a free web-based machine learning system that aims to automate RoB assessments of randomised controlled trials (RCTs). RobotReviewer has been tested internally by its developers where it performed well, but to date we have not identified any published independent evaluations. We compared and evaluated RobotReviewer against the current standard for RoB assessment, defined as double, independent, human researcher assessment with disagreements resolved by a third reviewer. METHODS: A case study has been undertaken where RobotReviewer was tested on a subset of RCT papers that had been previously assessed by two independent human researchers, as part of a systematic review. The results of the automated (i.e. RobotReviewer) assessments were compared with the manual, human reviewer assessments for similarity at each RoB domain in accordance with the Cochrane Risk of Bias Tool. RESULTS: 35 papers reporting an RCT were assessed for RoB by two independent human reviewers and RobotReviewer. The results of manual (i.e. human reviewer) and automated (i.e. RobotReviewer) RoB assessment were compared. The mean level of agreement between RobotReviewer and double, independent, human researcher assessment was 72% across all papers. 25% agreement was achieved across three papers, 50% agreement was achieved across eight papers, 75% agreement was achieved across 14 papers, and 100% agreement was observed across 10 papers. CONCLUSIONS: This study has provided practical insight into the current effectiveness of employing a machine learning system to support RoB assessment in a systematic review, as part of a health technology assessment.

PRM242: AN EXPLORATION OF THE METHODOLOGY OF PUBLISHED SYSTEMATIC LITERATURE REVIEWS ON "BURDEN OF DISEASE"

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OBJECTIVES: Understanding the burden of diseases is important for policymakers and health technology assessment bodies. However, there is no established methodological guidance on systematically identifying evidence relating to the clinical, economic or humanistic burden of a disease. We identified systematic literature reviews
(SLRs) on burden of disease and compared their methodologies to look for common themes or key differences. METHODS: We searched MEDLINE via PubMed for articles with “burden” in the title, and limited the results using the “Systematic Reviews” filter. Articles were screened in two stages by one reviewer, with input from a second reviewer when uncertain. Eligible articles had to report sufficient details on ≥2 methodological aspects: evidence sources, database search terms, eligibility criteria, or quality assessment tools. RESULTS: From 834 records identified through PubMed, 251 were SLRs on disease burden. Over 80% of SLRs reported clinical burden (e.g. prevalence, mortality, morbidity), 50% reported economic burden (e.g. costs, resource use, absenteeism, productivity losses), 20% reported humanistic burden (e.g. quality of life and other patient-reported outcomes) and 10% reported caregiver burden. Methodology was highly heterogeneous, partly reflecting diverse definitions of “burden” used across SLRs. Almost all SLRs searched MEDLINE and Embase, in addition to 0–20 other sources of evidence (e.g. other databases, congress abstract books, reference lists). Database search terms did not generally use validated filters for study designs; many did not use any specific search terms for burden outcomes. Formal quality assessment was only performed in half of the included studies, using a variety of published checklists. CONCLUSIONS: The variation in approaches for conducting SLRs on burden of disease may make it difficult for policymakers to compare the results of SLRs in different disease areas. Consideration of the similarities and differences between the methodologies identified in this review will be useful to inform future SLRs.

PRM243: 3-STEPS STRATEGY FOR PATIENTS EARLY ACCESS TO AN UNAUTHORIZED MEDICATION / DEVICE PROJECT DESIGN (BASED ON 23 PROJECTS ANALYSES INCLUDING EAP, CUP, NPP, IND, ATU)

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OBJECTIVES: Every expanded access project is unique, thus the goal of this research was to develop a systemic approach that could be implemented for any project on early access independent of the design. METHODS: 3-steps strategy has been developed, verified and tested on 23 expanded access projects of various designs, including EAP, CUP, NPP, treatment IND, and ATU. The first step in the strategy is to complete the objectives matrix: primary and secondary. Using market authorization plan, to mark the lists of countries as ‘proactively go’, ‘reactively go’ and ‘no go’. Based on the matrix for the objectives (ethical – to treat patients only; to get early real-word data/long term FUP, reimburse the cost/launch best price policy) the strategy at a second step creates an algorithm of the best submission approach per every country/site/patient or its combinations using the dedicated regulatory database. During the third step the strategy reflects a matrix of the objectives and submission processes and implements accordingly into the dedicated project processes, plans and systems unique per country/site/patient. RESULTS: 3-steps strategy supports multiple designs of the project for a successful early access but also downstream commercialization following marketing approval. For example, in countries where charging is permitted, prices used in early access will anchor payer expectations around price points. Also, familiarity with drug usage in early access should enable smoother uptake upon launch. 3-steps strategy was found to be cost-effective, supporting the timelines for launch, and fulfilling the objectives of the client and other involved stakeholders. CONCLUSIONS: Despite the complexity and variety of early access project designs in worldwide arena, 3-steps strategy can be implemented in each scenario. It results in fewer burdens for all parties involved, and is effective in meeting the unmet requirements of patient population to be treated within the speed of EAP.

PRM244: EMBEDDING RANDOMIZED CONTROLLED TRIALS INTO MEDICAL PRACTICE

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OBJECTIVES: To provide insight in how Pragmatic Clinical Trial (PCT) features can be embedded in RCTs and especially how registries and other routinely collected health data can be used to reduce costs, increase speed of recruitment and limit the amount of additional work needed for investigators, while keeping sufficient quality and acceptability. METHODS: Literature review and assessment of ongoing trials. RESULTS: In the TASTE and VALIDATE-SWEDEHEART study, among others, electronic databases were present, so that it was possible to define and fine-tune inclusion and exclusion criteria based on medical practice before the start of the trial as well as to test the relevance of CRFs and to set expectations around drop-out, missing values and site recruitment. For the Validate-SWEDEHEART trial, data substitute and support/validate RCT data and support its generalizability, using hybrid systems where adjudication is possible. Long term follow up and extension studies were enabled as most patients stay in the electronic databases. This shows that traditional RCTs can be made more pragmatic regarding follow up, eligibility criteria, recruitment, organization, setting and primary outcomes, while adherence and treatment prescription needs to be strictly defined to assign the relative outcome to treatment. Mitigation of potential risks regarding blinding, among others, will be discussed. CONCLUSIONS: RCTs can be embedded in current medical practice in a variety of ways to reduce costs and improve pace of study execution while remaining acceptable.
**PRM245: GAMIFICATION, WHAT IS IT AND HOW CAN IT BE USED IN HEALTH OUTCOMES RESEARCH?**

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**BACKGROUND:** Gamification is a novel approach which aims at applying elements from game design to other contexts. This method seeks to improve user experience and increase engagement, with medium to long-term benefits on behavior. So far gamification has been successfully applied to Business, e-Learning and Marketing, and starts attracting more and more attention in e-Health. **METHODS:** The aim of this paper is to introduce theoretical aspects on gamification and its possible impact on wellness and health-related context. By providing real-world example of how it is currently applied in health, we will showcase the means and methods that can increase patients and health professionals' fun, engagement, and communication. Motivation plays a key role when engaging into a brand new activity in autonomy for a recurring amount of time (intrinsic motivation vs extrinsic motivation). There is a wide variety of elements related to motivation affordances (e.g., points, leaderboards, feedback), however to be effective they must address the social situation of gameplay as well as the specificity of each health context. Platform of implementation for gamification is a non-negligible aspect as some of them may be more effective mediums for delivering health interventions. Limitations will be reviewed and we will provide suggestions so that future initiative may avoid known pitfalls. **CONCLUSIONS:** Gamification is growing on a fertile soil with the widespread of digital platform in the population (e.g., smartphones, tablets, and computers) and current technologies used in medical care for assessment and monitoring (e.g., ePRO, online questionnaires, wearable devices). Current applications in e-Health have been proved to provide short-term engagement through extrinsic rewards, but the long-term potential of gamification remains to be explored. Solutions must be sought from existing psychology theories and game design experience.

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**PRM246: MAPPING THE SYSTEMATIC REVIEW TOOLBOX**

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**OBJECTIVES:** The Systematic Review (SR) Toolbox is an open online resource of tools to support the systematic review process. The toolbox has been well-received by the systematic review community and is a Cochrane Collaboration recommended source of review production software. To ensure the toolbox resource remains current and useful to researchers, a literature mapping exercise was undertaken to develop a search strategy to regularly horizon scan for review production tools. **METHODS:** Research publications on tools to support the systematic review process were analysed using two tools to enable the mapping of the literature; Yale MeSH Analyser and VOS viewer text-mining software. Data was extracted on 1) MeSH subject headings and other keywords 2) free-text terms relating to systematic review tools. This data was used to develop a search strategy that would automatically search a number of sources at regular intervals, including MEDLINE, ensuring new tools are identified and indexed in the toolbox efficiently. **RESULTS:** 82 publications were analysed. MeSH headings, keywords, and free-text terms were collated and informed the development of the search strategy. The search strategy was designed and tested on the MEDLINE database (via Ovid) and set to automatically run at regular intervals. New publications identified by the search are assessed using the toolbox inclusion and exclusion criteria. Included publications are added to the toolbox. **CONCLUSIONS:** The mapping exercise enabled the development of an efficient search strategy to identify new tools to support the systematic review process. Future plans are to translate the search strategy to search a range of information sources in health care research.

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**PRM247: REAL WORLD DATA IN FRANCE – STATE OF THE ART**

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**Objectives:** So far, the use of real world data (RWD) in France is limited. The aim of the study is to make an inventory of RWD and the way they are used by the different stakeholders of the health care system in France (hospitals, pharmaceutical companies, public health agencies, doctors…). We want to compare the existing RWD in France and the new ‘SNDS’ (Système national des données de santé) and investigate the limitations within the use of RWD in France and how the creation of the SNDS could enable a better use of the RWD. **Methods:** We collected various forms of RWD by searching in the medicines recommendations made by the HAS (Haute Autorité de Santé), the database of the ATIH (technical agency on hospitalization’s information) and of the French national health insurance. **Results:** We built a table that summarized this information and that contained six columns: Type of RWD, content, access, limits, cost and an example. Two different tables have been created: the first one represents the various existing types of RWD (register, observational study, PMSI, SNIIR-AM) study and the second one shows the
new perspectives open by the creation of the SNDS. We also found new kinds of data that could be incorporated in the future into real world studies (health application, connected devices) and we listed new potential stakeholders that could enter the domain of RWD (Google, phone operators, startups…). Conclusion: The objectives of the SNDS helped us to conceptualize and synthesize what the RWD are in France and how they should evolve in the next few years. RWD are growing and should increase even more with the opening of the SNDS. The SNDS have an important potential and may help to go over the limitations that the French system is facing so far with RWD.

PRM248: A CONCEPTUAL MODEL OF THE ECONOMICS OF VISUALIZATION IN DIAGNOSTICS AND SURGERY

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OBJECTIVES: In recent years, there have been many important advances in medical devices designed to provide diagnostic and surgical imaging and visualization. This presents an important health economics and outcomes research challenge: how can we quantify the economic value of incremental improvements in imaging and visualization? This project was focused on developing a conceptual economic framework to describe the basic structure of economic evaluations of visualization. METHODS: The project had three parts. First, we conducted interviews with two groups of key opinion leaders: (1) medical devices product leaders in industry, and (2) physicians who use the devices. Industry experts were asked about design attributes and the engineering intent of improvements in visualization, and physicians were asked about clinical utility. Second, we conducted a comprehensive review of the literature on the economics of diagnostics and the clinical utility associated with visualization. Third, we used the interviews and the literature to construct a conceptual framework for economic evaluation. RESULTS: The primary goals of the conceptual framework were to: (1) develop an understanding of the clinical utility associated with visualization devices, and to identify measures that quantify clinical utility; (2) identify economic outcome measures associated with clinical utility; and (3) develop a template framework to which most “economics of visualization” problems could be applied. The conceptual model takes into account some general issues pertaining to economic evaluation of diagnostics, critical elements for health technology assessment agencies, and practical issues concerning measurement of outcomes. The conceptual model consists of a decision tree framework and a narrative description of the variables, pathways, and logic. CONCLUSION: As engineering and scientific advances in visualization accelerate, it is necessary to develop technology assessment tools that weigh the costs and benefits of improvements in visualization and the relationship with diagnostic accuracy and surgical visualization.

PRM249: DISEASE BURDEN MAPPING IN RARE DISEASES: AN EXAMPLE OF HYPOPHOSPHATASIA

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Objective: Rare diseases are often characterised by complex pathophysiology, a wide range of symptoms and outcomes, and a poorly understood patient experience. The authors sought to develop a new approach to describe the relationship between disease pathophysiology and patient outcomes, so as to maximise the value of sparse disease data and to visually communicate complex disease burden information to non-specialist audiences. The approach was applied using hypophosphatasia (HPP) as an example. Methodology: A literature review was conducted to identify all consequences of the disease. A disease burden map was created which visually linked specific manifestations with the impact on patients. Disease elements were categorised according to the proximity of the manifestations to the underlying pathophysiology (organs and systems affected, primary symptomology, morbidity, mortality and Health Related Quality of Life (HRQoL)). Frequency and severity of disease manifestations were represented visually through proportional area boxes. Clinical expert opinion was used along with published evidence to inform the structure of the map and the relative importance of the elements. Practical implementation: Three separate maps were developed for HPP according to age of onset: infantile, juvenile and adult. A structured qualitative and semi-quantitative process was undertaken to elicit input from five clinical experts. In juvenile HPP, the element with the highest burden was functional disability, resulting mainly from bone and muscle pathologies and associated with significant morbidity and reduced HRQoL. In infantile HPP, where patients rarely survive into late childhood, mortality represented the largest component of disease burden. The burden maps were utilised as part of a Highly Specialised Technology submission to NICE in the UK. Conclusion: Despite inherent issues of subjectivity, this approach has proved a useful tool in building consensus among clinical experts on the nature of disease manifestations and for communicating burden to non-specialist audiences.

PRM250: THE USE OF THE EORTC ITEM LIBRARY TO SUPPLEMENT EORTC QUALITY OF LIFE INSTRUMENTS
The European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group (QLG) has refined its strategy towards symptom measurement to meet the needs of researchers and clinicians in light of rapidly changing treatment for cancer patients. The standard use of the validated core questionnaire QLQ-C30 together with a disease-specific module can now be complemented by a user-created item list to cover novel side-effects of a tested drug/treatment. Therefore, the EORTC QLG has enhanced functionalities of the Item Library, a repository of over 850 unique items in up to 110 language versions, enabling users to develop their custom-made item list. The aim of the Item Library is to facilitate flexible, timely measurement of symptoms, complementing the use of fully validated quality of life instruments. The new strategy forms part of a larger research initiative in the EORTC QLG. The Item Library is already fully accessible to academic and pharmaceutical industry users. It is also undergoing further validation in order to answer all questions arising from the end users. Through multiple search options (symptoms, keywords, related items), users can identify items and scales that best address the side-effects to be measured. Selected items can then be added to a new questionnaire, including the corresponding conditional items, instructions, response scales and time frames. The finalised custom item list is subsequently reviewed by the Item Library’s content manager, to ensure that the questionnaire is composed correctly and contains all the necessary elements and information. The approved custom questionnaires become available for all other users to browse through, export or adapt for use in their trials, creating an invaluable resource for research and broadening the portfolio of available instruments.

**PRM251: ASSESSMENT OF ECONOMIC MODEL STABILITY BY REPEATED ONE-WAY SENSITIVITY ANALYSIS**

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**OBJECTIVES:** One-way sensitivity analysis (OWSA) is used to assess parameter uncertainty in health economic modeling by increasing and decreasing the base case value of each parameter and plotting the impact on the outcome in a tornado chart. OWSA provides useful information regarding which parameters are most influential. However, in cost-effectiveness analyses, where the outcome is an incremental cost-effectiveness ratio, OWSA may be challenging to interpret when the sign of the numerator or denominator changes and does not clearly display where these inflection points occur. We present a method to conduct repeated OWSA in order to better characterize the relationship between parameters and results across a range of values, and to identify where inflection points occur. **METHODS:** A Microsoft Excel with Visual Basic for Applications (VBA)-based hypothetical model was created to demonstrate the method and to compare and contrast a traditional “fixed” OWSA and repeated OWSA. The repeated OWSA analysis performs a OWSA at multiple intervals within a range specified by the user. Results are plotted on an x-y scatter-plot of the Δ % change in parameter value vs the ICER. Repeated OWSA displays which parameters result in a stable, predictable, ICER and also demonstrates at what point certain parameters result in an inflection in the ICER (ie, where the sign of the ICER changed due to a switch in the Δ cost or Δ effectiveness). Finally, the analysis displays the relationship between each parameter and the ICER result (eg, linear or non-linear). **CONCLUSIONS:** Repeated OWSA offers a potential improvement to fixed OWSA by providing a more complete view of how each parameter interacts with the ICER across a range rather than one snapshot at a fixed value. This analysis may be particularly useful in cases where there are small differences in costs or effectiveness, resulting in ICER volatility in fixed OWSA.

**PRM252: EXPECTED VALUE OF SAMPLE INFORMATION FOR INDIVIDUAL LEVEL SIMULATION MODELS TO INFORM STOP/GO DECISION MAKING BY PUBLIC RESEARCH FUNDERS: A METHODOLOGY FOR THE DAFNEPLUS DIABETES EDUCATION CLUSTER RCT**

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**OBJECTIVES:** This paper presents a conceptual methodology for calculating the expected value of sample information (EVSI) to inform the decision making of a UK public funder (NIHR) regarding whether to fund the second stage of the DAFNEplus research programme. The first phase of DAFNEplus programme involves redeveloping, piloting and refining DAFNE structured education courses for adults with type 1 diabetes. The second phase aims to test the effectiveness and cost-effectiveness of the revised course (DAFNEplus) versus a standard DAFNE course in a cluster randomised controlled trial (RCT). **METHODS:** To generate prior estimates of effectiveness of DAFNEplus
compared to DAFNE and the uncertainty around them, an expert elicitation exercise will be conducted using the Sheffield Elicitation Framework to estimate likely incremental changes at 12 months follow-up in: HbA1c; rate of severe hypoglycaemia; and rate of diabetic ketoacidosis. Five experts will include: medical experts; diabetes educators; psychologists; and potentially patient representatives. Summary statistics from the first phase of DAFNEplus will be presented to the experts. EVSI of the proposed trial will be calculated by conducting a cost-effectiveness analysis of DAFNEplus versus DAFNE using an existing individual level simulation model (the Sheffield Type 1 Diabetes Policy Model), the elicited distributions and Sheffield Accelerated Value of Information Tool (SAVI) by Strong et al. The EVSI will compared to the cost of the RCT. CONCLUSIONS: Elicitation of likely effects on clinical endpoints and their prior uncertainty, together with individual level simulation modelling and SAVI, makes it feasible to include health economic criteria in stop/go decisions by public funders. To generalise this approach to other diseases and settings, analysts will need to consider: how to synthesise prior evidence; the balance between existing prior data and eliciting expert judgement; the roles and biases of experts to elicit from; and wider decision making criteria of the research funder.

PRM253: A ROBUST, REPRODUCIBLE METHOD FOR EVALUATING THE SUITABILITY OF DISPARATE OBSERVATIONAL DATABASES FOR POOLED ANALYSIS, USING THE OMOP COMMON DATA MODEL

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BACKGROUND: Data pooling -- integration of patient-level data from different databases -- is used to increase sample size where individual databases are too small. Differences in data format and content, along with population heterogeneity, require careful evaluation to identify differences that may interfere with interpretation of results of subsequent pooled analyses. Evaluation for pooling can be difficult, time-consuming, and is not reproducible across databases. Use of a Common Data Model (CDM) provides opportunities for development of efficient, reproducible methods to evaluate appropriateness of pooling across a wide variety of databases. METHODS: We developed a method, utilizing the Observational Medical Outcomes Partnership (OMOP) CDM to efficiently assess format, content, and appropriateness of disparate databases for pooling. It takes advantage of existing OMOP data transformation processes, documentation and programs available in the public domain through the Observation Heath Data Sciences and Informatics (OHDSI) Collaborative. Method summary: Mapping: map databases into OMOP format. For many databases, mapping documentation is available through OHDSI. Transformation: transform databases into OMOP format using existing OHDSI utilities or developing denovo. Analysis: OHDSI ACHILLES reports enable interactive exploration of patient and data characteristics for any OMOP-format database. Evaluation: review by clinical experts to identify differences that may interfere with pooled results interpretation. PRACTICAL IMPLICATIONS: By design, OMOP data transformation normalizes data format and identifies content quality issues. OHDSI programs provide meaningfully comparable population characteristics, including diagnostic and treatment patterns, which can aid in understanding heterogeneity across disparate databases. De-duplication, if necessary, is facilitated by standardized-format data. CONCLUSIONS: Use of a CDM facilitates systematic evaluation of individual datasets for pooled analyses. This is especially useful for pooling data from different countries, where coding systems and practice patterns may vary. An additional benefit is that CDM-format data can be easily integrated / used for subsequent pooled analyses, assuming pooling is appropriate.

PRM254: COMPARISON OF WEIGHTING METHODS USED DURING THE CONSTRUCTION OF MULTIPLE-CRITERIA DECISION ANALYSIS TOOL FOR REPEATED USE IN LOWER INCOME COUNTRIES

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OBJECTIVES: In multiple-criteria decision analysis (MCDA) practice, the criteria taken into account regularly differ in relevance, therefore it is necessary to assign importance weights to them. The objective of this study was to compare the most common criteria weighting methods in the process of developing MCDA tools for repeated use in lower income countries in terms of level of detailedness, real world feasibility, and ability to fulfill the axioms of preference ordering. METHODS: The most widely used methods of determining importance weights of various criteria in decision making were reviewed and evaluated. With the construction of hypothetical decision problems, the number of questions required to be answered by decision-makers in order to quantify criteria weights were estimated. RESULTS: An inverse relationship between the detailedness of the methods and their simplicity was identified. A hypothetical decision problem with 6 criteria expects decision makers to answer 10 questions applying the ‘Simple Multi–Attribute Rating Technique’ (SMART) method with swing weighting approach, and 15 questions in case of the ‘Analytic Hierarchy Process’ (AHP). With ‘Discrete Choice Experiments’ (DCEs), applying full factorial design would result in an unmanageable number of questions; however, different techniques (for example, orthogonal
arrays) exist for reducing this number. The total number of questions using the ‘Potentially All Pairwise RanKings of all possible Alternatives’ (PAPRIKA) methodology is generally between 45 and 60, assuming 4 possible performance levels according to each criterion. At the same time, this approach also provides additional information on the shape of the scoring functions. CONCLUSIONS: When time and research budget is limited to develop MCDA tools for repeated use, selection of criteria weighting method should be based on the expected level of detailedness, availability of resources, and the size of the decision-making group that will participate in determining the criteria weights.

PRM255: REVISITING INDIRECT HEALTH PREFERENCE ELICITATION AS A BASE CASE

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In the context of constrained health budgets, cost-effectiveness of health technologies has become an important concern. The strengths of this approach include its ability to explicitly model assumptions of what policy makers value when making a decision, to contextualize decisions in terms of absolute versus relative effects, and to use results to inform efficient use of research resources. A key aspect of many cost-effectiveness models is the quality adjusted life year (QALY), which allows analysts to capture the value of reduced mortality and improved quality of life simultaneously. Measurement of QALYs requires the determination of quality weight which is bound at negative infinity (indicating death or health states worse than death) and one (indicating perfect health). While these weights can be elicited directly from patients through a standard gamble or time trade off, most national bodies recommend that preference for health states be determined by the general public. This recommendation comes despite the empirical evidence that these indirect health state valuations often differ in magnitude, and possibly in direction, to those directly elicited from patients. In this abstract, we assume that the purpose of cost-effectiveness analysis is to maximize population health and argue that recommendations to use indirect preference elicitation render this goal impossible to achieve. We use examples from the published literature to create two scenarios which illustrate how indirect preferences may be preferred for questions of prevention, but may lead to unjust and inefficient resource allocation that will meaningfully decrease population health when evaluating interventions to improve the cure disease. We argue that methods guidelines for cost-effectiveness analysis of health technologies ought to recommend that the source of health preferences match the population that will be most directly affected by the decision problem.

PRM256: ENGAGING PATIENTS IN THE DEVELOPMENT AND VALIDATION OF PATIENT-REPORTED OUTCOME (PRO) MEASURES AS PARTNERS, NOT JUST PARTICIPANTS


OBJECTIVES: There is growing recognition among researchers, regulatory agencies, policy makers and payers of the value in taking a more patient-centred approach to health outcomes research. Patient-reported outcome (PRO) measures assess the experience of health conditions from the patient perspective, capturing data that may not be accurately reported by clinicians or observers. Methods in which patients can be actively engaged in PRO development and validation beyond their traditional role as passive participants are presented and discussed. METHODS: The extent of patient engagement in PRO research can range from passive (participant) to active (researcher). ‘Active’ engagement requires patient direction in the planning/conduct of research. Specifically, input into the development of study documents (e.g. interview guides), selection of PRO measures or generation of new items, involvement in cognitive testing (e.g. reviewing results, informing instrument modifications) and in evaluation of measurement properties (e.g. scoring or meaningful changes in scores) are methods of active engagement. The convening of patient advisory groups represents a practical means of facilitating patient engagement in the research process. IMPLICATIONS: The optimal level of engagement depends upon the objectives of the research. In particular there is a need to balance methodological rigour with feasibility, cost and timeline considerations. Most importantly, implementation requires careful planning to ensure patients receive adequate support (e.g. PRO and regulatory training) to ensure that they are comfortable, empowered and able to contribute meaningfully to the research process as equal research partners. CONCLUSIONS: There is scope for patients to be more actively engaged in PRO measure development/validation, as research partners rather than just participants. Patient advisory groups present a practical way of engaging patients at key stages and help to ensure that PRO measures are truly patient-centred, valid and credible; assessing what is important to patients, in a way that reflects patients’ experiences.

PRM257: EFFICIENT SECONDARY USE OF REPRESENTATIVE SOCIAL AND HEALTH CARE DATA IN FINLAND: ISAACUS DATA LAKE, ANALYTICS AND KNOWLEDGE MANAGEMENT PRE-PRODUCTION PROJECT

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Background: Finnish residents have access to a comprehensive public welfare system and unique personal identity codes which enable the cross-linking of registries and databases. Sitra-funded Isaacus pre-production projects are aimed at preparing an operator that provides wellbeing data and open data from different information sources and registers on a one-stop-shop basis. The permit and guidance services for the users of this data will be made available in one place. The operator will be based on future legislation and it is planned launch date is early 2018.

Objectives: City of Kuopio has initiated a pre-production project "Well-being information on children and young people" that has the following feasibility objectives: to create the data lake, to utilize analytics for knowledge management, to enable real-world evidence-based client segmentation and, finally, to test a remote-operating platform.

Methods: The pre-production project utilizes social and health care data from child and adolescent (<18 years) clients of the Kuopio social services. A data lake together with its metadata is developed to compile client-associated and administrative big data scattered in various databases. Platform is created to support efficient secondary data use. The dataset from the data lake is analysed with the primary objective to support knowledge management through client segmentation based on similarities in client characteristics and/or resource use. The analysis also includes the new social welfare and healthcare reporting system ‘service packages’ information.

Results: Results of the analyses are presented in the conference. Obtained knowledge can be utilized to support more effective service provision in the City of Kuopio and will enable faster secondary use of similar data also elsewhere in Finland.

Conclusions: Service provision for the residents is expected to improve by using big data, analytics, knowledge management, segmenting, targeting, and consequent evidence-based criteria, which this preproduction project aims to establish for children and adolescents.

Prm258: Network Meta-analysis in the Evaluation of Vaccines

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Background: Head-to-head clinical efficacy randomized controlled trials (RCTs) for vaccines are often unfeasible due to logistical and/or ethical constraints and comparative real-world effectiveness studies are methodologically challenging. Without direct efficacy or effectiveness comparisons, relative risk/benefit of vaccines can be challenging to assess. Objectives: While network meta-analyses (NMAs) have been used extensively to estimate the comparative efficacy and safety of therapeutic interventions, the application of this method to compare vaccines is rare. To our knowledge, there is only one published vaccine NMA which compares the relative effectiveness of rotavirus vaccines. We discuss how NMAs can be used to evaluate the relative efficacy and safety of vaccines within a specific disease area; using vaccines to prevent herpes zoster (HZ) as another case example. Methods: NMA methodology can be applied to indirectly compare vaccines; however, issues such as waning immunity, indirect vaccine effect, changing epidemiology over time, and seasonality of the disease of interest pose unique challenges. Detailed feasibility assessments should be undertaken to systematically determine if NMA is appropriate from a methodological and clinical perspective. This requires close collaboration between methodologists and clinical experts. Recently, a comparison of vaccines for HZ was deemed feasible, in particular due to availability of evidence studied in large, well-designed RCTs, and due to the epidemiology of HZ. Key challenges faced included variations in effect modifiers such as patient age, follow-up duration, and outcome definitions. It was possible to leverage existing NMA guidance to provide credible and reliable estimates of the relative effect of HZ vaccines that have not been studied in head-to-head efficacy trials. Conclusions: NMAs provide a method to indirectly compare different medical interventions, including vaccines, in the absence of head-to-head data. With RCT data and real world evidence, NMAs can contribute to inform vaccine recommendations and public health decision making.

Prm259: Beyond Product Value - A Holistic Approach for Value Assessment

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The current regulated model of value assessment (HTA) and P&R decisions is based on a concept of product value. It requires evidence of incremental therapeutic or diagnostic value corresponding to an established unmet medical need. The primary objective is ensuring best use of resources to optimize population health. Benefits beyond medical outcomes and cost-effectiveness are generally not considered. However, medical technologies and additional services may add value in other ways, such as improving efficiency of care pathways or eliminating waste. Convenience, less burden, timely access to resources and CO2 reductions are important benefits to patients, HCP’s and society. Examples are remote care (e.g. telehealth), process or pathway optimization. These approaches are more common in MedTech where low IP protection, shorter product cycles, and low regulatory hurdles drive...
strategies to convince a more fragmented stakeholder landscape through contracting and collaboration. Funding is partly driven by the privately financed (second) healthcare market. Development of Market Access and HEOR strategies is traditionally guided by the regulatory framework with focus on HTA/P&R submissions. This approach is less suitable to identify gaps and opportunities for health solutions with benefits beyond improved clinical outcomes. We propose a framework with three levels of value potential 1) product value (technologies; regulatory model), 2) value-based health care (solutions; collaboration model) and 3) public value (citizenship; societal model). This framework enables a structured approach to define value propositions, identify gaps and opportunities and plan for different types of evidence and stakeholder engagement. The traditional „societal” perspective in economic analyses quantify the wider budget impact of improved health outcomes. First approaches to include the ecological dimension into economic analyses (Marsh et al 2017) include impact of CO2 burden, however, without addressing its value. Dialogue with key stakeholders should start regarding ways to include value beyond product into appraisals and decisions.

### PRM260: CONSIDERATIONS FOR THE SELECTION OF WRITTEN CHINESE VARIANTS IN THE PROCESS OF TRANSLATING AND LINGUISTICALLY VALIDATING CLINICAL OUTCOME ASSESSMENTS (COAS)

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**OBJECTIVES:** There are several predominant variants of both written and spoken Chinese. The written variants are Traditional and Simplified Chinese, and well-known spoken variants include Standard Mandarin, Cantonese, and Taiwanese. Understanding the relationship between these written and spoken variants and the appropriate circumstances for usage is vital to successful translation and linguistic validation of COAs targeted for use in populations that speak and write these variants of modern Chinese. **BACKGROUND:** Modern spoken Chinese is divided into at least seven major dialectical groups containing over 200 total dialects. Although many of these spoken dialects are not mutually intelligible, historically, there has been a common written system underlying the spoken variants. This common written system officially diverged in 1956 into two variants, Traditional and Simplified Chinese. Confusion frequently arises from the fact that use of these variants is not interchangeable, but dictated largely by national boundaries and political tensions. Traditional Chinese is used predominantly in Hong Kong, Taiwan, Macau, and overseas Chinese-speaking communities. Simplified Chinese is used predominantly in mainland China, Singapore, and Malaysia. Furthermore, formal education is typically given in only one of the written variants, and although the two are related, and most speakers are exposed to both in daily life, they differ enough that knowledge of and literacy in one variant does not perfectly transfer to the other. **CONCLUSIONS:** There are important differences between the Traditional and Simplified variants of written Chinese, as well as geographic and national variation in their use. Additionally, most formal education occurs in only one variant, and there is no clear relationship between spoken variants and their underlying written forms. Together, these factors necessitate careful consideration of the written variant and the subject population requested for translation services and linguistic validation of COAs in locations where modern Chinese is used.

### PRM261: SPECIAL CONSIDERATIONS FOR CONDUCTING QUALITATIVE INTERVIEWS WITH CANCER PATIENTS AND THEIR CAREGIVERS FOR THE PURPOSE OF DEVELOPING CLINICAL OUTCOME ASSESSMENTS

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**BACKGROUND:** Eliciting information directly from the patient is particularly important in oncology due to the symptoms, impacts and toxicities associated with the disease and treatment. When integrated into oncology clinical care, rigorously developed clinical outcome assessments (COAs) can improve outcomes and ensure the patient voice is heard. However, working with patients with advanced cancer or undergoing end of life care requires careful consideration. **AIM:** To discuss special considerations required when using traditional methods for conducting qualitative research in oncology, in a sensitive and appropriate manner, while maximising data retrieval. **CONSIDERATIONS:** When designing qualitative research studies in oncology, a number of factors should be considered, including; situational risk assessment (e.g. understanding the participants diagnosis, prognosis and treatment history), access to a support network (e.g. ensuring the patient/caregiver has sufficient emotional support following the interview) and appropriate safeguarding procedures (i.e. clear safeguarding process in place for researchers to follow if necessary). **TECHNIQUES:** Practical adaptations to research (e.g. interview length, location of interview, presence of another person for support) can help to make oncology patients/caregivers feel more comfortable and encourage spontaneous discussion. Clear pre- and post-interview guidance for researchers can help to ensure that high-risk participants (e.g. patients with terminal illness) are identified early in the research and appropriate risk assessment strategies are implemented. Post-interview follow up can be pursued on an ad-hoc basis if the researcher deems it necessary. Clear safeguarding procedures can protect both participant and
researcher. **CONCLUSION:** Developing and validating oncology specific COAs is fundamental to fully capturing the patient experience in oncology. Special consideration of the sensitivities specific to this patient population help to ensure the rigorous development of oncology specific COAs while ensuring participants (and researchers) are appropriately supported. These considerations also mean researchers are adequately equipped with the knowledge and resources to conduct the research in an ethical, supportive manner.

**PRM262: GROUP CONCEPT MAPPING AS A STRATEGY FOR DEFINING PATIENT-CENTERED OUTCOMES IN PROMS AND PRO-PMS**

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Although patient engagement in health research is commonly recognized as a priority, there is a lack of guidance regarding appropriate and feasible methods for defining patient-centered outcomes. This is critical when developing both patient-reported outcome measures (PROMs) and PRO-based performance measures (PRO-PMs). One area that has been particularly ignored is engaging patients in the creation of conceptual frameworks that define outcomes that matter to patients. Clinicians and researchers generally create these frameworks, relying on the incorporation of the patient voice through one-on-one interviews, surveys, and focus groups. However, each of these strategies are fraught with limitations, including patient response bias and potential limitations of generalizability. In addition, they do not leverage the potential of social research networks and group-based technological solutions to develop patient-centered conceptual frameworks. This presentation addresses the following objectives in PROM and PRO-PM development: (1) review of group concept mapping (GCM; Concept Systems®) as a viable method for engaging patients, (2) provision of examples of GCM applications in defining outcomes, and (3) discussion of strengths and limitations of this approach. GCM combines qualitative (statement generation and sorting) and quantitative (multidimensional scaling and cluster analysis) methods to generate visual maps depicting a conceptual model. This presentation will show examples of studies that have utilized GCM for the development of PROMs and a recent Robert Wood Johnson Foundation PRO-PM study to define patient perceptions of “good” healthcare. Strengths of GCM include evidence of validity and reliability, ability to incorporate multiple stakeholder views into a single conceptual framework, and the potential for application to measurement and evaluation. Potential limitations include problems with technical literacy, attrition, and managing response burden. Methods to address these limitations will be discussed. Overall, GCM represents a valuable participatory concept development strategy with the potential to enhance traditional researcher-driven methods in PROM and PRO-PM development.

**PRM263: USING A MIXED METHODS APPROACH TO DETERMINE THE ITEM-SCALE STRUCTURE AND SCORING FOR CLINICAL OUTCOME ASSESSMENTS**

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**BACKGROUND:** Factor analysis is a widely accepted approach to assess the suitability of an instrument structure and can be used in the content and psychometric validation of clinical outcome assessments (COAs). Qualitative insights into the importance of items and concepts should also be considered when developing a scoring algorithm, outlining how to combine individual items into a score in a meaningful way. **OBJECTIVES:** This study outlines quantitative methods to define a suitable item-scale factor structure for COAs and qualitative approaches to develop a scoring algorithm to weight items by importance. **RESULTS:** Factor analysis is used to assess the suitability of a hypothesized conceptual framework for a COA (confirmatory factor analysis) or to identify a suitable item-scale structure in the absence of a pre-defined conceptual framework (exploratory factor analysis). First or second-order confirmatory factor analysis can be used depending on the hierarchy and structure of the concept of interest. Once the item-scale factor structure is finalized a scoring algorithm can be developed. Many COAs are scored by assigning an equal weight to all items and summing or averaging items to form domain and total scores. Qualitative ranking exercises with patients and clinical experts can determine the relative importance of items. Weighting can then provide the percentage that each item should contribute towards an overall score. This can provide insights into which items are of greater relevance to a condition, and highlight concepts that are crucial or less critical to a health condition. Factor analysis and qualitative approaches to develop scoring algorithms should be used in combination to ensure that item-scale structures of COAs are both quantitatively and qualitatively valid. **CONCLUSIONS:** When developing a COA factor analysis and qualitative weighting or ranking exercises can be used in combination to determine item-scale structures and scoring for COAs.

**PRM264: CONCEPTUAL MODELING FRAMEWORK FOR GLOBAL FUNCTIONING OF ADHD PATIENTS**

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State-Transitions Models (STMs) in Attention-Deficit Hyperactivity Disorder (ADHD) are often in discrete time following a standard Markov process. Consequently, transitioning from one health state to another can only take place at the start or end of a predefined time interval and depends only on the present state. As a result, patient history is ignored. In addition, the utility measures related to the states of existing models are often based on Health Related Quality of Life (HRQoL) measures such as the EuroQol five dimensions questionnaire (EQ5D). However, it has been called into question whether measures such as the EQ5D can adequately capture the well-being and the level of functioning of children and adolescents with ADHD. Therefore, we propose a new approach for differentiating between the states by focusing on impairment. We use the Global Assessment of Functioning (GAF) - scores, obtained from real-world data, to model the disease progression of children and adolescents with ADHD. In addition, contrary to current studies, we choose to use continuous time semi-Markov modeling to deal with the limiting assumptions of existing STMs in ADHD as stated above. The methods will be illustrated using an applied example for ADHD. We aim to investigate whether the proposed conceptual modeling framework based on global functioning fits the observed real-world process better than the existing models. Sensitivity analyses will be performed to determine the impact of difference in goodness-of-fit on the long-term cost-effectiveness estimates comparing a Markov and semi-Markov approach in both discrete and continuous time.

**PRM265: DEVELOPING NEW PRACTICE MODEL TO ENSURE BETTER MEDICATION CONCORDANCE**

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**Introduction:** Tremendous research has been carried out relating nonadherence and its interventions since 1950. Interventions developed were not found to be effective in the clinical scenario. We intended to develop a model or conceptual framework to incorporate medication adherence in clinical scenario. **Methodology:** 5 steps process by Yosef Bareen for conceptual framework analysis was used 1: Extensive literature search was carried out to identify types of model were used for developing interventions. 2: Reviewing result to find the deficiencies in the model and rationale their impact on medication non-adherence. 3: Survey was conducted. 4: Model was developed. 5: Appraisal by different health care professionals. **Result** Model “practice model for medication concordance” is based on closed environment based on two dynamics: health related and patient related. Health dynamic comprises of two participants and patient dynamics have one participant. All information remains within these three active participants. Participants are initiator, mediator and recipient. Initiator may be a physician or pharmacist who initiates the concordance pathway by assessing patient, medication regimen, documents and monitor patient adherence with mutual agreement of patient. Initiator takes the responsibility of creating the environment of concordance. Mediator is another health professional who is responsible to support both initiator and recipient. Once the initiator has assessed recipient, mediator may assist the Initiator by providing supplies (medications or other), technical support (education, reminder aids) and follow up. Information about recipient will be provided to initiator for further evaluation. Mediator shares equal responsibility with initiator to achieve the outcome as set in goals. Recipient usually is one who receives the services from health professionals. Recipient can be patient himself or care taker of the patient which is the focus of the model hence the represent the major part of it. **Conclusion** Model allows health professionals and patient parallel in terms of information, responsibility and accountability.

**PRM266: MEASURING CHANGES IN PATTERNS OF TOBACCO PRODUCT USE OVER TIME: TRANSITION PROBABILITY APPROACHES**


Measuring patterns of tobacco use has typically involved assessing number of units and frequency of use of cigarettes. With the emergence of new types of products (e.g. e-cigarettes, water-pipes, heat-not-burn products), use of more than one tobacco product is increasing in popularity, and therefore quantifying the overall tobacco consumption of individuals is becoming more challenging. Novel products are different in design and consumption to cigarettes and their availability results in multiple and complex combinations that make the measurement of exposure to tobacco and nicotine containing products intricate. Moreover, these complex patterns of use present a challenge when assessing changes over time and evaluating their subsequent impact on health outcomes. Changes in patterns of tobacco product use over time (i.e. moving between different tobacco use status and combinations, the possibilities of single, dual or poly product use, progression from occasional to regular use, initiation, cessation, switching, and re-initiation between products) can be characterized by estimating the probabilities of transition between one tobacco-use state and another. This contribution presents an overview of analytical approaches to assess transitions in complex patterns of tobacco use. It addresses the practical implications of applying these analytical approaches across existing epidemiological surveys and datasets to characterize patterns and determine probabilities of changes in tobacco use status. In addition, it considers the utility of transition probability methods to provide a snapshot into
changes in the patterns of tobacco use and how this can be used to inform future tobacco use trajectories, associated health outcomes, and tobacco harm reduction efforts.

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**DISEASE: SPECIFIC STUDIES**

**INFECTION - Clinical Outcomes Studies**

**PIN1: CASE FATALITY RATE OF ENTERIC FEVER: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**OBJECTIVES:** Enteric fever, caused by S. Typhi and S. Paratyphi, is a febrile illness. It can present as a severe disease with complications including intestinal perforations and death. Reliable estimates of disease burden are needed to inform decision makers in the implementation of new control strategies. Until now, no meta-analysis has been conducted to summarize mortality from enteric fever. Therefore, we aimed to collect all studies reporting a case fatality rate (CFR) for enteric fever.

**METHODS:** For this systematic review and meta-analysis, we searched Embase, Medline, WoS, and PMC for articles published between January 1, 1970 and January 11, 2017 reporting mortality from enteric fever. Studies had to diagnose cases via serology or culture, be conducted in an endemic country, and include all ages. We used a random effects model to combine the estimates. The protocol was registered in PROSPERO (CRD42017057428).

**RESULTS:** We identified 40 eligible articles, which resulted in 44 outcomes. The average CFR was estimated to be 2.49% (95% CI: 1.65%-3.75%). The odds of dying from enteric fever is lower in children compared to adults (OR: 0.73, 95% CI: 0.37-1.44, n=15). The odds of dying from an antimicrobial resistant strain versus a susceptible strain is 1.73 (95% CI: 0.69-4.33, n=6). However, these differences were not found to be statistically significant.

**CONCLUSIONS:** The probability to die from typhoid may in crease further with rising antimicrobial resistance. More data is needed to investigate possible prognostic factors and to obtain more precise estimates.

**PIN2: HAART TREATMENT TRENDS IN HIV/AIDS PATIENTS IN A TERTIARY CARE HOSPITAL, MALAYSIA**

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**OBJECTIVES:** Current study is aimed to explore and to observe the use of HAART therapy and the combinations of antiretroviral drugs among HIV/AIDS patients.

**METHODS:** An observational retrospective study of all patients diagnosed of HIV infection and on HAART therapy from Jan 2007 to Dec 2012 was conducted at infectious disease department of Hospital Pulau Pinang, Malaysia. Patient socio-demographic details along with clinical features were recorded. Data was descriptively analyzed by using statistical package for social sciences (SPSS 20).

**RESULTS:** Out of 792 patients that underwent HAART therapy, 607 (76.6%) were male and 185 (23.3%) were female patients. Different regimens of the HAART therapy were used in the current study. Overall First line therapy of HAART was used 769 (97.1%) times in HIV patients while 110 (13.9%) times 2nd line therapy was used. Combination of AZT+3TC+EFV of first line antiretroviral drugs was used 331 (41.8%) times followed by TDF+FTC+EFV combination which was administered 271 (34.2%) times and D4T+3TC+NVP used 177 (22.3%) times. AZT and D4T in the First line drug combinations were changed many due to associated ADRs such as anemia and lipodystrophy. Combination of AZT+3TC+LOP-RITO of Second line drugs of HAART were prescribed in 48 (6.1%) patients followed by TDF+FTC+LOP-RITO (5.9%).

**CONCLUSIONS:** The study indicates the use of first line HAART therapy was higher in HIV/AIDS patients. The use of first line of antiretroviral drugs such as AZT, D4T and TDF were in the initial stages of HIV infection, though the therapy was changed either to different combinations or to 2nd line HAART therapy when the condition become worsen. However, a multicenter study with a large sample size may provide us with better understanding of the use of HAART therapy.

**PIN3: ASSESSMENT OF ISONIAZID PROPHYLAXIS THERAPY INITIATION APPROPRIATENESS, ADVERSE DRUG REACTION AND ADHERENCE AMONG HIV PATIENTS IN UNIVERSITY OF GONDAR REFERRAL HOSPITAL, NORTHWEST ETHIOPIA**

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**BACKGROUND:** Treatment for latent TB infection (LTBI) is an important strategy to reduce socioeconomic burden of
HIV/TB coinfection by providing Isoniazid prophylaxis therapy (IPT) for people living with HIV (PLWHIV). Appropriate initiation and good patient adherence are crucial to achieve this. **OBJECTIVES:** The aim of this study was to assess level of IPT initiation appropriateness, ADR and patient adherence in HIV patients on IPT during follow up in university of Gondar referral hospital. **METHODS:** A facility based cross sectional study design was conducted and simple random sampling technique was used for selected populations. A structured questionnaire was used and IPT initiation appropriateness was determined against WHO guideline; patient adherence was evaluated according to Morisky adherence scale and self reported ADR was also assessed. Data was analyzed using SPSS version 21 for windows and statistically significance considered when P<0.05. **RESULTS:** The obtained appropriateness level of IPT initiation was 116 (77.9%). According to Morisky adherence scale 121(81.2%) HIV patients were having good adherence with 95% CI (77.8 – 84.6). IPT adherence had statistically significant association with number of pills, ADR report and contraindication history. Out of a total of 52 patients who took IPT and experienced ADR, 31 (59.62%) took IPT longer than three months. The most common ADR encountered was constipation (30.8%). **CONCLUSIONS:** The level of adherence to IPT was generally high in PLWHIV. However, level of adherence to IPT and ADR reported seeks the attention of health care providers and researches for optimum clinical outcomes.

**PIN4:** COMPARATIVE EFFICACY AND SAFETY OF REGIMENS FOR TREATING PLASMODIUM FALCIPARUM MALARIA: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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**OBJECTIVES:** To compare and rank available ACT regimens for treating PF malaria. **METHODS:** We searched PubMed, Embase, and the Cochrane Central systematically for the randomized control trials (RCTs) of ACT regimen for treating PF malaria. Network meta-analysis (NMA) was performed to estimate risk ratio (RR) and 95% confidence interval (CI) from both direct and indirect evidences. We then ranked the comparative effects of all interventions with the surface under the cumulative ranking (SUCRA) probabilities. Inconsistency between direct and indirect estimates was statistically assessed globally. Primary outcome was adequate clinical and parasitological response (ACPR) at 28 days. Secondary outcomes were ACPR at 42 days, and serious adverse events. **RESULTS:** A total of 28 RCTs with 16 409 patients were included. The most commonly investigated regimens were artesether plus lumefantrine (ATM+LMF), dihydroartemisinin-piperazine (DHDATN+PPQ) and artesunate plus amodiaquine (ATS+AMQ). DHDATN+PPQ was associated with a significantly higher ACPR than artesunate plus mefloquine (RR 1.01, 95% CI 1.00 to 1.03), ATM+LMF (RR 1.02, 95% CI 1.01 to 1.04), artesunate plus chlorproguanil and dapsone (RR 1.12, 95% CI 1.07 to 1.16) but not significantly higher than artesunate plus mefloquine (RR 1.00, 95% 0.99 to 1.03). **CONCLUSIONS:** This NMA suggests that DHDATN+PPQ was the most effective ACT regimens and should be preferred as first-line regimens against PF malaria.

**PIN5:** SAFETY OF A SPECIFIC FIRST LINE ANTIRETROVIRAL REGIMEN: A REVIEW

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**OBJECTIVES:** To study the efficacy and safety of a specific first line antiretroviral (ART) regimen composed of tenofovir (TDF), lamivudine (3TC) and efavirenz (EFV), which was used until recently as the preferred first line treatment for adults in Brazil and is still amongst the recommended by the World Health Organization. **METHODS:** In April, 2017, we conducted a systematic search of the literature in MEDLINE via Pubmed, Cochrane CENTRAL, EMBASE and Lilacs for cohorts that reported on toxicity or CD4 lymphocyte count or viral load among HIV-1 infected adults on first line ART. Only reports on naïve patients were considered. One arm of treatment must have consisted of TDF+3TC+EFV. **RESULTS:** Our search yielded 441 abstracts, of which 36 registries were read in full, resulting in 5 papers that met all eligibility criterion. The cohorts included comprised 7275 patients mostly from African countries. The most frequent backbone comparators were zidovudine+lamivudine and stavudine+lamivudine, and as for 3º agents, nevirapine and ritonavir boosted lopinavir were most common. The average follow-up was 1 year from the start of treatment. The median age at treatment initiation was 43.6 years and the median CD4 count at baseline was 178.6 cells/mm3. Only one study disclosed effects on viral load, just as only another one reported on CD4 final count. Regarding toxicity, adverse events associated to efavirenz were reported in 4 of 5 studies, mainly associated to the central nervous system and rash. Zidovudine based regimens appear to be safer compared to tenofovir based treatment. **CONCLUSIONS:** Recently, the preferred first line regimen in Brazil traded the 3º agent efavirenz to dolutegravir, which appears to be wise, considering the adverse events associated to the former. Nonetheless, efavirenz is still widely used. It is difficult to study the efficacy and safety of one regimen specifically, however, it is of importance in order to optimize therapy.
**PIN6: SYSTEMATIC REVIEW OF HERPES ZOSTER EPIDEMIOLOGY: AVAILABLE EVIDENCE IN SPAIN RELATED TO SPECIFIC SUB-POPULATIONS**

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**OBJECTIVES:** To review available scientific evidence on incidence of herpes zoster (HZ) in the general population and in specific sub-populations in Spain. **METHODS:** A systematic review of the literature (up to October 31, 2016) was carried out, using the Medline (PubMed) and Embase databases, combining the following search terms: "herpes zoster", "diabetes mellitus", "chronic obstructive pulmonary disease", "chronic heart failure", "mental disorders" and "immunocompromised". Supplements for local scientific congresses, non-indexed Spanish journals and official regional epidemiological reports, potentially HZ-related, were also manually searched. Inclusion criteria were: reporting incidence of HZ in the Spanish general population and/or specific sub-populations; English or Spanish language. No restrictions were applied on study design or population age. **RESULTS:** Among 264 references retrieved (48 PubMed, 148 Embase and 68 manual searching), 30 were finally included. Incidence rate of HZ in the general population was reported in 9 studies, ranging from 2.1 to 5.5/1,000 population. In the remaining 21 references, assessing sub-populations, HZ incidence ranged from 9.0 to 15.0/1,000 patients with diabetes mellitus (DM), from 11.0 to 12.0/1,000 population with chronic obstructive pulmonary disease (COPD) or cardiovascular diseases. In asthmatic patients, 6.9 HZ cases/1,000 subjects were reported. The highest observed HZ incidence ranged from 1.3 to 400.0/1,000 population defined as immunocompromised. HZ incidence related to specific immunocompromised conditions were 10.0/1,000 cancer patients, 13.0/1,000 AIDS patients, from 5.0 to 240.0/1,000 transplanted patients and from 11.0 to 27.0/1,000 population with rheumatic diseases. Only 3 studies performed comparisons with general population, reporting an increased risk of HZ for DM (24%), COPD (39%) and COPD patients receiving inhaled corticosteroids (61%). **CONCLUSIONS:** Available studies in Spain are heterogeneous, but suggest that HZ incidence is higher in specific sub-populations (immunocompromised, cardiovascular diseases, COPD and DM) versus general population. More evidence is required for reliable identification of risk conditions for HZ occurrence.

**PIN7: IMPACT OF COMORBIDITIES ON THE RISK AND COST OF HOSPITALIZATION IN HIV-INFECTED PATIENTS: REAL WORLD DATA FROM THE ABRUZZO REGION**

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**OBJECTIVES:** Due to the success of highly active antiretroviral therapy, HIV-infection has been transformed into a lifelong condition. Therefore, HIV-infected patients are more likely to experience age-associated comorbidities. Little is known about the impact of the comorbidities on the risk of hospitalization and related costs in HIV patients. Our aim was to quantify the risk of hospitalization and costs associated with comorbidities in HIV-infected patients. **METHODS:** The study population included subjects aged ≥18 years with HIV infection, identified from the Abruzzo’s hospital discharge database during the years 2004-2013. Patients were then followed in the years 2014-2015 and all admissions were recorded. Patients’ comorbidities (Charlson Comorbidity Index, CCI) were extracted from ICD-9-CM codes in the hospital discharge abstracts. Poisson regression was used to compare the Incidence Rate Ratios (IRRs) of acute hospital admissions in patients with and without each comorbidity class. A generalized linear model under gamma distribution was used to estimate adjusted mean hospital costs. IRRs with 95% confidence interval (CI) were adjusted for age, gender and the other comorbidities. Costs were derived from official Italian DRG-based reimbursements. **RESULTS:** Among 1026 HIV patients identified (mean age 47 years), 30% experienced at least one comorbidity and 14.5% needed acute hospital admission during the follow-up period. The risk of acute hospitalization significantly increased among patients with renal (Adjusted IRR 2.27; 95%CI: 1.45-3.56), liver (IRR 2.21; 1.57-3.13), and chronic pulmonary comorbidities (IRR 2.31; 1.63-3.32). Adjusted mean hospital costs were €2,130 in patients without comorbidities, and €4,111 and €6,488 in those with CCI=1 or CCI≥2, respectively. **CONCLUSIONS:** The presence of renal, liver and chronic pulmonary comorbidities doubled the risk of hospitalization. A CCI≥2 was associated with a four-fold increase in hospitalization costs. Our experience underlines that antiretroviral treatment should be tailored in accordance with HIV-associated comorbidities, to minimize the risk of acute events during the chronic management of HIV-infection.

**PIN8: ROTAVIRUS VACCINATION MAY REDUCE ACUTE GASTROENTERITIS RATES ACROSS ALL AGE GROUPS IN ENGLAND**

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**OBJECTIVES:** Rotavirus is the main cause of severe acute gastroenteritis (AGE) in children under 5 but has not
been considered an important cause of AGE in older age groups. England introduced rotavirus universal vaccination for infants in July 2013. This study aims to evaluate the impact of rotavirus vaccination on all cause AGE episodes in England across all age groups using the Clinical Practice Research Datalink (CPRD) and Hospital Episode Statistics (HES) database. METHODS: We included all persons registered in CPRD between 1st July 2010 and 30th June 2016. Cut-off date to define pre- and post-vaccination periods was 1st July 2013. AGE general practitioner (GP) episodes and hospitalizations were defined using AGE related Read and ICD10 codes with a 14 day disease free period. We calculated crude episode rates of AGE, overall and stratified per age group, health care setting and calendar time. RESULTS: There were 28 AGE GP episodes per 1,000 person-years in the pre-vaccination period compared to 23 post-vaccination overall, a 18% (95% CI: 17.5-18.6) reduction. The largest decrease was observed in children < 5 years: 26.6% (95% CI: 25.5-27.6) reduction. A significant decrease was also observed among age groups not vaccinated, particularly among 65 to 74 year olds: 16.9% (95% CI: 15.1-18.6) decrease. Impact on AGE hospitalizations was minimal overall (2%, 95%CI: 0.3-3.1), but with reductions of 29% (95%CI: 26-32) -5 years, and 6% (95%CI: 2.3-9.6) in 85+ years. CONCLUSIONS: This ecological analysis suggests that the introduction of rotavirus vaccination in England may have resulted in a significant impact on all cause AGE episodes across all age groups, similar to what has been seen following the introduction of pneumococcal vaccination among infants. Although trends before vaccination suggested a stable background rate, we cannot rule out a coincidental decrease of AGE unrelated to rotavirus vaccination.

**PIN9: REAL WORLD EFFECTIVENESS OF TREATMENT WITH OBV/PTV/R ± DSV IN HCV PATIENTS WITH CIRRHOSIS IN POLAND**

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**BACKGROUND:** In chronic hepatitis C virus-infected patients cirrhosis is associated with less effective INF-based treatment and higher risk of complications. New IFN-free direct-acting antiviral therapies have greatly improved sustained virologic response (SVR) rates in patients with cirrhosis, nonetheless the rates are still lower than in patients without cirrhosis. **OBJECTIVES:** To assess the real world effectiveness of treatment with OBV/PTV/r ± DSV in patients with HCV infection and compensated cirrhosis participating in Polish public drug program. **METHODS:** Registry that included patients with cirrhosis treated with OBV/PTV/r ± DSV, who entered the drug program from Oct 1 2015 to Jan 31 2016 in seven non-randomly selected hospitals (N=265). Data on genotype, comorbidities, past treatment, end of treatment response, SVR24 and reason for early treatment cessation (including AE) was collected retrospectively. **RESULTS:** From 265 patients with cirrhosis receiving treatment (ITT population) 263 completed treatment (2 fatalities) and 256 had SVR24 assessed (4 lost to follow up and 3 fatalities) (PP population). Analysed group comprised 50% male, 54% treatment-experienced, prevailing comorbidities were hypertension (38%) and diabetes (16%). 250 patients achieved SVR24 – 94% in ITT population, 98% in PP population. Results are consistent with the efficacy in noncirrhotic patients from the same registry; from 238 patients with liver fibrosis stages F1-F3 (ITT) SVR24 was assessed in 225 patients (PP) and 222 achieved SVR24 (93% in ITT population, 99% in PP population). **CONCLUSIONS:** Real world data from Poland regarding OBV/PTV/r ± DSV therapy of HCV infected patients with cirrhosis confirms the high effectiveness of this regimen. Presented results are further reinforced by RWE study performed by Flisiak et al. (2017), where 90 patients with cirrhosis reached SVR24 (72% in ITT and 99% in PP population). The results indicate the effectiveness of Polish drug program.

**PIN10: ZOSTER VACCINE EFFECTIVENESS AGAINST INCIDENT HERPES ZOSTER AND POST-HERPETIC NEURALGIA IN ELDERLY IN THE UK**

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**OBJECTIVES:** Herpes zoster (HZ) is a painful skin rash that occurs most frequently in older adults and is caused by reactivation of latent varicella virus (VZV). Its most common complication is post-herpetic neuralgia (PHN). The UK introduced zoster vaccination in the national immunization program in 2013. The vaccine was routinely offered to 70 year-olds and, as part of the catch-up, to 79 year-olds. This study assessed the vaccine effectiveness (VE) against HZ and PHN in elderly within the total population. **METHODS:** This retrospective cohort study included subjects from birth cohorts 1943-1946 (routine) and 1934-1937 (catch-up) in the UK Clinical Practice Research Datalink (CPRD). Vaccinated subjects were compared to unvaccinated subjects using piecewise Cox regression model. HZ outcomes in community setting were analyzed, including HZ, PHN and other HZ complications (i.e. neurological but not PHN, ocular, disseminated and other). **RESULTS:** For the routine birth cohorts (79274 subjects), we found a VE for HZ of 76.4% (95% CI: 70.6%-81.1%) and for PHN of 68.3% (95% CI: 7.4%-89.1%) for the first 2 years of vaccination. For the subsequent 2+ years, the VE estimates of HZ was 56.1% (95% CI: 29.2%-72.7%). For the catch-up cohorts (48193 subjects), the VE estimates were comparable. We found insufficient evidence to determine the VE for other HZ complications. **CONCLUSIONS:** Within the total population, the HZ vaccine provided protection against HZ and PHN, but its protection declined over time. Immunosuppressed conditions need to be taken into account.
PIN11: EPIDEMIOLOGY AND OUTCOMES OF DIFFERENT TREATMENT STRATEGIES IN PATIENTS WITH PNEUMONIA CAUSED BY CARBAPENEM-RESISTANT ACINETOBACTER BAUMANNII IN MEDICAL INTENSIVE CARE UNITS

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OBJECTIVES: The prevalence of carbapenem-resistant Acinetobacter baumannii (CRAB) is emerging in the intensive care units (ICUs) in Taiwan. Pneumonia is a common site of CRAB infection and associated with high mortality in critically ill patients. The aims of this study were to study the epidemiology and treatment outcomes associated with different treatment strategies of CRAB pneumonia. METHODS: We conducted a multicenter retrospective study on adults (≥ 20 years) patients with CRAB pneumonia in the medical ICUs of three hospitals, including a medical center and two regional hospitals in Southern Taiwan during 2010-2015. The data were collected for patient characteristics, prescribing patterns, drug resistant patterns, and treatment outcomes. RESULTS: A. baumannii accounted for about 13% of all isolates in the MICUs, and up to 86% of them were CRAB. The prevalence of CRAB was continuously increasing during the study period. More than 94% of the CRAB were susceptible to tigecycline and colistin. Of the 215 patients with CRAB pneumonia included in the analyses for treatment effectiveness, 84 (39%) were treated with tigecycline monotherapy, 42 (20%) with tigecycline combined with colistin, 34 (16%) with colistin monotherapy, 28 (13%) with colistin combination, and 27 (13%) with tigecycline combination. Patients treated with tigecycline monotherapy had significantly higher mortality rate than colistin monotherapy (p = 0.04). CONCLUSIONS: CRAB was emerging in the MICUs in Taiwan. Tigecycline was the most common antibiotic prescribed for CRAB pneumonia patients; however, tigecycline monotherapy was associated with significantly higher mortality rate than colistin monotherapy.

PIN12: VACCINES FOR HERPES ZOSTER: A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS IN ADULTS ≥50 YEARS OF AGE

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OBJECTIVES: To perform a systematic literature review (SLR) of efficacy and reactogenicity/safety of vaccines for herpes zoster in adults ≥ 50 years of age based on evidence from randomized controlled trials. METHODS: A systematic search was performed in May 2017 using predefined terms in MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials in addition to manual searches of relevant non-indexed conferences. Standard SLR methodology was used to select relevant publications using predefined Population, Intervention, Comparators, and Study Design (PICOS) criteria. Quality was assessed at the trial level using the Cochrane Risk of Bias tool. Key outcomes extracted included efficacy (against herpes zoster (HZ), post-herpetic neuralgia, and other HZ complications, as well as HZ burden of illness mean score) and reactogenicity/safety (injection site/local reactions, systemic/general reactions, vaccine-associated systemic/general reactions, total discontinuations, and serious adverse events). RESULTS: Of 1,290 unique publications retrieved for screening, 25 publications (associated with 21 unique trials and 108,678 patients) were included. There were 21 full texts and four conference abstracts all published between 1998 and 2017. Only two HZ vaccines were evaluated in the included studies: the candidate HZ adjuvanted subunit vaccine and Zoster Vaccine Live, although various routes of administration, formulations, doses, and schedules were assessed. Eight included articles (representing four trials and one sub-study) reported efficacy outcomes of interest, while 23 articles (representing 20 trials) reported reactogenicity/safety outcomes of interest. CONCLUSIONS: This SLR provides a comprehensive overview of the literature reporting on the efficacy and reactogenicity/safety of HZ vaccines. Vaccines against HZ demonstrated favourable benefit risk profile. Given no head-to-head efficacy studies were identified, the relative merits of the individual formulations should be explored. Further investigation is needed to examine the appropriateness and feasibility of combining the extracted outcomes using meta-analysis or network meta-analysis and to define the best methodology to be used.


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OBJECTIVES: The objectives of this study were to assess trends in the median HIV ARV drug prices per DDD in the US in the period 1987-2015 and to compare the AWP and the NADAC for HIV ARV drugs at market entry. METHODS: The list of HIV ARV drugs at market entry in the US was extracted from the FDA website. We used the World Health Organization Anatomical Therapeutic Chemical (ATC) classification system website to collect defined daily dose (DDD) for each HIV ARV drug. We used the RedBook to collect the WAC and the AWP. The AWP were collected from approval date to deactivation date or December 31, 2015. We used the consumer price index-all urban consumers (CPI-U) to convert prices to 2015 US dollars. Descriptive analysis was performed. RESULTS: In the period 1987-2015, the FDA had listed 39 ARV drugs with 48 different pharmaceutical dosage forms and strengths approved in the US. The market entry inflation-adjusted AWP per DDD was $28.59 for zidovudine, the first HIV ARV that was approved in 1987. The lowest market entry inflation-adjusted AWP per DDD was $5.13 for lopinavir/ritonavir in 2000 and the highest was $102.97 for (cobicistat/elvitegravir/emericitabine/tenofovir alafenamide) in 2015. The median market entry inflation-adjusted AWP per DDD was $28.59 (interquartile range [IQR]=−$12.20) for HIV ARV drugs approved in the 1980s, $13.80 (IQR=$17.60) in the 1990s, $20.60 (IQR=$19.50) in the 2000s, and $39.04 (IQR=$24.04) in the period 2010–2015. The NADAC represented on average 75.2% of the AWP, with a range from 64.5% (ritonavir, 100 mg) to 95.9% (efavirenz/emericitabine/tenofovir disoproxil fumarate, tab, 600 mg-200 mg-300 mg). CONCLUSIONS: The prices of new HIV ARV drugs at market entry increased over time. The prices of existing drugs increased faster than the inflation rate. The high prices of HIV ARV drugs may impact affordability and accessibility to critical medications for both insured and uninsured population groups.

PIN14: GENDER INEQUALITY IN ACUTE GASTRO-ENTERITIS RATES IN ENGLAND

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OBJECTIVES: Norovirus and Rotavirus are the main cause of infectious acute gastroenteritis (AGE) across all age groups. As part of a wider study on the causes of medically attended AGE in England, we assessed whether these causes of AGE affected females and males differently. METHODS: We extracted all general practice and hospital inpatient episodes based on codes indicative of a potentially infectious gastroenteritis event between June 2007 and July 2013 in the CPRD and HES inpatient linked databases in England. This included both cause-specified and unspecified gastroenteritis. Confirmed non-infectious gastroenteritis were excluded. Relying upon the cause-specified episodes, we modeled the proportion of the cause-unspecified episodes for a range of infectious pathogens (Rotavirus, Norovirus, Clostridium difficile, other specified bacteria) in 4 age strata (under 5, 5-17, 18-64 and 65+ year old) and by gender. Pathogens for which little or no diagnostic records were available (parasites, other specified viruses) were excluded. RESULTS: We obtained data on a population of over 5.1 million for a total of 17.1 million person-years. Combined GP attendance and hospitalization rates for any AGE were 21.9% (95% CI: 21.2%-22.5%) higher among females compared to males. This difference was not consistent across the age groups: rates were 12.1% (95% CI: 11.1%-13.0%) and 11.4% (95% CI: 9.8%-13.0%) lower among 0-4 years and 5-17 year old girls, respectively, but 41.4% (95% CI: 40.3-42.5%) and 29.3% (95% CI: 28.0-30.7%) higher among women in the 18-64 and 65+ year age groups. A similar trend was seen for both Norovirus and Rotavirus with the exception that Norovirus rates were also higher among girls under 5. CONCLUSIONS: Infectious gastro-enteritis occurs more frequently among male children and female adults. Norovirus deviated from this pattern with rates being also higher among girls under 5. The cause-specified comparisons are based on modeling and require further validation.

PIN15: RETROSPECTIVE ANALYSIS OF THE BURDEN OF CYTOMEGALOVIRUS DISEASE IN IMMUNOSUPPRESSED PATIENTS AFTER HAEMATOPOIETIC CELL TRANSPLANTATION IN ENGLAND


OBJECTIVES: Cytomegalovirus (CMV) disease is a complication that may occur in association with haematopoietic cell transplantation (HCT). This retrospective, matched cohort study assessed the burden of CMV disease in HCT recipients in England using the Hospital Episodes Statistics database. METHODS: The impact of CMV disease on mortality, graft-versus-host disease (GVHD), relapse-free survival and healthcare resources up to 12 months after CMV disease diagnosis was assessed in recipients who underwent an HCT between April 2011 and May 2016. Each HCT recipient with CMV disease was randomly matched with two HCT recipients without CMV disease. Matching criteria were age, gender, indication for transplantation, previously received anti-thymocyte globulin and/or total body irradiation. RESULTS: Overall, 4863 HCT recipients were recorded. CMV disease was recorded as a primary/secondary diagnosis in 312 HCT recipients (6.4%), and commonly occurred ≤3 months post-transplant (n=210, 63.3%). HCT recipients without CMV disease had a significantly greater probability of overall survival (79.0%)
versus those with CMV disease (70.8%; p-log-rank=0.0125). The logistic regression model showed that CMV disease was significantly associated with greater risk of in-hospital mortality (hazard ratio 1.40, 95% confidence interval 1.04–1.89). Probability of GVHD post-transplant was not significantly different between HCT recipients with and without CMV disease (23.3% vs 20.0%, respectively; p-log-rank=0.88). Probability of relapse, conditional on survival, was 19% in those with CMV disease and 22% in those without (p-log-rank=0.30). Mean healthcare costs were significantly higher in HCT recipients with CMV disease (£24,476) compared with those without (£17,610; p=0.0001). Generalised linear models showed that CMV disease led to increases of 44%, 30% and 30% in total costs, cumulative in-patient days and number of hospital re-admissions, respectively. **CONCLUSIONS:** This study highlights the burden of CMV disease in HCT recipients with substantial increases observed in mortality and hospital resource use in England.

**PIN16: INCREASED EPISODE RATE OF MEDICALLY-ATTENDED ACUTE GASTROENTERITIS IN DIABETICS IN ENGLAND**

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**OBJECTIVES:** Previous reports suggest diabetes as the most prevalent chronic condition among gastroenteritis cases admitted to hospital but little evidence is available on the extent to which diabetes is a risk factor for medically-attended acute gastroenteritis (MA-AGE). **METHODS:** Patients registered in general practices contributing to CPRD (Clinical Practice Research Datalink) from January 2006 to December 2014 and eligible for linkage to HES (Hospital Episode Statistics) APC (Admitted Patient Care) data were included. The type-I diabetic, type-II diabetic and diabetes-free cohorts were defined based on diabetes-related diagnoses, treatments and test results. MA-AGE events were defined based on MA-AGE related Read and ICD-10 codes. Episodes were defined as events separated by a minimum 14-day disease-free period. Episode rates and 95% confidence intervals (CI) were calculated for the three cohorts overall, by age group, by gender and by healthcare setting (diagnosed in hospital vs by GP only). In addition, age-gender standardized episode rate ratios comparing the type-I and type-II diabetic cohorts to the diabetes-free cohort were calculated, overall and by healthcare setting. **RESULTS:** We observed an episode rate of 60.96 per 1000 person-years (95%CI: 59.33-62.62) in type-I diabetic and 62.56 (95%CI: 62.10-63.03) in type-II diabetics, compared to 32.58 (95%CI: 32.51-32.66) in diabetic-free. This increase is seen across all age groups and both genders, although varying in magnitude, and is higher in hospital than for GP only. The age-gender standardized episode rates ratio comparing the type-I and type-II diabetic cohorts to the diabetes-free cohort are 1.99 (95%CI: 1.96-2.03) and 1.78 (95%CI: 1.73-1.83) overall, 5.03 (95%CI: 4.88-5.18) and 2.85 (95%CI: 2.71-3.00) in hospital and 1.43 (95%CI: 1.43-1.48) and 1.59 (95%CI: 1.54-1.64) for GP only. **CONCLUSIONS:** MA-AGE episode rates are increased in the diabetic compared to the diabetes-free populations. The highest increase is seen for MA-AGE diagnosed in hospital among type-I diabetics.

**PIN17: INCIDENCE OF RESPIRATORY SYNCYTIAL VIRUS RELATED HEALTHCARE UTILIZATION IN THE UNITED STATES**

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**OBJECTIVES:** Respiratory Syncytial Virus (RSV) is the most frequent cause of acute respiratory infection worldwide. Understanding of age specific healthcare utilization is necessary to guide effective prevention strategies. We aimed to assess the incidence rates of RSV related healthcare utilizations in various age groups. **METHODS:** We used the Truven Health MarketScan® Commercial Claims and Encounters database to examine rates of RSV related healthcare utilization in 2008-2014. Incidence rates of healthcare utilization were calculated each year using the total number of enrolled subjects as denominator and those with principal diagnosis for RSV specific ICD9 codes (079.6, 466.11 or 480.1) as numerator. **RESULTS:** During the 7 years study period, the overall rate of all RSV related healthcare utilization was 1.2 per 1000 person-year (ranged 1.0-1.3) with the highest rate in infants <1 year of age (31.4 per 1000, ranged 26.4-35.0). Rates per 1000 person year for hospitalization setting, ER/UC visits and outpatient setting were also highest in infants <1 year and young children. RSV related healthcare utilization rates increased with age among elderly (aged 65-74 vs. 75-84 vs. >85). **CONCLUSIONS:** The annual RSV related healthcare utilization rates were substantial, especially in infants and young children. These results underscore the need to accelerate the development of RSV vaccines to reduce the healthcare burden of RSV.

**PIN18: PULMONARY TUBERCULOSIS TRENDS AND TREATMENT OUTCOMES IN THE GOMOA WEST DISTRICT, GHANA**

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OBJECTIVES: The objectives of the study were to assess the distribution of disease and treatment outcomes of pulmonary tuberculosis and identify factors associated with unsuccessful treatment outcomes. Identification of these factors help multifaceted interventions targeting these factors to be recommended. METHODS: The medical charts of all new persons diagnosed as pulmonary TB either by AFB smear culture or radiography and captured in the district tuberculosis register from January 2010 to December 2015 were reviewed. Patients were categorized as having a successful (cured or completed treatment) or unsuccessful (default, failure, death or unknown) treatment outcome. The association of demographic and clinical factors such as age, sex, employment, health insurance status, subdistrict of abode, co-morbidities, orientation of disease and bacilli smear score with success of treatment, was evaluated by univariate and multivariate logistic regression using Stata. RESULTS: Of 154 patients, 124 (83.2%) had successful treatment outcomes whereas 30 (16.8%) had unsuccessful treatment outcomes. Of those with poor treatment outcomes, 5 (3.36%) had treatment failure, 4 (2.68%) defaulted, 7 (4.70%) died, and 9 (6.04%) had unknown treatment outcomes. Forty-one (26.6%) of cases occurred in the Apam, 27 (17.5%) in Mumford, 28 (18.2%) in Dago, 17 (11.0%) in Onyadze, 15 (9.7%) in Oseedze and 26 (16.9%) in Oguaa subdistricts. On multivariate analysis, cases from Gomoa Oguaa subdistrict (AOR 4.34; 95% CI 1.32-14.24) and old age (above 65 years) were significantly associated with unsuccessful treatment outcomes. CONCLUSIONS: In this study area, treatment success rate was found to be high. However there is the need to focus intervention among older patients above 65 years and the Gomoa Oguaa sub-district in order to ensure higher rates of treatment outcomes. It is imperative to enhance pulmonary tuberculosis education and surveillance in the Apam sub-district to reduce incidence of cases.

INFECTION - Cost Studies

PIN19: STRATEGIES TO EFFECTIVELY PREVENT SURGICAL SITE INFECTIONS IN ITALIAN HOSPITALS: ECONOMIC BENEFITS


OBJECTIVES: Surgical site infections (SSI) represent one of the most frequent hospital acquired infections, and are associated with patient morbidity, excess mortality, longer inpatient stays, and increased costs. Skin preparation with 2% chlorhexidine gluconate (w/v) in 70% isopropyl alcohol in a single use applicator, has been found to lead to a statistically significant reduction in SSI rates compared with other antiseptics. An economic analysis has been developed on the basis of these clinical results to compare the cost impact of different skin preparation solutions from the perspective of Italian hospitals. METHODS: A decision tree model has been developed to compare the costs of 2% chlorhexidine gluconate (w/v) in 70% isopropyl alcohol in a single use applicator with povidone iodine (aqueous and alcoholic) in a generic cohort of 1000 patients undergoing surgery per year. Costs and rates of SSI were retrieved from the wider literature. The robustness of the results were tested with univariate sensitivity analysis. RESULTS: Over a cohort of 1000 patients, 2% chlorhexidine gluconate (w/v) in 70% isopropyl alcohol yearly prevents 26 SSIs compared with povidone iodine alcoholic, and 66 SSIs compared with povidone iodine aqueous. This equates to savings of €120 and €318 per patient respectively in hospitals and a total saving of €120,000 and €318,000 per year for the full cohort. The sensitivity analysis demonstrates that the rate of SSIs is the key driver of the analysis. CONCLUSIONS: The choice of the most effective agent for skin preparation, together with the implementation of a cohesive strategy against SSIs, can lead hospitals to reduce the clinical and economic burden of infections.

PIN20: INFECTION PREVENTION IN HEART SURGERY IN GERMANY: AN ECONOMIC ANALYSIS

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OBJECTIVES: Patients undergoing coronary artery bypass grafting (CABG) using bilateral mammarian arteries (BIMA) are at high risk for surgical site infections (SSI). In these patients, the use of 2% chlorhexidine gluconate (w/v) in 70% isopropyl alcohol (CHG-IPA) in a single use applicator has been found to reduce by 36% the rate of SSI compared with isopropyl alcohol (IPA) alone. An economic analysis has been developed to assess the economic impact of CHG-IPA for CABG-BIMA surgery in the perspective of a German hospital. METHODS: An economic model with a decision tree structure was developed to compare CHG-IPA and IPA alone in a cohort of 100 patients undergoing CABG-BIMA surgery. Costs and rate of surgical site infections were retrieved from German clinical and economic evidence. A univariate sensitivity analysis was performed to test the robustness of the results. RESULTS: Compared with IPA alone, CHG-IPA with single use applicator was associated with 3 fewer SSIs every 100 patients undergoing CABG-BIMA, leading to a total saving of €559,961 for the hospital (€560 per patient
undergoing surgery). The sensitivity analysis demonstrates that results are driven by SSI rates: a minimum relative reduction in the SSI rate (<1%) makes CHG-IPA economically advantageous compared with IPA alone. CONCLUSIONS: The choice of the antiseptic may play an important role both clinically and economically for German hospitals, especially in high-risk and high-cost procedures as CABG-BIMA surgeries.

**PIN21: ASSESSING THE ECONOMIC IMPACT OF THE INTRODUCTION OF DACLATASVIR IN COMBINATION WITH ASUNAPREVRIL FOR THE TREATMENT OF CHRONIC HEPATITIS C IN CHINA**

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**OBJECTIVES:** In China, an estimated 9,795,000 people are chronically infected with hepatitis C virus (HCV), which can lead to life-threatening and resource-intensive complications. Current standard of care has suboptimal efficacy and safety; however, novel direct-acting antiviral (DAA) regimens have improved rates of sustained virologic response (SVR) and tolerability. This study aimed to assess the health economic outcomes of daclatasvir-asunaprevir (DUAL), the first DAA to be approved in China, versus current treatments for patients with HCV genotype 1b (an estimated 5,563,560 patients), from the Chinese payer perspective. METHODS: A published HCV Markov model was used to perform lifetime cost-effectiveness analyses (CEA) of 24 weeks DUAL (SVR: 92.4%, discontinuation: 0.6%, regimen cost: ¥57,810/RMB) versus 48 weeks pegylated interferon-alfa+ribavirin (PR, SVR: 62.4%, discontinuation: 3.9%, regimen cost: ¥53,977/RMB) and 48 weeks interferon-alfa+ribavirin (IR, SVR: 43.0%, discontinuation: 19.0%, regimen cost: ¥45,016/RMB). A budget impact model was developed to predict 2017/18 cost implications of introducing DUAL in China, applying forecast uptake rates and market share, assuming no discontinuation and that 35% of costs are covered by the patient. Published model inputs were specific to the Chinese setting and a 5% annual discounting rate applied. RESULTS: The CEA demonstrated improvements in benefit associated with initiation of DUAL: incremental quality-adjusted life years of 1.29 and 2.10 and incremental life-years of 0.85 and 1.40 per patient, versus PR and IR, respectively, with lifetime per-patient cost savings of ¥29,638 and ¥37,472, respectively. Introducing DUAL treatment is expected to result in an additional 31,333 patients achieving SVR in 2017/18, with a net budget impact of ¥18.90 million in 2017 and ¥0.07 million in 2018. CONCLUSIONS: Introducing DUAL treatment for HCV in China is predicted to offer significant health-related benefit and a reduction in total lifetime cost, whilst having minimal impact (approximately 0.001% of total Chinese reimbursement expenditure) on total 2017/18 budget.

**PIN22: BUDGET IMPACT OF INTRODUCING CEFTAZIDIME-AVIBACTAM (CAZ-AVI) FOR COMPLICATED INTRA-ABDOMINAL INFECTION (CIAI), COMPLICATED URINARY TRACT INFECTIONS (CUTI), AND HOSPITAL ACQUIRED PNEUMONIA INCLUDING VENTILATOR-ASSOCIATED PNEUMONIA (HAP/VAP) TO A HOSPITAL FORMULARY IN ITALY**

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**OBJECTIVES:** CAZ-AVI, a fixed-combination drug containing ceftazidime and avibactam, has been approved in Europe for cIAI, cUTI, HAP including VAP, and aerobic Gram-negative infections with limited treatment options (LTO). The objective of this study is to quantify the budgetary impact of adding CAZ-AVI to a hospital formulary in Italy. METHODS: A model was developed to estimate budget impact of adding CAZ-AVI to a hospital formulary over 3 years. Number of eligible patients were estimated from Italian epidemiological data. Cure and adverse event rates were extracted from clinical trials. Hospital length of stay associated with treatment cures/failures was derived from clinical trials of CAZ-AVI. Cost inputs were retrieved from published Italian Tariff lists. Current and future market shares were based on market research data and manufacturer’s forecast model. Given uncertainty around market share estimates in aerobic Gram-negative infections with LTO, analysis for this indication was not included. RESULTS: The introduction of CAZ-AVI was estimated to carry a marginal impact to the hospital budget. The total cost per treated patient, prior to CAZ-AVI introduction, was estimated to be €12,102 [€4,360 (cUTI), €18,051 (HAP/VAP) after the introduction of CAZ-AVI, an average of 0.5% increase in the budget. Reduction in hospital bed days and hospitalization costs was estimated with introduction of CAZ-AVI. Hospitalization costs represented the largest component of the total costs (93%) while pharmacy and adverse event costs made up 6% and 1%, respectively. The budget impact remained marginal even in sensitivity analysis of lower resistance rates (90% decrease in resistance rates resulted in 0.7% increase in total budget). CONCLUSIONS: The analysis suggested that adding CAZ-AVI to a hospital formulary in Italy would lead to a marginal increase in the hospital budget and a reduction in hospital bed days.
PIN23: COST IMPLICATIONS OF TEDIZOLID INTRODUCTION FOR THE TREATMENT OF COMPLICATED SKIN AND SOFT TISSUE INFECTIONS IN A RUSSIAN MULTI-FIELD HOSPITAL

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OBJECTIVES: Tedizolid is a novel oxazolidinone for the treatment of complicated skin and soft tissue infections (cSSTIs) including those caused by methicillin-resistant Staphylococcus aureus (MRSA). We aimed to estimate budget impact following the introduction of tedizolid for the treatment of suspected or documented MRSA cSSTIs in a Russian multi-field hospital. METHODS: Budget impact model of MRSA cSSTIs management was built based on the results of network meta-analyses (R. McCool et al., 2015; J.F. Logman et al., 2010), randomized controlled trials, observational studies and experts’ opinion. Tedizolid introduction as linezolid replacement in a simulated cohort of 100 inpatients with suspected or documented MRSA cSSTIs was assessed for 1 year time horizon. Treatment durations for tedizolid and linezolid were modelled at 6 and 10 days, respectively, consistent with drug labels and meta-analyses data. Direct and opportunity medical costs were considered. Need for second-line treatment courses, de-escalation therapy and gram-negative coverage was accounted for each regimen. Unit costs were extracted from official sources. Univariate sensitivity analysis was conducted on key model parameters. RESULTS: The budget for the treatment of 100 inpatients with suspected or documented MRSA cSSTIs with linezolid and tedizolid was €94578 and €55230 respectively, including €61265 and €60538 of medications costs respectively. Replacement of linezolid with tedizolid will result in €39348 total budget savings (including €727 savings on drugs) and hospital bed usage optimisation by 31.6%. Results were sensitive to change in linezolid and tedizolid treatment courses duration and costs and to the amount of cSSTI management reimbursement. Tedizolid introduction becomes cost-ineffective for treatment courses ≥9 days long. Uncertainty of other parameters within reasonable limits had no impact on the results. CONCLUSIONS: Tedizolid is a cost saving alternative to linezolid for the treatment of suspected or documented MRSA cSSTIs in a Russian multi-field hospital.

PIN24: BUDGET IMPACT ANALYSIS OF USING TEMOCILLIN, A NARROW-SPECTRUM ANTIBIOTIC, AS AN ALTERNATIVE TO BROAD-SPECTRUM CARBAPENEMS

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OBJECTIVES: Bacterial resistance is one of the major causes of mortality and costs in all healthcare systems. Narrow-spectrum beta-lactams, like temocillin, are recommended to spare the use of broad-spectrum antibiotics in order to decrease their selection pressure for resistant organisms. Considering the positive correlation between consumption of antibacterials and related bacterial resistance, the present research aims to explore the budget impact of introducing temocillin in Iran as part of an antibiotic stewardship program to spare the use of carbapenems such as imipenem. METHODS: The historical trend of imipenem-resistant Pseudomonas in Iran was detected by systematic review and pooled analysis of reporting articles. It was assumed that temocillin takes 10% of imipenem market share after its launch and this market share was optimised by 31.6%. Results were sensitive to change in linezolid and tedizolid treatment courses duration and costs and to the amount of cSSTI management reimbursement. Tedizolid introduction becomes cost-ineffective for treatment courses ≥9 days long. Uncertainty of other parameters within reasonable limits had no impact on the results. CONCLUSIONS: Tedizolid is a cost saving alternative to linezolid for the treatment of suspected or documented MRSA cSSTIs in a Russian multi-field hospital.

PIN25: A BUDGET-IMPACT ANALYSIS (BIA) OF IMMUNIZING ADULTS WITH COPD WITH THE 13-VALENT VACCINE (PCV13) AGAINST COMMUNITY-ACQUIRED PNEUMONIA AND PNEUMOCOCCAL DISEASE

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OBJECTIVES: Streptococcus pneumoniae is the leading cause of community-acquired pneumonia (CAP). The incidence of pneumococcal-pneumonia (PP) is greatest at the extremes of age and with comorbidity. The incidence of CAP is estimated at 10.1/1000 inhabitants. In Austria 32,907 hospitalized CAPs were documented in adults; 31%
(10,015) with S.Pneumoniae and 65% (6,510) of it corresponds PCV13-serotypes. 44% (2,864 VT CAPs) are attributable to COPD patients. 110 cases develop an invasive PP. The aim of the BIA is to quantify the monetary impact of an increased proportion of PCV13 vaccinated person’s in the different risk-groups (GOLDII+ and GOLDIII+ in different age-groups) compared to a constant situation. METHODS: A multi-cohort, COPD population-based model was developed over a 5-year time-horizon, which includes the following states: hospitalized and outpatient CAPs, invasive-pneumococcal-diseases (IPDs), exacerbations and mortality. Patients without immunization are considered for PCV13 vaccination according to the selected vaccination-rates. A repetition-vaccination is considered. The model includes a serotype shift over time. Results show within which risk-groups savings could be achieved (treatment costs avoided offset PCV13 cost) and within which risk-groups additional health expenditure were generated from the payer’s perspective. RESULTS: Among risk-groups with COPD GOLDII+ vaccination leads in all age-groups (≥18, ≥50, ≥60, ≥65) to cost-savings over 5-years (from 16.3 million € [≥18] to 23 million € [≥50]). Calculations are based on the present pharmacy-selling-price, which is paid out-of-pocket. Between 1,923-1,075 CAPs and 110-156 IPDs could be avoided over 5-years. Among risk-groups with COPD GOLDII+ reimbursement would increase health-expenditure between 15.2 million € (≥18) and 3.9 million € (≥50); between 2,747-1,565 CAPs and 135-229 IPDs could be avoided. In GOLDII+ age-groups a PCV13 reimbursement-(break-even)-price between 53-66€ would result in a 0 effect to health-care budgets. CONCLUSIONS: An increase of immunized persons – due to the incentive of reimbursement – would reduce disease-burden significantly and lead among high-risk patients to huge savings.

PIN26: CALCULATING THE RETURN ON INVESTMENT FOR IFN-FREE DAAS: THE CASE OF GREECE

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Calculating the Return-on-Investment for IFN-free DAAs: The case of Greece Konstantinos Drakos, Kakouros Michael, Efthymiou Xenofon, Anastasiou Dimitrios ABSTRACT OBJECTIVES: The present study investigates the HCV infected Greek population for a 20-year horizon covering the period 2016-2036, considering the health outcomes and healthcare costs of alternative screening and treatment strategies. We place special emphasis on the investigation of an Interferon (IFN)-free Direct-Acting Antivirals (DAAs) treatment option across all fibrosis stages. The main objectives are to conduct a Return-on-Investment analysis as well as considering broader macroeconomic costs due to HCV. METHODS: The first part of the analysis builds a health-state transition (Markov Chain) model where all cohorts are tracked sequentially over annual cycles to evaluate five alternative screening and treatment strategies with respect to their clinical outcomes and healthcare costs among the Greek population with HCV over a 20-year horizon (2016–2036). The second part of the analysis focuses on LrD and conducts an economic analysis designed to investigate the macroeconomic payoff of adopting an IFN-free DAAs treatment option across all fibrosis stages. RESULTS: Our results show that comprehensive treatment with IFN-free DAAs at stages F0-F4 exhibits by far the highest return on investment in terms of LYs gained in SVR12 per 10,000 euros invested. As it regards the macroeconomic payoff, we find that for every euro spent on IFN-free DAAs full treatment costs, 20 cents are gained in the form of GDP loss averted. CONCLUSIONS: The macroeconomic loss is estimated by calculating the GDP loss due to patients’ premature deaths. The main finding is that for every euro spent on IFN-free DAAs full treatment costs, 20 cents are gained in the form of GDP loss averted. This result is of a macroeconomic nature, over and above any QALY gains. Therefore, the societal cost born by the payer, is 20% outweighed by GDP losses averted.

PIN27: SUBCUTANEOUS IMMUNOPROPHYLAXIS AS A COST-EFFECTIVE TREATMENT ALTERNATIVE FOR HEPATITIS B VIRUS-RELATED TRANSPLANT PATIENTS IN FRANCE

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OBJECTIVES: HBV-related liver disease in advanced stages can only be treated by liver transplantation. Long-term combination prophylaxis with virustatics and HBV-specific immunoglobulins (HBIG) is necessary to protect the liver from being re-infected after transplant. In France, HBIG is available in 2 administration routes: an intravenous infusion (IVHBIG) and a subcutaneous injection (SCHBIG). The objective of this analysis is to evaluate the economic impact of those two routes of administration from the public payer perspective. METHODS: In a center of excellence for hepatology in Paris, which performs over 100 liver transplants per year, ten patients were switched from IVHBIG to SCHBIG. Patients were monitored regarding treatment regime and costs of both alternatives. Costs included were the product prices of SCHBIG, IVHBIG and virustatics, the costs for product administration and for biologic tests, transportation and therapeutic education. A model was built to compare the costs of both prophylaxis methods over a 3-year time frame from a public payer perspective. RESULTS: The total cost for 3 years of prophylaxis was €505,000 for the group treated with IVHBIG and €265,000 for SCHBIG group. Treatment expenditure was mainly driven by the product cost for HBIG. After switching from the intravenous to the subcutaneous route, the dosage of HBIG could be reduced to 23% of the original dose while keeping protective HBIG trough levels in the blood serum. Therefore, even
though the price per unit is higher for SCHBIG, the total costs were significantly lower. Additionally, the possibility of self-administration led to savings as transportation and infusion in the day care hospital were avoided. **CONCLUSIONS:** The result of the budget impact model shows that the use of SCHBIG leads to cost savings from a public payer perspective when compared to IVHBIG. Thus, the switch from IVHBIG to SCHBIG can be recommended from a cost-effectiveness point of view.

**PIN28: O INDICATIVE BUDGET IMPACT OF POSACONAZOLE VERSUS ITRACONAZOLE IN INVASIVE FUNGAL INFECTION PROPHYLAXIS IN ADULT PATIENTS WITH AML/MDS**

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**OBJECTIVES:** Patients with haematologic malignancies are at high risk of breakthrough invasive fungal infections (bIFIs), which are associated with high morbidity and mortality. Anti-mould prophylaxis and treatments have been introduced which have improved patient outcomes. This analysis estimates the budget impact of posaconazole and itraconazole, two prophylactic agents that prevent bIFIs in patients with acute myeloid leukaemia (AML) and myelodysplastic syndromes (MDS). **METHODS:** We developed a budget impact model looking at the costs of a hypothetical cohort of 100 patients in a posaconazole primary prophylaxis pathway versus an itraconazole primary prophylaxis pathway. The key cost and efficiency drivers considered are: drug acquisition, diagnostic test, antibiotic and hospitalisation costs associated with a bIFI. Key data on the costs of an infection come from a peer-reviewed published observational study in the UK. Differences in bIFI rates between posaconazole and itraconazole were demonstrated in multi-centre Phase 3 randomised controlled trials. **RESULTS:** For 100 patients, posaconazole has higher drug acquisition costs versus itraconazole (£216,398 versus £461,322) in AML, which increases to £355,262 for the posaconazole pathway versus £753,892 for the itraconazole pathway in patients with MDS. **CONCLUSIONS:** Looking across the continuum of care, posaconazole is associated with lower overall costs versus itraconazole. It is important to note that switching drugs will incur initial reductions in drug expenditure; however it has the potential to increase the overall NHS activity and therefore cost. The impact on patient outcomes, financial stewardship and operational efficiency is aligned to the principles of medicines optimisation.

**PIN29: INDICATIVE BUDGET IMPACT OF POSACONAZOLE VERSUS FLUCONAZOLE IN INVASIVE FUNGAL INFECTION PROPHYLAXIS IN ADULT PATIENTS WITH AML/MDS**

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**OBJECTIVES:** Patients with haematologic malignancies are at high risk of breakthrough invasive fungal infections (bIFIs), which are associated with high morbidity and mortality. Anti-mould prophylaxis and treatments have been introduced which have improved patient outcomes. This analysis estimates the budget impact of posaconazole and fluconazole, two prophylactic agents that prevent bIFIs in patients with acute myeloid leukaemia (AML) and myelodysplastic syndromes (MDS). **METHODS:** We developed a budget impact model looking at the costs of a hypothetical cohort of 100 patients in a posaconazole primary prophylaxis pathway versus a fluconazole primary prophylaxis pathway. The key cost and efficiency drivers considered are: drug acquisition, diagnostic test, antibiotic and hospitalisation costs associated with a bIFI. Key data on the costs of an infection come from a peer-reviewed published observational study in the UK. Differences in bIFI rates between posaconazole and fluconazole were demonstrated in multi-centre Phase 3 randomised controlled trials. **RESULTS:** For 100 patients, posaconazole has higher drug acquisition costs versus fluconazole (£216,398 versus £461,322) in AML, which increases to £355,262 for the posaconazole pathway versus £753,892 for the itraconazole pathway in patients with MDS. **CONCLUSIONS:** Looking across the continuum of care, posaconazole is associated with lower overall costs versus fluconazole. It is important to note that switching drugs will incur initial reductions in drug expenditure; however it has the potential to increase the overall NHS activity and therefore cost. The impact on patient outcomes, financial stewardship and operational efficiency is aligned to the principles of medicines optimisation.

**PIN30: PREDICTION OF COSTS ON ANTIRETROVIRAL THERAPY IN THE REPUBLIC OF BELARUS**

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OBJECTIVES: The purpose of the pharmacoeconomic research was to determine ways to increase efficiency and accessibility of antiretroviral therapy (ART) in Belarus. METHODS: We have used the following methods: "naïve" approach, trend extrapolation method and pharmacoeconomic modeling. Markov models have been built on the basis of the results of medicines clinical trials, cohort studies, epidemiological statistics on HIV infection in Belarus in 2012-2017. Nine antiretroviral therapy (ART) regimens have included a combination of 3 antiretroviral drugs of various classes: reverse transcriptase nucleoside inhibitors, reverse-transcriptase non-nucleoside inhibitors and protease inhibitors. RESULTS: 54 models have been obtained for nine ART regimens depending on the level of CD4+ cells/µl of blood (>500, 500-350, 350-200, 200-100, 100-50, 50-0). For each model we have defined a hypothetical number of years necessary to achieve a normal level of CD4+ cells of blood. We have calculated an average annual cost of therapy for one patient including: death, ART cessation, increase in CD4+ cells, constant level of CD4+ cells after ART initiation. Scheme-8 Zidovudine + Lamivudine + Nevirapine has the lowest cost of therapy: $183.19 for CD4+ >500 cells/µl, $193.05 for >350, $235.77 for <350. 7400 people with different levels of CD4+ received ART at the beginning of treatment in 2016 in Belarus and costs were $4135078.42. With "naïve approach", the content of CD4+ >500 cells/µl and treatment according to Scheme-8 costs will be $1355606.00. Projected number of patients receiving ART in 2017 in Belarus will be 7871±363 (cubic trend, p<0.05). Total financial costs for getting CD4+ >500 cells/µl will be $1441888.49 ± 66497.97. CONCLUSIONS: We have determined the most effective and least expensive ART regimen. To reduce the cost of ART it is advisable to start the treatment process at the level of CD4+ >500 cells/µl. The saved money will allow to increase availability of ART in Belarus.

PIN31: COST PER LIFE SAVED OF ADJUNCTIVE IGM-ENRICHED IMMUNOGLOBULIN TREATMENT OF SEPSIS IN GERMANY

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OBJECTIVES: Despite the development of new antibiotics, sepsis continues to lead to death in at least one in four patients. It is also a major cause of child mortality, accounting for 26% of all neonatal deaths worldwide. According to German guidelines, one of the strategies in sepsis management is the adjunctive treatment with IgM-enriched immunoglobulins. This research aims to investigate the cost per life saved of treating sepsis patients with IgM-enriched immunoglobulins. METHODS: A cost per life saved model was developed for Germany. Effectiveness data was obtained from a systematic literature review including only sepsis studies published after 2005 with mortality as a main outcome. The costs were calculated using the list price of IgM-enriched immunoglobulin in Germany and the DRG (Diagnosis Related Groups) revenue for ICU. RESULTS: Based on five studies (N=502) of adult sepsis patients, treatment with IgM-enriched immunoglobulins reduced the absolute mortality rate by 25.5%, rendering a NNT of 3.93. The average treatment costs in Germany are 4106€ leading to 16114€ costs per life saved. Four studies in pediatric sepsis patients (N=335) showed an absolute mortality reduction of 32%. For a 2-year-old patient treated with IgM-enriched immunoglobulins, the cost per life saved is 2214€. Two studies showed that the ICU length of stay is 2.5 days shorter for pediatric patients treated with IgM-enriched immunoglobulins compared to standard treatment, which yields additional cost savings of 5000€ in Germany. CONCLUSIONS: The findings suggest that the treatment of septic patients with IgM-enriched immunoglobulins is cost-effective. Therefore IgM-enriched immunoglobulins can be recommended as adjunctive treatment of patients with sepsis.

PIN32: COST-UTILITY ANALYSIS OF DARUNAVIR-BASED REGIMENS FOR TREATMENT-EXPERIENCED PATIENTS WITH MULTIDRUG-RESISTANT HIV-1 INFECTION IN THAILAND.

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OBJECTIVES: HIV drug resistance (HIVDR) has significantly increased in Thailand. In patients who treatment failure on first- and second-line antiretroviral therapy (ART), the next regimen is to use at least two new active antiretroviral agents (ARVs). Nonetheless, new ARVs have not yet been included in the National List of Essential Medicines (NLEM) in Thailand. These are high-cost drugs, economic evaluation and budget impact analysis are needed to support NLEM decision making. This study aims to assess 1) The cost-utility analysis of raltegravir (RAL), etravirine (ETR) and maraviroc (MVC) plus darunavir (DRV)-based regimen 2). Budget impact analysis of RAL, ETR and MVC for treatment experienced patients with HIV drug resistance in Thailand. METHODS: A Markov model, which monitored a cohort of patients aged 17 years and over with first- and second-line HIV regimens resistance in Thailand, was developed to evaluate the cost-utility of alternative treatment regimens in accordance with the Thai expert opinions as follows 1). current practice: DRV/r+tenofovir (TDF)+lamivudine (3TC), 2). DRV/r+RAL+TDF+3TC, 3). DRV/r+RAL+TDF+3TC+ETR and 5). DRV/r+RAL+MVC from a Thai societal perspective with lifetime horizon. The model incorporated cost data, which were calculated for the year 2015, and the effectiveness data from a review of published studies. Outcome measures were life years, quality-adjusted life-years (QALYs) and
incremental cost-effectiveness ratios (ICER). Future costs and outcomes being discounted at 3% per annum. Probabilistic sensitivity analysis (PSA) was conducted to deal with uncertainties around parameters. RESULTS: The third regimen, 3) DRV/r+RAL+TDF+3TC, was the lowest lifetime cost, which was 5.7 million baht, and approximately increased 10 QALYs. The incremental cost-effectiveness ratio for the third regimen compared with current practice was $ 332,227. CONCLUSIONS: All alternative regimens for treatment experienced patients with HIV drug resistance in Thailand were not currently cost-effective at the willingness to pay (WTP) 160,000 baht/QALYs.

PIN33: COST-EFFECTIVENESS OF FIDAXOMICIN VERSUS VANCOMYCIN AND METRONIDAZOLE IN PATIENTS WITH CLOSTRIDIUM DIFFICILE INFECTION IN SPAIN


OBJECTIVES: Two prospective, multicenter, double-blind, phase 3 trials conducted in patients with Clostridium difficile infection (CDI) showed fidaxomicin to be non-inferior to vancomycin for clinical cure, but associated with higher sustained clinical cure and a lower risk of disease recurrence. A network meta-analysis (NMA) was undertaken to determine the efficacy of fidaxomicin versus metronidazole, using vancomycin as the common treatment arm. This analysis aimed to determine the cost-effectiveness, from a Spanish national payer perspective, of fidaxomicin versus vancomycin and metronidazole in patients with CDI. METHODS: A semi-Markov model was developed with a 12-month time-horizon, comprising six health states. The cohort is followed for up to three lines of therapy. Vancomycin and rescue therapy, respectively, are the assumed second- and third-line treatments in both arms. Rescue therapy is assumed to provide 100% clinical cure and 0% risk of recurrence. Clinical data for the intervention and comparators were derived from clinical trials and the NMA. Cost and utility data were sourced from the literature; costs were inflated to 2016 values where required. Cost-effectiveness of fidaxomicin versus vancomycin and metronidazole was assessed in the base-case analysis and in the following subgroups: non-severe or severe CDI, primary CDI episode, first recurrence, age (≥75 years), and use of concomitant antibiotics. RESULTS: First-line fidaxomicin treatment was associated with cost savings (~€820.44 and ~€2,330.30) and gains in quality-adjusted life years (0.008 and 0.013) for all patients, versus vancomycin and metronidazole, respectively. Fidaxomicin dominated vancomycin across all subgroups except the severe CDI subgroup, and metronidazole across all comparisons. CONCLUSIONS: Fidaxomicin dominated metronidazole and vancomycin in all comparisons, except in the severe CDI subgroup comparison with vancomycin, where fidaxomicin was cost-effective. Excluding patients with severe CDI, fidaxomicin remained dominant in all sensitivity analyses, supporting the base-case results. Outcomes were driven by the reduced recurrence rate with fidaxomicin treatment.

PIN34: PUBLIC HEALTH AND ECONOMIC BENEFITS OF QUADRIVALENT INFLUENZA VACCINE IN MEXICO

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OBJECTIVES: To estimate the public health and economic burden in Mexico that would have been avoided, over the last 6 influenza seasons (from 2010-2011 to 2015-2016), if QIV had been used instead of TIV. METHODS: A static model published by Reed et al. in 2012 estimating the public health impact of QIV compared to TIV over 10 seasons in the United States was adapted to Mexico for the influenza seasons from 2010-2011 to 2015-2016. B-lineage cross-protection was included as well as public health and economic impact based on published sources. Data was obtained from inpatients and outpatients of the Mexico Emerging Infectious Diseases Clinical Research Network cohort study. The analysis was stratified by age (6-59 months, 5-17 years, 18-49 years, 50-59 years, 60 years and older) to account for heterogeneity of data, and focused on vaccination recommendations. RESULTS: During those 6 seasons, QIV would have additionally averted more than 321,000 influenza cases, 121,000 GP consultations, 3,800 hospitalisations and 330 deaths compared to TIV in this population (societal perspective cost reduction near to 13 million euros). Most benefits would have been observed for the 6-59 months group (44% of all cases avoided societal cost offsets of more than 4.6 million euros) and the elderly (32% of hospitalisation and 90% of death avoided). In adults 18-59 years, loss avoid was estimated in 1.2 million euros. CONCLUSIONS: The introduction of QIV instead of TIV would prevent a significant amount of influenza-related burden in years with high B circulation and mismatch like 2015-2016 in Mexico. However, more robust local data are needed to estimate accurately the impact of QIV. Herd effect and co-morbidities were not taken into account that could underestimate the potential impact of QIV in the recommended population.
**PIN35: THE ECONOMIC BURDEN OF CONGENITAL CYTOMEGALOVIRUS-RELATED HOSPITALIZATIONS IN THE UNITED STATES**

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**OBJECTIVES:** Cytomegalovirus (CMV) infection occurs in approximately 60% of people in the United States (US). CMV can be transmitted from a pregnant woman to her fetus (i.e., congenital CMV [cCMV]). Roughly 20% of children with cCMV may develop permanent disability (e.g., hearing loss; developmental disabilities). While the epidemiology of cCMV has been documented, limited real-world evidence exists to quantify the associated economic burden. This study describes changes in cCMV-related hospitalizations and associated resource use (i.e., cost; length of stay [LOS]) in the US from 2004 to 2013 for infants <1 year old. **METHODS:** cCMV-related hospitalizations (ICD-9-CM diagnosis code 771.1) for infants from the 2004 through 2013 HCUP Nationwide Inpatient Samples (NIS) were analyzed. Annual cCMV-related hospitalizations per 100,000 population (standardized to the 2015 US population) were estimated using NIS sampling weights and US Census data. Additionally, per-hospitalization costs (in 2016 US dollars) and LOS were assessed. **RESULTS:** cCMV-related hospitalization rates among infants in the US fell 15%, from 20.9/100,000 in 2004 to 17.8/100,000 in 2013. However, during this period, mean (standard deviation [SD]) LOS increased, from 28.7 (36.2) days in 2004 to 36.7 (52.4) days in 2009, before falling to 29.1 (39.2) days in 2013. Mean (SD) costs increased from $93,683 ($138,604) in 2004 to $103,773 ($175,737) in 2013, peaking in 2011 at $128,052 ($202,961). Final (SD) costs increased from $93,683 ($138,604) in 2004 to $103,773 ($175,737) in 2013, peaking in 2011 at $128,052 ($202,961). Finally, the total burden of cCMV-related hospitalizations (i.e., aggregate costs across all cCMV-related hospitalizations) increased slightly, from $73M in 2004 to $77M in 2013, but did increase to >$80M in 2009, 2011, and 2012. **CONCLUSIONS:** cCMV-related hospitalization rates among infants in the US fell during the early 2000s, but the economic burden of cCMV in this population varied appreciably during this period. Further research to understand factors which may influence the observed variability in cCMV-related hospitalization rates and costs is warranted. Such research may help plan optimal resource allocation.

**PIN36: THE COST OF ILLNESS FOR INVASIVE MENINGOCOCCAL B DISEASE IN GERMANY**

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**OBJECTIVES:** The burden of meningococcal B (MenB) is characterized by a high case-fatality rate, serious effects of sequelae on the patients’ everyday life and the corresponding impact on health expenditures. This study is the first estimating the economic burden of MenB-related invasive meningococcal disease (IMD) cases in Germany. **METHODS:** A cost-of-illness study has been conducted from third-party payer and societal perspectives for 18 age-groups. Direct costs for the acute IMD phase included inpatient, rehabilitation and public health responses-related costs. Probabilities for sequelae (hearing loss, limp amputation, seizures, scarring, renal disease, blindness, neurological and psychological impairments like attention deficit hyperactivity disorder [ADHD]) were based on a literature review and related costs were collected for the first and subsequent years, respectively. Indirect costs included future productivity losses of patients due to IMD-mortality and sequelae as well as productivity losses of patients and parents during the acute phase. Friction-cost method and human-capital approach were employed. Secondary data, literature and expert opinion were used as data sources. Costs after 2015 were discounted at 3% following German guidelines. **RESULTS:** The average total cost per case including sequelae is 51,367€ using friction-cost and 198,529€ using the human-capital approach. Direct costs account for 21,126€ and are highest for the age-group <1 year (23,594€) but decrease over age to 10,410€ for patients >80 years. Seizures and renal disease have the highest sequelae cost with 157,939€ and 132,709€ per sequelae case and ADHD/anxiety and neurological and psychological disabilities cause the highest cost per IMD survivor with 4,238€ and 3,572€, respectively. **CONCLUSIONS:** Despite the rare occurrence of MenB-related IMD of on average 343.25 cases per year between 2001 and 2016, costs per age-cohort sum up to 17,631,752€. The avoidance of IMD cases and outbreaks not only reduces the disease burden, but also the economic burden for the German healthcare system and society.

**PIN37: HUMAN PAPILLOMA VIRUS IN ITALY: COST OF ILLNESS AND POTENTIAL SAVINGS DUE TO HPV9 PRIMARY PREVENTION**

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**OBJECTIVES:** The objective of this study is to estimate the economic burden associated with Human Papilloma
Virus considering the new universal vaccination strategy in Italy (National Immunization Plan 2017-19), and total direct medical costs preventable associated with nine major HPV-related diseases. METHODS: A Cost of Illness incidence based model was developed in order to estimate incidence and costs of invasive cervical cancer, cervical dysplasia, cancer of the vulva, vagina, anus, penis, head and neck, anogenital warts, and recurrent respiratory papillomatosis from the Italian National Health System Perspective. For each of the nine conditions, we used available Italian secondary data to estimate the lifetime cost per case, the number of incident cases of each disease, the total economic burden, and the relative prevalence of HPV types 6, 11, 16, 18, 31, 33, 45, 52, 58 in order to estimate the aggregate fraction of the total economic burden attributable to HPV infection. RESULTS: The total direct costs (expressed in 2017 Euro) associated with the annual incident cases of the nine HPV-related conditions included in the analysis were estimated to be €503.2 million, with a plausible range of €492.7–€51.9 million. The fraction attributable to the HPV9 was €320.0 (range €298–€342 million), accounting for approximately 63.6% of the total annual burden of HPV-related disease in Italy. CONCLUSIONS: Comparing our data to the previous analysis conducted in 2011, the introduction of primary and secondary prevention strategy was an important step forward in public health because of the reduced incidence rates of HPV related diseases and consequently costs (from €503.2 to €534.5 million estimated in 2011). Moreover the new HPV9 vaccine represents an important investment for the public health that could prevent about 64% (range 60% - 68%) of total Economic Burden compared to 59% in the vaccination strategies available in 2011 preventable costs.

PIN38: INVESTIGATING THE ECONOMIC IMPACT OF HIV-ASSOCIATED RENAL AND BONE CO-MORBIDITIES IN UK INPATIENTS USING THE HES DATABASE

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OBJECTIVES: Several studies have suggested people living with HIV (PLWH) are at increased risk of certain co-morbidities, including renal disease and osteoporosis. There are currently limited UK data on the additional cost associated with co-morbidities in this group. We aimed to use a national database, the Hospital Episode Statistics (HES), containing information including all admissions to characterise and assess economic implications of inpatient episodes. METHODS: We analysed 5 years of HES data (April 2011-March 2016) to extract episodes coded with a HIV diagnosis and a concurrent diagnosis of co-morbidities of interest – renal disease and osteoporosis; non-HIV episodes for each co-morbidity were also extracted as a control group. Relevant ICD10 codes for each co-morbidity were obtained from the Charlson co-morbidity index. Cost per episode (tariff derived from both diagnosis-based Healthcare Resource Group and matched NHS reference costs) was evaluated between the groups. RESULTS: A total of 83,388 HIV coded episodes were identified, with 5,103 renal disease and 1,608 osteoporosis coded episodes. The average age for episodes coded as renal disease (48 vs. 68; p<0.01) and osteoporosis (53 vs. 76; p<0.01) were two decades lower for PLWH than controls. Average cost per episode was higher in PLWH compared to the non-HIV control group: renal; £1,899 vs. £937 (p<0.01) and osteoporosis; £2,799 vs. £2,132 (p<0.01). We estimate the additional HIV-associated economic burden of these co-morbidities to be £5.98M over 5 years, assuming the difference in cost is applied to the total number of HIV episodes for these co-morbidities. CONCLUSIONS: HIV-associated renal and bone co-morbidities present 20 years earlier and add significant additional economic burden. Early identification and proactive management of patients at increased risk could reduce this burden. This large dataset is valuable in highlighting increased inpatient episode cost. With an ageing population of PLWH, financial impact will increase further.

PIN39: ECONOMIC BURDEN OF HERPES ZOSTER IN SPAIN

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OBJECTIVES: Herpes zoster (HZ) and its complications, including post-herpetic neuralgia (PHN), is a severe and painful disease, mainly observed in people ≥50 years old. The economic burden of HZ in Spain is not well documented, with only isolated regional data available. The aim of the study was to estimate HZ-related healthcare resources utilization and costs in Spanish adults ≥50 years. METHODS: A prospective, observational study was performed using surveillance networks in 3 regions in Spain (Madrid, Valencia and Cataluña). HZ cases in adults ≥50 were recruited, stratified by age group, through primary care centers. Both payer and societal perspectives were considered in the costs calculated during the 3 months following HZ rash onset or up to 9 months for PHN. Unit costs were taken from regional healthcare services tariffs and medication costs from public pharmacist’s retail prices. The costs associated with working days lost were evaluated by multiplying number of days lost by the average daily earnings from National Statistics Institute 2014. RESULTS: 545 HZ cases were included and 25 patients developing PHN were evaluated. HZ patients had on average 1.7 primary care visits per episode, 7 patients (1%) had
emergency room visits and 11 (2%) were hospitalized. Regarding medication, 85% patients were prescribed antivirals for systemic use and 55% were prescribed analgesics. 16 patients (3%), all aged 50-64 years, lost on average 9.9 days of work per HZ episode. Overall costs were €240 (payer perspective) and €296/HZ episode (societal perspective). Costs were higher in the 70-79-year-old age group (€331-€439) due to higher proportion of subjects hospitalized. For PHN patients, overall costs were €571 and €712/HZ episode from the payer and societal perspectives respectively. **CONCLUSIONS:** HZ and PHN have an important economic burden both for payers and society in general. Any intervention preventing HZ could contribute to avoid considerable costs in Spain.

**PIN40:** THE ECONOMIC BURDEN OF ACUTE BACTERIAL RHINOSINUSITIS AND ACUTE OTITIS MEDIA IN TURKEY: AN EPIDEMIOLOGY BASED COST OF ILLNESS STUDY WITH RESPECT TO CLINICAL PRACTICE AND AVAILABLE GUIDELINES

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**OBJECTIVES:** To estimate economic burden of acute bacterial rhinosinusitis (ABRS) and acute otitis media (AOM) in Turkey via an epidemiology-based cost of illness study with respect to clinical practice and available guidelines. **METHODS:** Tree age pro model was used for this analysis. Probability of each health condition in clinical practice or in guideline based management of pediatric and adult patients with ABRS and AOM was also determined. Average per patient direct cost in primary, secondary and tertiary-care management of ABRS and AOM was calculated based on cost items related to outpatient’s, laboratory and radiological tests, drug treatment, hospitalizations and interventions. Total annual treatment cost was calculated via prevalence-based extrapolation of per patient annual treatment costs for different health conditions managed in clinical practice and per guideline recommendations as well as in case of 5% higher antibiotic resistance. **RESULTS:** Average per patient annual treatment costs in clinical practice were US$ 24.29 for pediatric ABRS, US$ 26.83 for adult ABRS, US$ 25.70 for pediatric AOM and US$ 27.10 for adult AOM, while adherence to guidelines was associated with per patient US$ 3.09, US$ 5.84, US$ 2.95 and US$ 2.13 cost reductions, respectively. Total annual treatment cost was US$ 101,499,040 for ABRS and US$ 57,191,330 for AOM in clinical practice along with 20% (US$ 20,260,100) and 9.8% (US$ 5,626,990) cost reductions, respectively in case of adherence to guidelines. In case of 5% higher antibiotic resistance, total annual antibiotic treatment costs were increased by 18.3% (US$ 18,593,590) in ABRS and by 14.1% (US$ 9,063,630) in AOM. **CONCLUSIONS:** In conclusion, our findings indicate that ABRS and AOM pose a considerable burden to health economics in Turkey, with antibiotic prescription identified as the main cost driver and emphasize the likelihood of substantial cost savings by adherence to guideline recommendations and reduced antibiotic resistance.

**PIN41:** HEPATITIS C VIRUS: DETERMINANTS OF PATIENTS’ MANAGEMENT COSTS

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**OBJECTIVES:** While Hepatitis C Virus (HCV) is a significant economic burden for healthcare providers, limited evidence is available on determinants of resources absorption, both in treatment-experienced and treatment-naive HCV patients. The present study aimed to investigate the principal determinants of HCV management costs. **METHODS:** A multi-centred observational study was conducted within 5 Hospital Authorities in Northern Italy. Demographic, clinical and economic information were collected from the enrolled patients, related to 2014. Cost data (haematological exams, diagnostic and specialist procedures, territorial drugs, anti-viral therapy and HAART) were analysed from the Italian NHS perspective. Descriptive statistics and regression analyses were used to determine patterns and determinants of costs. **RESULTS:** The sample was composed of 324 treatment-experienced and 1,245 naïve patients, for whom the same trends emerged: i) the management cost of HCV depends on the severity of the disease, demonstrating significant differences according to the Metavir Score (p = 0.000), ii) H/C patients absorb more economic resources than HCV patients (p=0.000), with a higher consumption of both haematological exams and specialist visits. The HCV duration (β=0.087, p=0.000), the infection severity (β=0.181, p=0.000), the type of genotype (β=0.189, p=0.000), the achievement of a sustained virological response (SVR) (β=0.327, p=0.000) and the previous clinical history (β=0.218, p=0.000), in the treatment-experienced patients, are antecedent to a variation of HCV management costs (Adjusted R²=0.376). The level of liver fibrosis and the SVR alone explains the 11.2% and 12.9% respectively, of costs variance. The number of comorbidities (β=0.070, p=0.000), the level of liver fibrosis (β=0.075, p=0.000), and the presence of a concomitant HIV infection (β=0.889, p=0.000) determines higher HCV management costs (Adjusted R²= 0.782) in the treatment-naive patients. **CONCLUSIONS:** Economic information
related to clinical pathway could be useful for health policy decision-makers, in order to optimise the appropriateness of resources allocation for the HCV management.

**PIN42: HERPES ZOSTER RELATED HEALTHCARE BURDEN AND COSTS IN BOTH IMMUNOCOMPROMISED (IC) AND IC-FREE POPULATIONS IN THE UNITED KINGDOM**

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**OBJECTIVES:** Individuals with immunocompromising (IC) conditions are at a higher risk of developing Herpes Zoster (HZ) than IC-free individuals. The study objective was to assess the healthcare burden of HZ in IC and IC-free individuals ≥18 years of age (YOA). **METHODS:** We conducted an observational retrospective study in a cohort of IC (N=621,588) and IC-free (N=621,588) individuals, matched by age, gender and GP practice, registered in the Clinical Practice Research Datalink (1999-2012) and linked to the Hospital Episode Statistics inpatient data. Healthcare resource utilization (HCRU, i.e. primary and secondary care consultations, hospital inpatient stays, and prescriptions) was analyzed from 7 days before the HZ diagnosis date to: (1) 30 days, (2) 365 days after the HZ diagnosis date for subjects with (1) HZ only (No postherpetic neuralgia) and (2) subjects with postherpetic neuralgia only. Healthcare costs were computed by multiplying the number of units of resources by the unit costs and summed over all HCRU categories to obtain a total cost per individual. Values were expressed in 2014 UK pound sterling (£) and presented for HZ cases overall, stratified by age category (i.e. 18-49, 50-59, 60-69, 70-79 and ≥80) and IC status. **RESULTS:** The percentage of HZ-cases hospitalized were higher in IC subjects (e.g. 2.7% versus 0.4% in IC and IC-free individuals, respectively aged 18 to 49 YOA and 9.5% versus 7.5% in IC and IC-free individuals respectively aged ≥80 YOA). Similarly, HZ-related mean treatment costs per subject were higher in IC subjects (£189 versus £104 in IC and IC-free individuals, respectively aged 18 to 49 YOA and £557 versus £401 in IC and IC-free individuals, respectively aged ≥80 YOA). Costs varied considerably by IC condition. **CONCLUSIONS:** Individuals with IC conditions not only have a higher risk of HZ than IC-free individuals, but also incur higher HZ-related healthcare costs.

**PIN43: OUTCOMES AND COSTS OF TREATING HEPATITIS C WITH DIRECT-ACTING ANTIVIRALS: RESULTS FROM THE GERMAN HEPATITIS C-REGISTRY**

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**OBJECTIVES:** Chronic HCV infection is associated with a significant health burden. Long-term consequences are the development of liver cirrhosis and hepatocellular carcinoma. The introduction of direct-acting antivirals (DAAs) has dramatically changed hepatitis C treatment and sustained virologic response rates (SVR) of >90% were observed in clinical trials. Especially interferon-free regimens allow a shorter treatment duration and show favorable toxicity profile. Nevertheless new treatment options were accompanied with higher pharmaceutical costs. The aim of the current study was to analyze outcomes and treatment costs in a real-world setting. **METHODS:** Data were derived from the German Hepatitis C-Registry (DHC-R). The DHC-R is a prospective, multicenter real-world registry study comprising approximately 10,500 patients. Patients are treated at the discretion of the physician. This analysis included all patients with HCV genotype (GT) 1 and 3 who initiated and finished treatment between 02/2014 and 02/2017 and were documented in the pharmacoeconomic substudy. **RESULTS:** A total of 2,673 patients receiving antiviral treatment were analyzed; 88.0% had GT-1 and 12.0% GT-3 infection. Mean age was 54.6 years, 52.3% were male. Estimated mean duration of infection was 20.6 years. About half of the population (48.1%) was treatment-naive and 30.2% had liver cirrhosis. 93.5% of all patients achieved SVR (GT-1: 94.0%, GT-3: 89.1%). Average total treatment costs were £67,979 (£67,131 pharmaceutical costs, £624 ambulatory care, £24 hospital costs). Treatment costs were considerably lower in GT-1 compared to GT-3 patients (£65,650 vs. £85,039). Average costs per SVR (cure) of £69,841 for GT-1 and £95,443 for GT-3 were calculated. **CONCLUSIONS:** This analysis confirms high SVR rates for newly introduced DAAs in a real-world setting. Although costs for antiviral treatment have further increased, costs per SVR estimated are comparable to first generation DAAs. Detailed analyses stratified by treatment status, degree of cirrhosis and regimen should follow.

**PIN44: COST-EFFECTIVENESS OF INTERFERON-FREE TREATMENT STRATEGIES FOR HEPATITIS C AFTER GENERIC ENTRY OF DIRECT-ACTING ANTIVIRALS IN THE KAZAKHSTAN**
OBJECTIVES: Following the long phase of interferon-based HCV treatment, direct-acting antiviral agents (DAAs) were developed. Availability of DAAs has changed the treatment landscape of hepatitis C virus (HCV) infection. However, access to DAAs is limited by their exceptionally high pricing, up to USD23,000 per 12-week course in Kazakhstan. The high price of DAAs has restricted their use in Kazakhstan. This study examined whether generic DAAs could be cost-saving and how long it would take for the treatment to become cost-saving/effective. METHODS: We constructed Markov models to compare the outcomes of no treatment versus treatment with DAAs for the HCV-infected population in Kazakhstan. Model parameters were estimated from a systematic review of clinical trial results. Cost-effectiveness of HCV treatment using available DAAs was calculated, from a Kazakh payer perspective, assuming 3% annual discounting. The main outcome of the models was cost per quality-adjusted life-year (QALYs), total costs, and incremental cost-effectiveness ratio of DAAs versus no treatment. One-way and probabilistic sensitivity analyses were conducted. RESULTS: The models indicated that, compared with no treatment, the use of generic DAAs in Kazakh HCV patients would increase the life expectancy by 8.14 years, increase QALYs by 3.95, avert 19.01 DALYs, and reduce the lifetime healthcare costs by $2,100 per-person treated. Payback for the upfront costs of DAA drugs would be achieved in an overall average of less than 10 years - under 5 years for patients at advanced stages of HCV disease and almost 12 years if treatment begins at earlier stages. The results were robust to multiple sensitivity analyses. CONCLUSIONS: Treatment with generic DAAs available in Kazakhstan will improve patient outcomes, provide a good value for money within 2 years, and be ultimately cost-saving. Therefore, in this and similar settings, HCV treatment should be a priority from a public health as well an economic perspective.

PIN45: COST OF HOSPITAL TREATMENT FOR SEVERE AND MODERATE-TO-SEVERE INFLUENZA IN RUSSIA

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BACKGROUND: Respiratory viral infection (RVI) both in children and adults is one of the leading causes of hospitalizations in Russia every year. Presently the Russian mandatory medical insurance system (MMIS) defines low tariffs for RVI hospitalization (€401.37-€575.22) and a lot of cases are thought to be eligible for out-patient care. Still some influenza patients may need expensive hospital care, but the cost has never been calculated. OBJECTIVES: The aim of this study was to estimate the cost of hospital treatment for severe and moderate-to-severe influenza in adult patients. METHODS: The list of resources used in severe and moderate-to-severe influenza hospital treatment was made by experts - clinical practitioners in the field of infectious diseases. Pharmacotherapy and laboratory tests for identifying influenza virus by polymerase chain reaction (PCR) were considered to be cost drivers by experts, when use of other resources was considered to be equal to routine care in an infectious ward. The drug costs were calculated on the basis of registered maximal manufacture's prices. The cost of PCR was submitted by regional hospitals. Other medical costs were calculated based on average cost per inpatient-day in the infectious ward of the regional hospitals (excluding drugs) and average length of hospital stay of influenza patients with different degree of severity. RESULTS: The cost of drugs is €1,605.48 and €129.12 per patient with severe and moderate-to-severe influenza, respectively. The total cost of hospitalization is €2,300.87 for a severe influenza case and €664.28 for moderate-to-severe patient. 1st place in the drug costs structure belongs to antibiotics (56 % of drug costs) in moderate-to-severe influenza, and to plasma protease inhibitors (38%) in severe flu. PCR makes a small share in total costs. CONCLUSIONS: Cost of severe and moderate-to-severe influenza calculated based on expert treatment recommendations is much higher than defined tariff in Russian MMIS.

PIN46: HCV NETWORK OF SICILIAN REGION: A BEST PRACTICE TO MONITOR COST AND CONSEQUENCE OF TREATMENTS

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OBJECTIVES: The availability of new direct-acting antivirals (DAAs) has radically changed the hepatitis C care scenario, leading to major efficacy results but creating a sustainability issue. Epidemiological studies report that in Sicily there are about 30,000 citizens with a diagnosis of chronic hepatitis due to HCV. The need to guarantee diagnostic and therapeutic appropriateness uniformity in the territory, in accordance with treatment priority criteria,
and to provide easier access to healthcare, led to the creation of a Sicilian Network for the management of HCV. METHODS: The HCV Network in Sicily consists of a web-based platform, which allows to manage the prescriptions and the delivery of DAA drugs for all resident HCV patients. The platform permits chronic hepatitis treatment control, cirrhosis and HCV post-transplant relapse and also allows to plan the clinical control of patients who do not have the criteria for treatment with DAAs. The network consists of 41 centers and 84 gastroenterologists or infectologists connected to each other through the web-based platform. The HCV Sicily Network database analysis allowed an assessment of treatment cost for each therapeutic regime. Furthermore, the correlation between the therapies administered, the results obtained, and the related adverse events was evaluated. RESULTS: From May 2015 to December 2016, 11,317 patients have been recorded in the web platform and 5,931 patients started the treatment. The analysis showed that the HCV Network improves therapy management and allows a better assessment of clinical benefit. The data obtained from the Network also provided information on HCV epidemiology in Sicily and estimated the cost of treatments administered to patients. In addition, it showed antiretroviral therapy short term tolerability and efficacy data in a big patient cohort. CONCLUSIONS: The Sicily HCV Network is an excellent monitoring system of patients with hepatitis C and an important tool to evaluate cost and consequence of treatment with DAAs.

PIN48: CALCULATING THE INDIRECT COSTS OF ADULT PNEUMOCOCCAL DISEASE AND THE RATE OF RETURN TO THE 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13) IN OLDER ADULTS, WITH AN APPLICATION TO DENMARK

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OBJECTIVES: To assess vaccines, HTAs should consider their broader socioeconomic effects, including those on market and nonmarket productivity (indirect costs, ICs). They should also consider decision criteria beyond cost-effectiveness that incorporate such effects, like social rates of return (RoR). We develop a method for measuring vaccination’s productivity benefits and social RoR and apply it to the case of PCV13 in older Danish adults. METHODS: We measure ICs from death and disability per treatment episode of inpatient community-acquired pneumonia (ICAP), outpatient CAP (OCAP), bacteremia, and meningitis in Danes aged 50–85. Losses include market and nonmarket work (housework, caregiving, and volunteering time valued at the unskilled wage), and span the duration of disability or, with death, the rest of life with background mortality risks. We calculate a RoR to PCV13 Adult in terms of averted direct costs (DCs) and ICs, allowing for herd effects and serotype replacement from child vaccination. We perform separate calculations for diabetics aged 65–85. We use data from EuroStat, Statistics Denmark, Danish prices/charges, and the published literature. RESULTS: ICs per episode exceed per capita GDP (PCGDP) for ICAP, approach PCGDP for bacteremia, exceed five times PCGDP for meningitis, and exceed 20 times DCs for OCAP. ICs consist largely of nonmarket productivity—specifically housework—lost to death. The RoR to PCV13 in the general older adult population is 149% and is driven by averted ICAP-related costs. In elderly diabetics, ICs per episode are higher and the RoR a stunning 1,191%. Main results are robust in sensitivity analyses. CONCLUSIONS: The ICs of pneumococcal disease are considerable, even among older retired adults. The RoR to PCV13 in Danish older adults is high, especially for elderly diabetics, and compares very favorably with that of highly-regarded development interventions. Failing to account for productivity in valuing vaccination can result in considerable undervaluation.

PIN49: ECONOMIC EVALUATION OF ALTERNATIVE MEASLES-MUMPS-RUBELLA CHILDHOOD VACCINATION SCHEDULES IN DENMARK

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OBJECTIVES: To determine the economic impact of alternative measles-mumps-rubella (MMR) childhood vaccination schedules in Denmark when considering avoided hospitalizations for any infectious disease. METHODS: A Danish register-based study of the average cost per any infectious disease hospitalization in Danish children, dependent on vaccination status and age in months was performed. The age dependent risk of any infectious disease hospitalization and the average cost per any infectious disease hospitalization were combined in a decision analytical model and the cost associated with moving the recommended time of MMR vaccination at 15 months-of-age and 4 years-of-age (schedule A; the base-case) forward in schedules B: 13 months-of-age and 15 months-of-age, C: 6 months-of-age and 15 months-of-age and D: 6 months-of-age and 13 months-of-age was examined; assuming coverage rates as in the current vaccination schedule. Scenario analyses of the cost of MMR vaccination in different programmes and at different coverage rates of MMR vaccination were performed. RESULTS: In the base case, the decision analytical model predicts undiscounted incremental savings in schedules B, C and D compared to A. The largest incremental saving was found in schedule D with a saving of 14.9 million DKK, followed by schedule C (11.3 million DKK) and B (5.1 million DKK). The incremental undiscounted
savings were sensitive to increasing the MMR vaccination coverage to 95% from A actual coverage rates in schedules A, B, C and D. Increasing coverage rates to 95% in schedule A would require an additional 10.5 million DKK for vaccinations but could lead to 8.8 million DKK in savings on hospitalizations, resulting in -1.7 million DKK. Changing coverage to 95% generated incremental savings and the savings were highest for D (17.3 million DKK), then C (12.6 million DKK) and B (3.1. million DKK). CONCLUSIONS: The study suggests that alternative MMR vaccination schedules are associated with savings.

PIN50: INCLUSION OF SAFETY/ADR-RELATED OUTCOMES IN ECONOMIC EVALUATIONS FOR SEASONAL INFLUENZA VACCINES: A REVIEW OF AVAILABLE STUDIES

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OBJECTIVES: In this study we assessed how economic evaluations (EE) on seasonal influenza vaccines include Adverse Drug Reactions (ADRs) and what the impact of its inclusion on the health economic outcomes would be. METHODS: We searched MEDLINE, EMBASE and The Cochrane Library to identify full-text published studies in peer-reviewed journals. Full EEs on seasonal influenza vaccines, discussing ADR-related outcomes, published in any language up to December 5th 2016 were considered as eligible. The protocol for this review was published in PROSPERO. RESULTS: Forty-nine EEs included ADR-related parameters, apparently reflecting approximately 25% of EE-papers in the initial search. Notably, ADR-related costs included the direct medical costs of ADRs management, physician visit, hospitalizations and medication/treatment in 44 articles, and broader costs of time loss seeking treatment for ADRs, caregiver time, productivity loss/work absenteeism, traveling fee and household costs in 13 articles. Furthermore, ADR-related disutility/QALY were considered in 18 articles with explicit specification of duration and frequency of health losses. The most commonly included ADR was the Guillain-Barré syndrome. In those papers that allowed such estimation, direct costs of ADRs reflected less than 1% of total direct costs. Most studies specified a cost-effectiveness analysis design from the societal perspective. Mainly the EEs were comparing influenza vaccination with no vaccination (34 articles). Analyses on children were most frequent (18), followed by analyses over elderly (10), pregnant/postpartum woman and infants (7), and other groups of adults (risk groups, workforce). Data on the costs and health impacts of ADRs were derived from public databases (costs), population-based studies and surveys (utilities/QALYs) and clinical trials (frequencies). CONCLUSIONS: Seemingly, the majority of influenza vaccine EEs do not include potential ADRs of the influenza vaccine. Of those studies that allow such estimation, costs of included ADRs are very modest.

PIN51: COST-EFFECTIVENESS ANALYSIS OF DACLATASVIR/SOFOSBUVIR (DCV/SOF) FOR THE TREATMENT OF HCV PATIENTS WHO FAILED AFTER FIRST LINE TREATMENT WITH SECOND GENERATION OF DAA IN ITALY.

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OBJECTIVES: DCV in combination with SOF has shown a very good efficacy and safety profiles for treating HCV patients. Recent real life data from the Italian Platform for the Study of Therapies for Viral Hepatitis (PITER) cohort, shows the failure to eradicate HCV RNA following a DAA treatment regimen remains a rare, but important challenge from clinical and economic perspectives. The aim of this analysis was to evaluate the cost-effectiveness of the DCV/SOF regimen versus HCV alternative treatments for patients who failed to achieve SVR12 after a first DAA treatment from the Italian health care system perspective, based on data from the PITER cohort. METHODS: A Markov model of chronic HCV patients was used to develop two scenarios: 1) DCV+SOF versus LDV+SOF in Gt1 and Gt4 HCV patients; 2) DCV+SOF versus no retreatment option in HCV Gt1, Gt3 and Gt4 patients. The percentage of patients who failed first line treatment with SOF/SIM/RBV or SOF/RBV and were retreated or not, were used to populate the model. HCV resources consumption and SVR rates were quantified using PITER real life data. Transition probabilities and utility rates were derived from the literature. The outcomes were expressed in terms of Quality Adjusted Life Years (QALYs). Probabilistic sensitivity analysis (PSA) was performed considering a cost-effectiveness threshold of € 30,000/QALY. RESULTS: In the base-case analysis DCV+SOF is cost-effective from the INHS perspective in both scenarios, with an ICER of €3,461.52 and €6,888.69 costs/QALYs compared to LDV+SOF and no treatment respectively. The PSA showed robust results, ICERs remain below threshold in 94% and 99% simulations in Scenario 1 and 2 respectively. CONCLUSIONS: The results show that DCV+SOF is a cost effectiveness option in HCV patients who failed to reach SVR12 after first line DAA treatment.
OBJECTIVES: To evaluate the cost-effectiveness of dolutegravir (DTG) when compared to raltegravir (RAL) and ritonavir-boosted darunavir (DRV/r) in treatment-naive HIV-1-infected patients in Russia. METHODS: The assessment of cost-effectiveness was based on a decision tree analysis. Response rates defined by the probability of virologic suppression (HIV RNA<50 copies/mL) at 48 weeks were obtained from a published network meta-analysis. Responders were distributed across CD4 health states allowing the calculation of quality-adjusted life-years (QALYs). Baseline patient characteristics were informed using pooled data from DTG phase 3 clinical trials (SINGLE, SPRING-1, SPRING-2 and FLAMINGO). Costs obtained from Russian data included antiretroviral drug costs, treatment costs such as routine care, costs of treating cardiovascular conditions, opportunistic infections and drug-related adverse effects, and mortality costs. Utility values and mortality rates were obtained from published literature. A 48 week analysis was conducted using the societal perspective. Outcomes included QALYs, life-years (LYs), incremental cost per QALY ratio (ICER) and incremental cost per responder (ICPR). The analysis assumed no incremental mortality benefit due to better virologic response in the base case. The year of analysis was 2017. RESULTS: The rate of response among patients receiving DTG was 0.84 versus 0.73 for DRV/r and 0.80 for RAL. Total costs for treatment with DTG were 162,066 RUB, compared with 233,195 RUB for treatment with DRV/r and 369,723 RUB for treatment with RAL. In the ICPR analysis DTG dominated both DRV/r and RAL. Patients treated with RAL generated 0.740 QALYs compared to 0.738 with DTG and 0.736 with DRV/r. DTG dominated DRV/r in terms of ICER whilst RAL compared with DTG had an ICER of 124,492,962.35 RUB/QALY. CONCLUSIONS: With lower costs, higher response rates and comparable QALYs, DTG can be considered as a cost-effective alternative among the three treatment options.

/*PINS53: COST-EFFECTIVENESS ASSESSMENT OF HERPES ZOSTER VACCINATION IN GERMANY

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OBJECTIVES: With over 306,000 cases every year, leading to an annual bill of €182M to society, Herpes Zoster (HZ) and its complications have a significant burden on the German health-care system. This health economic analysis was designed to support an informed decision-making for a potential HZ vaccination recommendation in the German population aged ≥60 years. We compared two HZ vaccines, a two-dose candidate HZ adjuvanted subunit vaccine (HZ/su) and Zoster Vaccine Live-attenuated (ZVL). METHODS: The ZOster ecoNomic Analysis (ZONA) model is a static, multi-cohort Markov model that followed ≥60-year-old subjects over lifetime from the year of vaccination. Both HZ/su and ZVL introduction were compared to no vaccination. Model inputs included demographics, epidemiology, vaccine characteristics, utility, and costs. Costs and outcomes were presented over the lifetime of individuals, both discounted at 3% per year. The incremental cost-effectiveness ratio (ICER) was calculated based on the societal perspective. We assumed 40% coverage for both vaccines, with a second dose compliance of 70% for HZ/su. Model uncertainty will be addressed by performing scenario and sensitivity analyses. RESULTS: The cohort consisted of 22,5M people aged ≥60 years. Vaccinating with HZ/su resulted in 1M HZ and 197K postherpetic neuralgia (PHN) cases avoided, a gain of 38,546 quality-adjusted life-years (QALYs), an incremental €84,961 per QALY gained, respective and 197K postherpetic neuralgia (PHN) cases avoided, a gain of 38,546 quality

/*PINS54: COST-EFFECTIVENESS ANALYSIS OF SEQUENTIAL VACCINATION OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13) AND 23-VALENT PNEUMOCOCCAL POLYSACCHARIDE VACCINE (PPSV23) ON ADULT POPULATION IN SOUTH KOREA

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OBJECTIVES: Currently in South Korea, National Immunization Program (NIP) offers 23-Valent Pneumococcal Polysaccharide Vaccine (PPSV23) in order to prevent pneumococcal diseases among the over-65 elderly population; however, 13-Valent Pneumococcal Conjugate Vaccine (PCV13) is not included in the program. This study provides a comparative analysis of PCV13 versus PPSV23 for Korean adolescent population. METHODS: Analysis was designed in Markov model and from a healthcare perspective for a full life-cycle. Epidemiological and cost data used for analysis, such as incidence and mortality of pneumococcal diseases and serotype coverage, were drawn from Health
EFFECTIVENESS ANALYSIS OF VANCOMYCIN AND LINEZOLID: A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: Vancomycin and linezolid are the first-line treatments for Methicillin-resistant Staphylococcus aureus (MRSA) recommended in IDSA guideline. Linezolid has an easier dosing regimen but a higher acquisition cost in the US compared to vancomycin. This review is to evaluate if linezolid is a cost-effective treatment for MRSA.

METHODS: We conducted a systematic literature review of cost-effectiveness studies of linezolid and vancomycin. We searched PubMed and Embase with the keywords: “cost-effectiveness”, “vancomycin”, “linezolid”, and “MRSA”. We excluded non-human studies, studies conducted in countries other than the US, and literature reviews from this review.

RESULTS: Seven studies met the inclusion criteria and were included in this review. In these studies, linezolid and vancomycin were indicated for nosocomial pneumonia, surgical site infection, or complicated skin and soft tissue infection (cSSSI). Five out of seven studies used a decision tree model structure. Treatment duration of linezolid or vancomycin ranged from three days to 21 days, and time horizon of the model ranged from 35 days to two years. Six studies used number of patients cure as their effectiveness measure while one used number of lives saved. All seven studies included drug acquisition cost and cost of hospital stay as cost components. Five studies were funded by the manufacturer of linezolid. Four out of seven studies showed linezolid dominated vancomycin, two showed linezolid was cost-effective, and one showed linezolid was not cost-effective.

CONCLUSIONS: The results of this review indicated that linezolid is likely a cost-effective treatment for MRSA in nosocomial pneumonia and cSSSI. Evidence from published cost-effectiveness studies need to be interpreted carefully for potential bias.
**PIN57: A COST EFFECTIVENESS ANALYSIS OF SEASONAL QUADRIVALENT INFLUENZA VACCINE IN ITALY USING A STATIC MODEL**

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**OBJECTIVES:** Seasonal influenza is caused by two subtypes of influenza A and two lineages of influenza B viruses. Trivalent influenza vaccines (TIVs) contain two A strains but only a single B-lineage strain, which can lead to mismatches with actually circulating B lineage. Quadrivalent influenza vaccines (QIVs) containing both B-lineages strains have therefore been developed for improved protection against influenza. Here, we examine whether switching from TIV to QIV would be cost-effective for the recommended population in Italy. **METHODS:** A static cost-utility model was used to estimate the public health and economic impact of switching from TIV to QIV in the recommended population in Italy during an average influenza season (average epidemiological data from 2003-4 to 2012-13 season, pandemic season excluded). Whenever possible, epidemiological and cost data were obtained from Italian sources. Economic analysis was performed from payer and societal perspectives; discount rates for costs and outcomes were 3.0%. Univariate and probabilistic sensitivity analyses were performed. **RESULTS:** Over a mean influenza season, QIV is expected to avoid an additional 3,469 GP visits, 446 hospitalizations and 133 deaths related to influenza. This translated into savings of €1.6 million from avoided hospitalizations and approximately €2 million due to indirect costs linked to lost productivity. The incremental cost-effectiveness ratio (ICER) was €23,426 per QALY from a payer perspective and €21,096 per QALY from a societal perspective. When considering the switch to QIV for individuals ≥ 65 years of age, the ICER was €19,170 per QALY. Probabilistic sensitivity analysis showed that switching to QIV was cost-effective in >97% of simulations with a willingness-to-pay threshold of €28,000/QALY. **CONCLUSIONS:** Despite simulations didn't account for herd protection, the model showed that the switch from TIV to QIV in Italy is expected to be a cost effective intervention.

**PIN58: COST-EFFECTIVENESS ANALYSIS OF TIGECYCLINE IN COMPARISON WITH IMPENEM/CILASTATIN OR PIPERACILLIN/TAZOBACTAM IN THE TREATMENT OF COMPLICATED INTRA-ABDOMINAL INFECTIONS: A PERSPECTIVE OF IRANIAN HEALTH SYSTEMS**

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**OBJECTIVES:** Complicated intra-abdominal infections (cIAIs) are a public health issue characterized by a high disease burden. Also, increasing rates of resistance and therapeutic failure made cIAIs as one of the major causes of morbidity and mortality worldwide. This study was aimed to develop an economic model to evaluate the cost-effectiveness of tigecycline (TG), a broad-spectrum glycyclcline, in comparison with Imipenem/Cilastatin (Im-Cl) or Piperacillin/Tazobactam (Pi-Tz) for the treatment of adults with cIAIs based on the perspective of Iranian health system. **METHODS:** Utilizing a decision-tree model, all patients received TG 100mg/day, Im-Cl 2g/day, or Pi-Tz 3.375g/day as initial antibiotic therapy considering a maximum time horizon of 30 days. The measure for effectiveness was length of stay (LOS) estimated using published data on pathogen prevalence, in-vitro eradication rates, clinical success rates, and mortality rates. Information on direct medical costs were derived from literature, hospital records, and official databases. The model estimated the cost per patient and incremental cost-effectiveness ratios (ICER). Both deterministic and probabilistic sensitivity analysis were conducted to show the robustness of the model over the uncertainty of key parameters. **RESULTS:** LOS was shorten with TG rather than Im-Cl and Pi-Tz (15.1, 16.4 and 15.8 days, respectively). However, the cost per patient in TG groups was higher than in Im-Cl and Pi-Tz groups (107,087,997 IRR, 102,078,797 IRR, and 100,253,667 IRR, respectively). The Monte-Carlo simulation showed that TG would be cost-effective in more than 50% of cases at the willingness to pay threshold of 3,500,000 and 9,500,000 IRR per each hospitalization day avoided versus Im-Cl and Pi-Tz, respectively. **CONCLUSIONS:** The cost-effectiveness analysis showed that TG would lead to less hospitalization days and more cost in the treatment of cIAIs in Iran with the ICER of 3,853,231 versus Im-Cl and 9,763,329 IRR versus Pi-Tz and could be considered as a treatment option specially in case of bacterial resistance.

**PIN59: COST-EFFECTIVENESS EVALUATION OF PHID-CV VERSUS PCV-13 IN SLOVAKIA**

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**OBJECTIVES:** The 10-valent pneumococcal non-typeable Haemophilus influenzae protein D conjugate vaccine
(PHiD-CV) and the 13-valent pneumococcal conjugate vaccine (PCV-13) have been successfully used in the Slovak national universal mass vaccination programme (UMV) to protect against invasive pneumococcal diseases (IPD), pneumonia and acute otitis media (AOM) since 2011. Six years after the introduction of PCV in paediatric UMV in Slovakia, we have estimated cost-effectiveness of the two vaccines. METHODS: A previously published Markov cohort model was adapted to the Slovak setting using local demographic (birth cohort n=55,602), clinical, epidemiological data and local serotype distribution. Only direct medical costs were included and costs and outcomes were discounted annually by 5%. The analysis was performed from a payer's perspective in a lifetime horizon. Vaccine efficacy assumptions for a 2+1 schedule (at 3rd, 5th, and 11th month of age) were based on published trial data. In the base case, we used a vaccination coverage of 95.7%, as observed for PCV in UMV in 2016. Univariate and probabilistic sensitivity analyses (PSA) were carried out on key parameters. RESULTS: Under our model assumptions, both vaccines had a similar impact on IPD and pneumonia, but PHiD-CV generated a greater reduction in AOM cases compared to PCV-13 (5,938 cases). Hence, at price parity, PHID-CV was dominant over PCV-13 since it returned 25 additional discounted quality-adjusted life years gained and saved 200,283€ (discounted) to the public payer. At the real 25% lower price of PHiD-CV compared to PCV-13 and full reimbursement of both vaccines, the cost-saving increased to €2,272,722 (discounted). In PSA, 95.4% simulations (n=500) were in the dominant quadrant. CONCLUSIONS: PHiD-CV is estimated to provide both additional health benefits and cost-savings compared to PCV-13, at price parity. From the public payer perspective, a substantial budget saving is estimated using PHiD-CV compared to PCV13 in paediatric UMV in Slovakia.

PIN60: COST-EFFECTIVENESS OF QUADRIVALENT INFLUENZA VACCINE FOR NATIONAL IMMUNIZATION PROGRAM IN SOUTH KOREA

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OBJECTIVES: In Korea, National Immunization Program(NIP) for influenza began in 1997 for elderly people aged 65 or above, and children under 6 were included in the vaccination from 2016/2017 season. However, the burden of influenza is still high. The goal of this study is to estimate the effectiveness of replacing the existing trivalent vaccine with quadrivalent vaccine to increase the matching rate. Furthermore, this study aims to measure cost effectiveness of adjuvant vaccine in the elderly. METHODS: Cost-effectiveness analysis was conducted from societal perspective. We extracted the rates of incidence, complication, and hospitalization, and the medical costs of influenza by age groups using the National Health Insurance Service's Database from the 2013/2014 season through the 2014/2015 season. A Markov model was used for analysis in the elderly(≥65 years). However, for children(≤59 months), the decision tree model was used for analysis since aged between 6 to 64 years will be excluded from NIP. We included direct non-medical cost and caregiver's time cost. All costs and effectiveness was discounted at 3% annually. RESULTS: From the base case analysis, compared with trivalent influenza vaccine, the quadrivalent influenza vaccine was moderately cost-effective (ICER=43,338,743 KRW/QALY) for children, and more cost-effective (ICER=20,371,157 KRW/QALY) for the elderly. Moreover, adjuvant vaccine was dominant to trivalent. Sensitivity analyses indicated that the ICER is sensitive in variance of vaccine matching rate, cost of vaccine, and distribution of influenza B. CONCLUSIONS: Compared with trivalent influenza vaccine, the introduction of quadrivalent and adjuvant influenza vaccine would reduce influenza disease burden and be cost-effective in Korea. It is recommended to introduce quadrivalent influenza vaccine to NIP under certain conditions. Further study using a dynamic transition model seems necessary to estimate effectiveness of influenza vaccine.

PIN61: COMPARING THE ESTIMATED HEALTH AND ECONOMIC BENEFITS OF HERPES ZOSTER (HZ) VACCINES IN THE UK

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OBJECTIVES: The one-dose live-attenuated HZ vaccine was introduced into the UK vaccination programme for the elderly in September 2013. An alternative investigational two-dose HZ/su vaccine is currently in development. To investigate the overall health and economic benefits of the one-dose HZ vaccine in comparison to the investigational two-dose vaccine in the UK programme. METHODS: A Markov model was developed to compare the economic impact and case burden of HZ and postherpetic neuralgia (PHN) for the two types of vaccine in the UK for adults aged 70 to 79 years old. Vaccine effectiveness assumptions were taken from a recent observational study from Kaiser Permanente Northern California for the one-dose HZ vaccine, while assumptions for the investigational vaccine were taken from the clinical trial publications. However, a key limitation is the lack of data on the investigational vaccine’s first dose efficacy and duration. Hence a first dose efficacy range of 25% - 65% and duration of one year were modelled. Different series completion rates were applied for the two-dose vaccine varying from 45%
- 75%, based on compliance rates reported for hepatitis vaccines in adults. The waning of the investigational HZ/su vaccine after 2 doses was assumed to be either 15 years or 20 years. **RESULTS:** For 1000 vaccinated individuals, the one-dose HZ vaccine prevented more cases of HZ and PHN than the two-dose investigational HZ/su vaccine when the two-dose completion rate was at 45% and the efficacy for the first-dose was 25%. **CONCLUSIONS:** The one-dose HZ vaccine could lead to better health and economic benefits if the two-dose investigational HZ/su vaccine cannot achieve very high series completion rate in a real world situation. Given the uncertainties about one-dose efficacy and duration of effect, further analyses are needed to determine the likely overall impact of the two-dose vaccine in the UK.

**PIN62: IMPLEMENTATION OF A SOCIETAL COST-EFFECTIVE MODEL OF A SWISS CANTON SCHOOL VACCINATION CAMPAIGN THROUGH A HOSPITAL PHARMACY LOGISTICS PLATFORM**

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**OBJECTIVES:** The Public Health Service of canton of Vaud (PHSCV) is increasingly confronted with supply disruptions involving school vaccination program. In order to avoid vaccination coverage breakdowns, all vaccination recommendations (i.e. dT, dT-IPV, dTpa, dTpa-IPV, HB, HPV and MMR) were supplied by the hospital pharmacy logistics unit (HPLU). The aim was to establish if this supply model is cost-effective compared to a traditional supply. **METHODS:** All costs of different transport modes were taken into account (2014-2015 vs 2015-2016). Incidence and costs of disease management were included to highlight the dominant strategy. A failure mode and effects analysis (FMEA) on the two transport systems (i.e. good distribution practice (GDP) supplier VS the free of charge post system) as well as on the school establishments’ fridges have been carried out. **RESULTS:** During 2015-2016, 18’430 doses were delivered and no disruption was recorded compared to one major breakdown of dTpa-IPV in 2014. Logistics costs were $ 6’000 (GDP supplier costs) and $ 47’500 (HPLU costs). The HPLU avoided new cases of recorded diphtheria (12 cases at $ 70,000 / case), hepatitis B (195 cases at $ 99,900 / case) and measles (16 cases at $ 15,500 / case). No cases of poliomyelitis, rubella and tetanus were reported. Mumps, pertussis and human papillomavirus are not subject to declaration. Without taking into account a case of poliomyelitis or human papillomavirus, the model avoids relative costs of $ 92,700 per new case. The FMEA showed no increased risk even though the fridges (83.6%) are not of pharmaceutical quality. **CONCLUSIONS:** A HPLU circumvents supply shortage by reserving the doses of vaccine and thus guarantees the school vaccination coverage through a cost effective model. Given this, it has been decided to continue and to sign a convention between the PHSCV and the Hospital Service of Pharmacy.

**PIN63: ESTIMATING LIFE YEARS AND QUALITY-ADJUSTED LIFE YEARS IN HEAVILY TREATMENT-EXPERIENCED (HTE) PATIENTS**

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**OBJECTIVES:** Modelling HIV is complicated by the requirement for individualised care. In highly treatment experienced (HTE) subjects, therapeutic options are limited. The study objectives were to develop and validate a de novo disease progression and cost-effectiveness model and estimate the value of achieving viral suppression, in terms of life years (LYs) and quality-adjusted life years (QALYs), in HIV-infected HTE adults. **METHODS:** Following a review of the published literature, a lifetime Markov state transition model was developed using Microsoft Excel, with health states reflecting CD4 count, viral load and death. Model parameters (rates, costs and utilities) were sourced from published literature and external validation to published cost-effectiveness studies in treatment-experienced cohorts was conducted. LYs and QALYs were estimated for a hypothetical cohort reflective of HTE subjects, with a mean age of 43.0 years, 32% female and a mean CD4 count of 200 cells/μL under two scenarios: [1] viral load suppression, indicative of successful treatment; and [2] increasing viral load, indicative of failing or no treatment. Health benefits were discounted at 3.5%. **RESULTS:** The model was validated to five published studies, providing an overall R2 of 0.90, a root mean square percent error of 9.5% and a mean absolute percentage error of 7.6%. For scenario [1], predicted LYs and QALYs for patients were 16.69 and 13.26, respectively (27.68 and 22.02 undiscounted); for scenario [2], predicted LYs and QALYs were 9.35 and 7.11, respectively (12.19 and 9.27 undiscounted). Consequently, viral suppression was associated with incremental discounted gains in LYs and QALYs of 7.34 and 6.15, respectively. **CONCLUSIONS:** The de novo HIV model used in this study exhibited a high degree of correlation with published models reporting outcomes for treatment-experienced cohorts. The model’s application highlights the potential significant health gains associated with successfully treating the HTE HIV-infected population, for which few treatment options exist.
OBJECTIVES: To assess cost-effectiveness of a vaccine that would protect against both Lyme Borreliosis (LB) and tick-borne encephalitis (TBE) in a highly endemic setting in Slovenia. METHODS: A Markov model was developed to estimate cost-effectiveness of a potential single combination vaccine against LB and TBE from the societal perspective. The model expressed time in annual cycles, followed a target population through their lifetime, and applied an annual discounting of 3%. A target population entered the model in a susceptible state, with time dependent probabilities to acquire LB/TBE infections and their acute manifestations. Disease manifestations were either resolved within one cycle, or a patient developed LB/TBE sequalae. The vaccination, which consisted of initial immunization and one revaccination, reduced the probability of contracting LB/TBE infection, thus affecting costs and utilities. Estimates of LB/TBE direct and indirect costs, and data on natural course of LB/TBE were obtained from local Slovenian databases. Effectiveness of the potential combined LB/TBE vaccine was derived from the studies on existing TBE and LB vaccines, while utility estimates were collected from various literature sources. RESULTS: A potential combined LB/TBE vaccine was predicted to have an incremental cost of €771,305 per 10,000 vaccinated persons, an incremental utility of 16.74QALYs and a base-case incremental cost-effectiveness ratio (ICER) of €46,061/QALY. Vaccine cost, effectiveness and discount rates were identified as the most influential model parameters. A vaccine price of €9.13 would lead to cost savings and pharmacoeconomic dominance of the vaccination strategy. CONCLUSIONS: The base-case ICER was below commonly accepted thresholds of cost-effectiveness (3xGDP/capita=€52,500/QALY in Slovenia), indicating that a combined LB/TBE vaccine might be a cost-effective option in Slovenia. This analysis represents a rare example of cost-effectiveness assessment prior market authorisation. Although some key parameters were unknown, our model sets up a tool to analyze pharmacoeconomic criteria that can help development of a cost-effective health technology.

OBJECTIVES: Clostridium difficile infection (CDI) is associated with considerable morbidity, mortality and healthcare resource utilisation. This research aims to model and evaluate the cost-effectiveness of bezlotoxumab, a new antitoxin agent + standard of care (SoC) compared with placebo + SoC patients with recurrent CDI (rCDI) in the U.K. METHODS: We developed a computer-based Markov health state transition model to simulate the natural history of CDI. Patients with CDI were followed from infection until death. Costs and effectiveness were evaluated using a third-party payer perspective. Recurrence rates were taken from point estimates taken from pooled data of the two phase 3 clinical trials. Transition probabilities and costs of rCDI were obtained from the literature. Cost-effectiveness analysis was conducted in three different patient populations: the entire clinical trial population, CDI patients at higher risk of rCDI—aged 65 years or above, and those with a prior history of rCDI within 6 months. Costs and benefits were discounted annually at 3.5% RESULTS: The model predicted that treating patients with bezlotoxumab + SoC resulted in 0.1170, 0.1022, and 0.1628 incremental discounted QALYs gained per patient for the trial population, ≥65 years and those with a prior history, respectively. The increment discounted costs were £1,321.15, £630.38, and £670.58 in these three groups. Incremental cost-effectiveness ratios were estimated at £11,287.55, £6,170.30, and £4,117.84 per QALY gained for the trial population, ≥65 years and those with a prior history, respectively. Key influential parameters include CDI-specific mortality, cost of an rCDI episode, and underlying recurrence rate. CONCLUSIONS: Based on the Markov model, bezlotoxumab in combination with SoC might be a cost-effective option in the United Kingdom. This analysis represents a rare example of cost-effectiveness assessment prior market authorisation. Although some key parameters were unknown, our model sets up a tool to analyze pharmacoeconomic criteria that can help development of a cost-effective health technology.
OBJECTIVES: To evaluate adherence to treatment, healthcare resource use and costs in "single tablet" E/C/F/TDF vs "multi-tablet" regimens using PIs or INIs + dual NRTI backbone (BB). METHODS: Preliminary analysis from an observational retrospective study was performed through the administrative and laboratory databases of two out three Infectious Diseases Departments participating to this study (ASST Valle Olona, Busto Arsizio and IRCCS San Raffaele, Milan). HIV patients were included if they had at least one prescription for an antiretroviral agent between 01/2012 and 02/2015. Follow-up was: 48 weeks; all analyses were stratified according to treatment status (naïve/experienced). Average adherence, healthcare resource use and related costs were analyzed. A multivariate regression model with the covariates: age, sex, treatment experienced, non-adherence, viral load (VL) ≥50 and CD4 ≤ 200 at baseline was used. RESULTS: 666 patients (198 ECFTDF, 428 PI+BB and 40 INI+BB) were included. The average age was 41.7±10.0, 45.1±9.8 and 44.8±13.4 years (p<0.001); male 88%, 80%, 90% (p=0.019); treatment experienced 47%, 50%, <1%; previous AIDS 2%, 8%, <1% (p=0.015); previous hospitalizations 5%, 6%, 10% (p=0.387); baseline CD4 ≤200 8%, 19%, 48% (p<0.001); VL ≥50 at baseline was 100% for naïve patients. For experienced was 29% and 62% for E/C/F/TDF and PI+BB respectively (p<0.001). Non-adherence to treatment for ECFTDF was 7.7%, PI+BB 33.8% and INI+BB 17.9% and the mean annual patient cost was respectively €10,423, €10,461 and €11,708 (p=0.194). Multivariable model revealed lower non adherence for E/C/F/TDF (PI+BB +31.50%, p<0.001; INI+BB +4.61%, p=0.352) and lower mean annual cost [PI+BB +995€ (95%IC:2-1987), p=0.05; INI+BB +379€, (95%IC:1553-2309), p=0.701]. CONCLUSIONS: ECFTDF was associated with significantly greater adherence and lower mean annual cost compared to PI+BB. Given the limited number of INI+BB patients, differences observed were not statistically significant and further analysis including patients from the third infectious disease department is needed to confirm these preliminary results.

PIN67: EVALUATION OF RESOURCE UTILIZATION AMONG INFANTS, YOUNG CHILDREN AND ELDERLY PATIENTS DIAGNOSED WITH RSV INFECTION IN THE UNITED STATES

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OBJECTIVES: We described health resource utilization (HRU) among infants, young children and the elderly in a large clinical database. METHODS: Using de-identified Optum Integrated claims and electronic medical records, we included patients experiencing their first RSV infection (ICD-9 diagnosis codes 480.1/079.6/466.11 and ICD-10 codes J12.2/J07.4/J21.0/J21.0/J20.5) between 01January 2008 and 31March 2015. We evaluated HRU attributable to RSV in terms of hospital cost (USD 2015), length of stay (LOS), ICU admissions, and we evaluated hospital ReAdmissions for Respiratory disease ≤30 days after discharge of hospitalization with RSV (RAR≤30). RESULTS: We included 12,959 patients with a first clinical diagnosis of RSV and at least one year of follow-up. 6,475 (50.0%) were infants/young children (0-5 years) without predefined pre-existing morbidities (WPPM) whilst 1,441 (11.1%) were infants/young children born pre-term, 954 (7.4%) were elderly (≥65 years). For infants/young children WPPM, the median LOS and cost per RSV hospitalization (N=722) was 4 days (IQR 3-5) and USD 7,683 (IQR 5,147-13,316). For pre-term infants/young children, the median LOS and cost per RSV hospitalization (N=282) was 5 days (IQR 3-7) and USD 10,501 (IQR 5,662-21,090). For elderly, the median LOS and cost per RSV hospitalization (N=219) was 8 days (IQR 5-22) and USD 14,070 (IQR 8,918-26,180). Excluding hospital births, 21.4%, 22.7% and 26.0% of RSV hospitalizations were ICU admissions for RSV among infants/young children WPPM, pre-term infants/young children and elderly, respectively. Median LOS in ICU was 2 days (IQR: 1-5) for infants/young children WPPM, 3 days (IQR: 2-5) for pre-term infants/young children and 6 for elderly (IQR: 4-13). The elderly had the highest frequency of RAR≤30 of 21 (9.6%) among RSV admissions. Median LOS for these respiratory readmissions was 11 days (IQR: 6-35) and cost was USD 11,577 (IQR: 5,067-19,790). CONCLUSIONS: RSV is associated with substantial hospital HRU in infants/young children, but there is also substantial hospital HRU in the elderly.

PIN68: SYSTEMATIC LITERATURE REVIEW OF ECONOMIC EVALUATIONS AND HEALTHCARE RESOURCE UTILISATION STUDIES IN THE TREATMENT OF CLOSTRIDIUM DIFFICILE INFECTION

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OBJECTIVES: The aim of this systematic literature review (SLR) was to identify and summarise all available evidence for Clostridium difficile infection (CDI), with regards to: health economic models that evaluate and compare alternative treatment strategies and studies that evaluate the economic burden of CDI and its treatment, in terms of healthcare resource utilisation (HCRU). METHODS: A systematic search was conducted in December 2016; focused
on capturing existing economic models and HCRU studies. Databases searched included: MEDLINE®, Embase®, EconLit, National Health Service Economic Evaluation Database (NHS-EED), Database of Abstracts of Reviews of Effects, and Health Technology Assessments (HTA). A comprehensive hand-search of conference abstracts, HTA body websites and the Tufts CEA registry were undertaken. Screening of abstracts and full-texts were performed by two independent researchers with consensus being facilitated through a third-party. Data extraction was carried out by a single researcher and validated by a second researcher. RESULTS: The search identified 4,995 records. Overall, 95 full text articles and 6 conference abstracts were included; of which 39 were health economic modelling studies and 62 HCRU studies. The economic studies were mostly cost-utility analyses (CUAs) based on decision-tree models comparing similar treatment regimens including fidaxomicin, vancomycin, metronidazole, and fecal microbiota transplant. The majority of models focused on treating initial CDI populations (69%), while the remainder focused on CDI recurrence. The HCRU studies were mostly retrospective studies conducted in general/hospitalised patient population. The majority of these studies were conducted in initial CDI populations (84%) and 16% in CDI recurrence. CONCLUSIONS: The results of this SLR provides a comprehensive summary of all published evidence available for treatment of CDI and can be used to support the development of and inputs required for global adaptations of health economic models. There is a lack of HCRU evidence for recurrent CDI populations, which identifies an area of possible future research.

PIN69: HEALTH CARE RESOURCE UTILIZATION AND COSTS ASSOCIATED WITH HIV-POSITIVE PATIENTS WITH COMORBIDITY VERSUS HIV-NEGATIVE PATIENTS WITH COMORBIDITY

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OBJECTIVES: The success of antiretroviral therapy (ART) has led to human immunodeficiency virus (HIV) being considered a treatable chronic condition. However, the need for life-long therapy in HIV-positive patients presents a number of challenges including long-term renal, cardiovascular (CV) and bone toxicities. The study objective was to evaluate the impact of HIV on health care resource utilization and costs among patients with comorbidities, using the Quebec public drug plan database (RAMQ). METHODS: HIV-positive patients who had received ART for at least 6 months from January 2006 to June 2012 were selected and categorized in 4 groups: 1) patients with CV, bone or renal comorbidity, 2) patients with CV comorbidity, 3) patients with bone comorbidity and 4) patients with renal comorbidity. Three controls of HIV-negative patients with the same comorbidities were matched for age groups and gender to each HIV-positive case. Comorbidity date was defined as the date of the first medication, diagnosis or medical procedure related to comorbidities. Health care resource utilization and costs were measured in the 2 years following comorbidity date. RESULTS: A total of 1,983 HIV-positive patients with comorbidity were identified, in which 1,498 had CV comorbidity, 915 had bone comorbidity and 191 had renal comorbidity. The mean total health care cost per year was higher in HIV-positive than in HIV-negative patients with comorbidity (CAN$22,037;SD=16,935 vs. CAN$3,620;SD=7,418, p<0.01). For patients with CV and bone comorbidity, similar results were obtained. For patients with renal comorbidity, the mean total health care cost per year was higher for HIV-positive than for HIV-negative patients (CAN$29,759;SD=24,827 vs. CAN$9,193;SD=17,659, p<0.01) and costs in both groups were higher than groups with other comorbidities. CONCLUSIONS: HIV-positive patients with renal, bone or CV comorbidities had increased health care costs when compared to HIV-negative patients with the same comorbidities. Renal comorbidity had the highest health care costs.

PIN70: ANTVIRAL MEDICINES ASSESSMENT: WHAT IS DRIVING HIGH CLINICAL ADDED VALUE IN FRANCE?

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OBJECTIVES: To analyse the basis of clinical added value (CAV) appraisal regarding the high cost of new medicines including hepatitis C treatment In France. The CAV appraisal is done by the French National Authority for Health (HAS) on a 5-point scale from I (major) to V (no CAV). The CAV level is partly used by the economic committee for healthcare products to negotiate drug prices. METHODS: A retrospective and descriptive study analysing HAS appraisals of all new antiviral indications assessed between 2010 and 2015 were conducted. For each CAV appraisal, information regarding the level of evidence and clinical effectiveness was collected. RESULTS: Twenty antiviral drugs (47 indications) were assessed. All obtained a favourable opinion for reimbursement with 11 a major to moderate CAV, 14 a minor and 22 no CAV. No one obtained a major CAV. The majority of studies (46% [22/47]) were non-active comparator studies based on virological response and supported an important to moderate CAV in 32% (7/22), as sofosbuvir that granted the highest CAV level (important CAV). Among the 19 comparative trials, 68% (13/19) were of superiority design supporting a major to moderate CAV in 31% (4/13) of the cases. A higher proportion of important to moderate CAV were observed in trials using a relevant primary endpoint (28%) versus no
one for a study using an exploratory endpoint such as pharmacokinetic endpoint. **CONCLUSIONS:** A high proportion (53%) of CAV is recognized in virology compared to the other therapeutic areas (15%) while non-active comparator studies are made. This report shows that HAS appraisals remain multi-factorial. HAS' expectations in terms of level of evidence take into account the medical need, therapeutic area specificity and a rapid evolution of the therapeutic strategy. The emergence of anti-viral drug resistance can also influence the CAV appraisal.

**INFECTION - Patient-Reported Outcomes & Patient Preference Studies**

**PIN71: REAL-WORLD EVIDENCE OF DIRECT-ACTING ANTIVIRALS PERSISTENCE ON PLANNED HEPATITIS C TREATMENT**  
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**OBJECTIVES:** The objective of this study is to evaluate the persistence on treatment of patients on direct-acting antivirals (DAA) therapy for hepatitis C in a Portuguese University Hospital (CHUC). **METHODS:** This was an observational study where hospital pharmacy dispensing data were collected over the period Jan/2015-May/2017. Persistence was defined as remaining in therapy and not discontinuing (end of treatment). Crude survival estimates were obtained by Kaplan-Meier method. The risk of HCV treatment discontinuation was estimated by a Cox proportional hazard model. Adherence was a second exploratory endpoint calculated by the pill count approach. **RESULTS:** A total of 626 patients were included: mean(SD) age 49.9(10.9) years and 74.4% male. Genotype 1 (72.4%) was the most frequent, 67.4% of patients were treatment naïve and 38.8% metavir F1. Ledipasvir/sofosbuvir was used in 83.2% of the cases. Planned treatment duration was: 12 weeks (69.0%); 24 weeks (29.1%). For these two major subgroups, 68.3% and 63.2% were treatment naïve and 8.1% and 64.8% were metavir F4, respectively. An estimated 8.9% (95% CI = [6.0%;11.7%]) and 16.5% (95% CI = [10.6%;22.0%]) of patients ended treatment before 12 and 24 weeks planned treatment duration, respectively. Men [hazard ratio of discontinuation = 0.77, 95%CI = [0.61:0.97]) and non-cirrhotic patients [HR = 0.70, 95%CI = [0.49:1.0]) were more likely to persist on treatment. Adherence to DAA treatment of 95% or higher was observed in 98% of the 12 weeks and 24 weeks subgroups, respectively. **CONCLUSIONS:** Real-world data confirms very high persistence and adherence rates to DAA for the treatment of hepatitis C.

**PIN72: HEPATITIS A AND HEPATITIS B RECOMBINANT VACCINE ADHERENCE IN THE UNITED STATES**  
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**OBJECTIVES:** Estimate the completion and adherence of the HepA/HepB recombinant vaccine three-dose schedule in the US. **METHODS:** We conducted a retrospective database study of claims from the 2008-2015 MarketScan Commercial Claims and Encounters (CCAE), Medicare Supplemental, and Medicaid databases. Completion of 2 and 3 doses of Twinrix and adherence with the 3-dose recommended schedule were measured. Individuals age ≥19 at first dose were included if they had 6 months of continuous health plan enrollment prior to the first dose. Individuals who were on the accelerated 4-dose schedule were excluded. Median time to completion, the proportion of patients who completed 2 and 3 doses, and adherence to the recommended schedule within specific time periods of the first dose were estimated using Kaplan-Meier survival curves. **RESULTS:** 178,033 individuals initiated the series. Average age at initiation was 45.02 years, and 88.6% of initiators were in the CCAE database. Males composed 43% of the sample. Overall, 39.8% of individuals received a second dose within the recommended 1 month; this ranged from 22.7% in the Medicaid sample to 41.3% in the CCAE sample. Adherence to the recommended spacing for the second dose was highest in individuals aged 60-64 at initiation (45.5%) and lowest in individuals aged 19-49 (37.3%). The KM-estimated median time to the second dose was 6 months. Only 18% of initiators received a third dose within the recommended 6 months of the second dose, and 32.3% had received a third dose within 30 months of the first dose. Of those who received a second dose, the median time to the third dose was 16 months. **CONCLUSIONS:** Adherence to the recombinant HepA/HepB vaccine regimen is suboptimal. Only 18% received the third dose within the recommended schedule. Research is needed to fully understand the factors associated with completion and adherence to multi-dose vaccines in order to improve vaccination rates.

**PIN75: INFLUENZA-RELATED ATTITUDES OF HEALTHCARE WORKERS AT INSTITUTIONS FOR ACUTE AND CHRONIC DISEASES**  
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OBJECTIVES: The objective of our study was to learn the vaccination coverage against seasonal influenza, nonspecific and specific prevention habits, and attitudes related to vaccination. METHODS: We conducted a quantitative, cross-sectional survey with non-random sampling method among the healthcare workers of the Harkány Spa Hospital, the Emergency Patient Care Department, Department of Emergency Medicine and the Intensive Anaesthesiologic and Therapeutic Institute of the Clinical Center of the University of Pécs (n=254). The questionnaire involved the following question types: sociodemographic data, specific/nonspecific prevention against influenza, and attitudes, habits related to vaccination. Data analysis (with 95% probability) was carried out by descriptive statistics, x^2 test with Z-test and Bonferroni correction, Spearman’s correlation, Kruskal-Wallis test, and as a post hoc test Mann-Whitney U test with Bonferroni correction, and multinominal logistic regression concerning normality. We used SPSS 22.0 program for data analysis. RESULTS: The questionnaire was completed by 121 healthcare workers in acute care, and 133 employees in chronic care. 55.5% of them never had vaccination against seasonal influenza. Workers in acute care (β=1.155; 95%OR=3.17 [1.27;7.92]; p=0.013) and persons with higher education (β=0.714; 95%OR=2.04 [1.09;3.81]; p=0.025) were more likely to be vaccinated than people in chronic care. People in acute care (Mann-Whitney U=3509.500; p<0.001;) had hand disinfection more times and wore mask (χ^2=32.668; p<0.05) protective gloves (γ^2=58.307; p<0.05) and goggles (γ^2=58.307; p<0.05) more frequently than people in chronic care. People in chronic care did not believe that seasonal influenza was a severe disease (Mann-Whitney U=1046.500; p<0.001), therefore, according to them, they did not belong to a group vulnerable to influenza (Mann-Whitney U=1167.000; p<0.001). CONCLUSIONS: Education of professionals in chronic care and information provision concerning specific and nonspecific prevention against influenza to healthcare workers play an essential role in workplace communication. It should be treated as a priority issue due to the increase in compliance value.

PIN77: HEALTH-RELATED QUALITY OF LIFE, WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT ASSOCIATED WITH CLOSTRIDIUM DIFFICILE INFECTION IN CHINA, BRAZIL, EUROPE AND THE UNITED STATES

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OBJECTIVES: To assess the health-related quality of life (HRQoL), work and activity (WA) impairment associated with Clostridium difficile infection (CDI). METHODS: Data aggregated from the 2013-2016 US, 5EU, China and Brazil internet-based cross-sectional National Health and Wellness Surveys (NHWS) were used. NHWS includes the revised Medical Outcomes Study 36-Item Short-Form and the Work Productivity and Activity Impairment General Health questionnaire. Respondents (≥18 years) were classified as 1) currently treated doctor-diagnosed CDI (CT), or 2) doctor-diagnosed CDI not currently treated (NT), or 3) never experienced CDI (NO), based on self-reports.
Regression modeling assessed the association between CDI status and outcomes after adjusting for Charlson Comorbidity Index, education, age, sex, and country. **RESULTS:** Of 352,780 respondents, 299 and 2,111 met criteria for CT and NT, respectively. About 45% of respondents were US-based. CT and NT were older (mean 48, 53 vs. 46), more often unemployed (50%, 57% vs. 41%), and had higher mean CCI (2.61, 0.92 vs. 0.20) than NO. More females were NT (67%) than CT (49%) or NO (53%). After adjustment for covariates, CT and NT reported significantly lower mean HRQoL than NO: mental component summary score (39, 43 vs. 46), physical component summary score (39, 41 vs. 46), and health utility (0.58, 0.64 vs. 0.71) (all p<0.05). These differences met commonly accepted thresholds for minimal clinically important difference. CT and NT reported significantly greater percent of work time missed (21%, 16% vs. 8%), impairment while working (43%, 34% vs. 22%), overall work impairment (52%, 39% vs. 26%) and activity impairment (61%, 49% vs. 34%) due to health than NO (all p<0.05). **CONCLUSIONS:** CDI is associated with clinically meaningful and statistically significant lower HRQoL and statistically significant higher WA impairment compared to those with no history of CDI. The potential impact of CDI on HRQoL and WA impairment requires further evaluation.

**PIN78:** QUALITY OF LIFE AND UTILITY DECREMENT ASSOCIATED WITH CLOSTRIDIUM DIFFICILE INFECTION IN FRENCH ACUTE CARE FACILITIES

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**OBJECTIVES:** To estimate the impact on quality of life and the QALY decrement associated with Clostridium difficile infection (CDI) in the hospital setting. **METHODS:** An observational prospective study was performed in 7 French acute-care facilities in 2016 where patients presenting with a bacteriologically-confirmed CDI were randomly enrolled. The EQ-5D-3L was filled in by patients at 7 (+/-2) days after CDI diagnosis to describe their perceived state of health at that date and also to retrospectively assess their state of health as of immediately before the episode (baseline). Individual utility decrement was obtained by subtracting the corresponding utilities using the French tariffs. The QALY loss was calculated by multiplying the days spent from baseline (first symptoms) to the date of the interview, by the decrement of utility. A multivariate analysis of variance of the utility decrement according to CDI and patients and infection characteristics was performed. **RESULTS:** 80 patients were enrolled and had evaluable data. The median age was 71 years (min/max: 30/98) and 45% were male. The utility scores were negative in 14 patients (18%) at baseline and in 43 patients (54.4%) during the CDI episode. The utility scores dropped from a mean 0.542 (0.391) at baseline to 0.050 (0.404) during the CDI episode with a mean adjusted utility decrement of 0.482 points (0.4) and showed statistically significant differences according to CDI severity (Zar score ≥ 3) (p=0.001), baseline utility (positive/negative) (p= 0.032), gender (p=0.041) and age (cut-off at 65y) (p=0.041). No association with the Charlson index was found. The associated QALY loss in absence of mortality was 10.22 (19.44) QALD (Quality-Adjusted Life Days) or 0.028 (0.053) QALY. **CONCLUSIONS:** The impact on quality of life of CDI episodes aside from the consequence of excess mortality is major and translates in a substantial QALY loss despite their short duration.

**PIN79:** THE IMPACT OF VACCINATION AND PATIENT CHARACTERISTICS ON INFLUENZA VACCINATION UPTAKE

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**OBJECTIVES:** To improve information for patients and to facilitate a vaccination coverage that is in line with the EU and World Health Organization goals, we aimed to quantify how vaccination and patient characteristics impact on influenza vaccination uptake. **METHODS:** An online discrete choice experiment (DCE) was conducted among 1,261 representatives of the Dutch general population aged 60 years or older. In the DCE, we used influenza vaccination scenarios based on five vaccination characteristics: effectiveness, risk of severe side effects, risk of mild side effects, protection duration, and absorption time. A heteroscedastic multinomial model was used, taking all five vaccination characteristics as well as 19 different patient characteristics into account. **RESULTS:** Vaccination and patient characteristics both contributed to explain influenza vaccination uptake. Assuming a base case respondent and a realistic vaccination scenario, the predicted uptake was 58%. One-way changes in vaccination characteristics and patient characteristics changed this uptake from 46% up to 61% and from 37% up to 95%, respectively. The strongest impact on vaccination uptake was whether the patient had been vaccinated last year, whether s/he had experienced vaccination side effects, and the patient’s general attitude towards...
vaccination. **CONCLUSIONS:** Although vaccination characteristics proved to influence influenza vaccination uptake, certain patient characteristics had an even higher impact on influenza vaccination uptake. Policy makers and general practitioners can use these insights to improve their communication plans and information regarding influenza vaccination for individuals aged 60 years or older.

**PIN80:** A MULTICENTER, OBSERVATIONAL STUDY TO EVALUATE COMORBIDITIES IN PATIENTS ABOVE 50 YEARS OF AGE – AGING POSITIVE: A COMPARISON OF MEDICAL CHARTS AND PATIENTS SELF-REPORTED DATA

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**OBJECTIVES:** The primary objective of AGING POSITIVE is to characterize non-AIDS-related comorbidities of interest among HIV-infected patients ≥ 50 years old. This poster focuses the results of an exploratory objective: to compare patient self-reported data on comorbidities, current co-medication and healthcare resource use with the equivalent data collected from the medical charts. **METHODS:** Multicenter, cross-sectional study conducted in seven Portuguese centers specialized in the treatment of HIV/AIDS. Data was collected from hospital medical records and through a patient self-administered questionnaire. Concordance between data obtained by investigator through medical records and the patient-reported knowledge was analyzed using Kappa concordance coefficient for qualitative variables and intraclass correlation coefficient for quantitative variables. **RESULTS:** A total of 401 patients were recruited between Nov/15 and Jun/16. Patient's mean age was 59.3 years (SD) and the mean infection duration was 12 years (SD 6.17). All patients filled the questionnaire. The most frequent comorbidities were the same for data collected from medical charts and self-reported data – hypercholesterolemia, hypertension and depression/chronic anxiety. The comparative analysis showed a statistical significant concordance between non-AIDS comorbidities of interest collected from self-administered questionnaire and equivalent data collected from medical charts. For all comorbidities, the rate of concordant answers was greater than 93% (except for hypercholesterolemia: 87.8%) and the Kappa concordance coefficient show a good and very good agreement. The comparative analysis of co-medication also depicted a general good and very good concordance (except for hepatitis C which showed a moderate concordance), with a statistical significant Kappa concordance coefficients and a higher rate of concordant answers. Lipid lowering agents, antihypertensives and antidepressants/anxoylitics were the most frequent co-medications. Results of healthcare resources showed a moderate and good correlation in comparison of self-reported versus medical charts data. **CONCLUSIONS:** Data in medical charts and patient-reported knowledge is highly concordant both in terms of comorbidities as co-medication.

**PIN81:** PRIORITIZING PATIENT-RELEVANT ATTRIBUTES OF HIV MEDICATIONS: A MIXED METHODS APPROACH

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**OBJECTIVES:** Since the advent of highly active combination antiretroviral therapy (ART), HIV infection has been transformed into a life-long manageable disease. As the number of effective therapeutic options has increased, the number of inputs for decision-making has increased, and trade-offs of regimen attributes have become more complex. The study’s objective was to identify preference-relevant characteristics of ART and to understand key factors in the ART selection process from provider and patient perspectives. **METHODS:** A mixed methods approach was used, including interviews with patients and providers and ranking tasks. Participants were enrolled between March 2016 and May 2017 in the Southeastern United States. Interviews were coded following direct content analysis and complemented by quantitative analysis of attribute mentions. Ranking tasks were analyzed via count analysis. **RESULTS:** 28 interviews (16 patients, 12 healthcare providers) and 26 ranking tasks with patients were conducted. 61.1% of patients were male (mean age: 50.7 years, mean duration on ART: 14.8 years). Providers had 15.5 years of professional experience on average. Qualitative analysis of patient interviews revealed a variety of decision relevant aspects; the majority could be grouped in four categories: side effects (14/16 patients), administration characteristics (14/16 patients), dosing (13/16 patients), long-term effects (12/16 patients), and other considerations, like patient involvement, relationship with provider, and efficacy. The degree of concordance between patients and providers differed across categories. Ranking results showed differences in priorities regarding depression, nausea, diarrhea, changes in physical appearance, and drug interactions. Expectations for the involvement of patients in the ART selection process varied greatly among and between patients and providers. **CONCLUSIONS:** A large number of relevant attributes were identified and assigned to categories. Study results also indicate considerable heterogeneity in priorities across patients, in providers’ perception of patient priorities, and in patients’ preferred level of involvement in HIV treatment decisions.
OBJECTIVES: Cytomegalovirus (CMV) disease is associated with increased mortality and morbidity in haematopoietic cell transplant (HCT) recipients. This study aimed to identify patient-reported outcomes (PROs) affected by CMV infection and CMV treatment in HCT recipients. METHODS: An EMBASE literature review of transplantation publications (post-2002) that included PRO instruments and ≥50 transplant recipients was conducted to identify studies using PRO instruments in CMV management and CMV reactivation. However, as this search did not identify any studies matching the criteria, the search was expanded to include studies of HCT recipients that used PRO instruments in general. Two experts in HCT were interviewed to determine the impact of CMV infection and treatment on PROs from their perspective, and ten HCT recipients were asked about their experience of the transplant, CMV infection and CMV treatment. Based on information provided by HCT experts and recipients, an additional search was conducted to identify PRO instruments specifically measuring fatigue. RESULTS: Overall, 976 references were identified. The most widely-used PRO instruments were the short-form health surveys SF–36 and SF–12. The HCT experts highlighted the difficulty of isolating the impact of CMV, and that the main impact on transplant recipients was due to the burden of taking medication intravenously, the stress/anxiety from having an infection, re-hospitalisation and antiviral therapy toxicity. During the transplant recipient interviews, fatigue and stress/anxiety from the infection were the most common symptoms attributed to CMV disease. In the expanded fatigue search, 2285 publications reporting 252 different methods of measuring fatigue were identified: 416 publications used scales specifically designed to measure fatigue. CONCLUSIONS: This study highlighted that fatigue and anxiety are key symptoms of CMV infection and/or CMV treatment. There are no CMV-specific PRO instruments validated in CMV patients that can adequately assess HCT-related fatigue and anxiety.

PIN83: PATIENTS’ EXPERIENCES LIVING WITH CHRONIC HEPATITIS B INFECTION: A MULTINATIONAL QUALITATIVE STUDY

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OBJECTIVES: Chronic hepatitis B (CHB) is an incurable viral infection of the liver and a major risk factor for cancer. We sought to understand patients’ experiences of CHB from pre-diagnosis through to treatment and beyond, including any differences according to nationality or coinfection status. METHODS: Qualitative data were sourced from a literature review (MEDLINE, Embase, PsycINFO, conference proceedings) and semi-structured interviews with patients and clinicians from Italy, Japan, Spain and USA. Publications and interview transcripts were analysed using a thematic synthesis approach facilitated by ATLAS.ti v7.5. RESULTS: Fourteen publications, 84 patient interviews and 30 clinician interviews were analysed. A ‘patient journey map’ was developed to portray overarching themes throughout time, in addition to a conceptual model highlighting specific symptoms, impacts and treatment-related side effects. Many patients with CHB were asymptomatic - a significant barrier to diagnosis - but initial symptoms included tiredness, appetite loss, nausea or vomiting; the frequency and severity of these increased with increasing disease progression. Diagnosis was often accompanied by shock and uncertainty for the future. Throughout life, CHB significantly impacted emotional and psychological wellbeing including perceived stigmatization, and was associated with numerous lifestyle limitations and work-related impacts. Patients described 'never feeling free' from the illness. Treatment side effects were especially prominent in patients receiving interferon-based therapies, further impacting their lives. Whilst the symptoms and impacts of CHB on patients’ lives were ubiquitous across country and co-infection status, differences in transmission route, treatment decision-making and disease understanding were apparent. CONCLUSIONS: Experience of CHB varies, but fatigue and impacts on psychological and emotional wellbeing are prominent. Experiences varied throughout time in response to key events such as shock and uncertainty at diagnosis and treatment-related side effects, amidst ongoing limitations and perceived stigmatization. The findings of this research can inform the content of patient-reported outcome measures for CHB patients.

PIN84: QUALITY OF LIFE IN PATIENTS WITH LYME DISEASE IN SLOVAK REPUBLIC

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OBJECTIVES: The incidence of Lyme disease (LD) in Slovak Republic is assumed about 2000-3000 cases per year
with about 100 cases of encephalitis as its complication. No study was published about the impact of LD on quality of life (QoL) and work ability (WA) in Slovak Republic. **METHODS:** The sample consisted of 50 patients, 32 women and 18 men, with average age being 55.8 years. 11 patients were classified as LD with neuropathia, 24 patients – LD with arthro-myopathia, 13 – LD with fatique syndrome, 2 – LD with heart syndrome. The average duration of disease was 4 years. Primary method used for the analysis of QoL was a combined questionnaire: A. Demography, B. Clinical part. C. Quality of life, D. Socio-economic part. QoL and WA were evaluated on numeric scales from 0 - the worst to 10 - the best. Standard statistical tests were used in results evaluation. **RESULTS:** Significant statistical differences (p less than 0.05) in QoL were found: in the time of best health – 9.0, without LD – 8.1, in the time of diagnosis – 4.4, current (observed, treated when necessary) – 5.2. The results gained in WA were: 9.2 vs 8.3 vs 5.2 vs 4.7. The results from QoL and WA were in strong correlation. The myo-arthropatic pain was the same in the time of diagnosis-4.40 as by the treatment- 4.34, the fatique was similar – 4.5 vs 4.7, as symptoms of heart failure- 5.9 vs 6.3.

Willingness to pay was for full health without LD was 75.0 € monthly by average monthly income 420.0 €. **CONCLUSIONS:** LD has a significant impact on patients’ QoL and WA. There are significant differences in both areas in duration of LD. The treatment had positive impact on QoL and WA. Longer time of LD duration had worse QoL and WA.

**PIN85: SYSTEMATIC LITERATURE REVIEW OF HEALTH-RELATED QUALITY OF LIFE IN CLOSTRIDIUM DIFFICILE INFECTION**

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**OBJECTIVES:** The aim of this systematic literature review (SLR) was to identify and summarise all available evidence for Clostridium difficile infection (CDI), with regards to health-related quality of life (HRQL). **METHODS:** A systematic search was conducted in December 2016; focused on identifying utility and HRQL studies. Databases searched included: MEDLINE®, Embase®, EconLit, National Health Service Economic Evaluation Database (NHS-EED), Database of Abstracts of Reviews of Effects (DARE), and Health Technology Assessments (HTA). A comprehensive hand search of conference abstracts, HTA body websites and the Tufts CEA registry were undertaken. Screening of abstracts and full-texts were performed by two independent researchers with consensus being facilitated through a third party. Data extraction was carried out by a single researcher and validated by a second researcher. **RESULTS:** The search identified 1,232 records. Overall, 3 full text articles and 1 conference abstract were included. The HRQL studies identified varied with regards to the method of elicitation, using the Short Form Health Survey (SF-36 or SF-12), Euroqol-5d-3l questionnaire (EQ5D), and time trade-off methods to elicit preferences for various health states. Only a single study by Shupo et al. reported utility weights for CDI-related health states (Shupo et al. 2012), which were based on the EQ-5D (completed by an unknown number of healthcare providers in the UK) as well as time trade-off methods (valued in a representative sample of the UK population). Utility values reported by this study were described by the authors as being “unrealistically low for patients with CDI.” **CONCLUSIONS:** The lack of utility weights available to represent CDI-related health states is underlined by the fact that cost-utility analyses in CDI refer to utility studies conducted in alternative populations. Alternative methods such as discrete choice experiments should be explored for this patient population.

**INFECTION - Health Care Use & Policy Studies**

**PIN86: A MULTICENTER, OBSERVATIONAL STUDY TO EVALUATE COMORBIDITIES IN PATIENTS ABOVE 50 YEARS OF AGE – AGING POSITIVE: CHARACTERIZATION OF THE HEALTHCARE RESOURCE USE**

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**OBJECTIVES:** The primary objective of AGING POSITIVE is to characterize non-AIDS-related comorbidities of interest among HIV-infected patients ≥ 50 years old. This poster focuses the results of a secondary objective: to describe healthcare resource use (hospitalizations and medical appointments) in the previous 12 months. **METHODS:** Multicenter, cross-sectional study conducted in seven Portuguese centers specialized in the treatment of HIV/AIDS. Data was collected from hospital medical records and through a patient self-administered questionnaire. **RESULTS:** A total of 401 patients were recruited between Nov/15 and Jun/16. Patient’s mean age was 59.3 years (SD), the mean infection duration was 12 years (SD 6.17) and the mean duration of ART was approximately 10 (SD 6.07) years. Accordingly to the medical records all patients had medical appointments at the HIV-specialist during the previous year (mean 3.43; SD 2.72). 49.0% had medical appointments at other hospital-specialist (mean 3.50; SD 3.48) and 56.4% had medical appointments with the general practitioner (GP) mean 3.58; SD 3.48. Approximately 7% of the patients were hospitalized, with a mean of 1 hospitalization and median duration of 7 days. Almost ¼ of the patients (64/266) had no medical appointments at GP or other hospital-specialist. The
PIN87: DOES THE REIMBURSEMENT OF IN-PATIENT HOSPITAL SERVICES ADEQUATELY COVER NOVEL ANTIBIOTIC PHARMACEUTICALS IN THE U.S., EU4 AND ENGLAND? DISCUSSION OF CURRENT MECHANISMS IN PLACE

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OBJECTIVES: Diagnosis-related group (DRG) codes bundle in-patient hospital services into categories for which standard payments are made. In some countries, payment policies allow for adjustments to DRG codes and additional, alternative and temporary funding (AATF) mechanisms can provide reimbursement for novel pharmaceuticals. This research examined the existing hospital in-patient funding mechanisms and AATF options to establish how effectively current funding facilitates access to novel antibiotics in scope markets (United States [U.S.], EU4 [France, Germany, Italy, Spain] and England). METHODS: Funding mechanisms were compared using a targeted range of current DRG codes for the treatment of infectious and parasitic diseases in the scope markets. The criteria for AATF under current market regulations were also examined. The accessibility of these funding options was explored for 13 EMA approved antibiotics between 01/01/2011 and 01/06/2017. RESULTS: All markets, except Spain, have AATF mechanisms to reimburse novel pharmaceuticals. In some situations, a novel antibiotic cost can constitute 70%+ of the DRG payment amount while evidence suggests that generics only make up a small percentage of the DRG amount. Although the broad criteria for AATF funding options are published, formally, multidrug resistance is not a criterion taken into consideration when allocating AATF. This is reflected in the low frequency of AATF funding being achieved (England [4/13], France [2/13], and the U.S. [1/13]). CONCLUSIONS: The resources available through DRG code-based funding utilised for hospital in-patient services are often insufficient to fund novel and innovative antibiotics. A minority of antibiotics have qualified for AATF; leading to a possible increase in in-patient hospital budgetary pressures due to limited funding. AATF mechanisms are vital to support appropriate reimbursement and access to new effective antibiotic therapies delivering patient benefits. BIBLIOGRAPHY: 1 Barlas, S., 2014 Dec. Generic Prices Take Flight. Pharmacy and Therapeutics, 39(12), pp. 843-845.

PIN88: ADDRESSING UNCERTAINTY IN WOUND MANAGEMENT USING A MODIFIED DELPHI METHODOLOGY

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OBJECTIVES: The increasing prevalence and rising costs of Venous Leg Ulcers (VLU), Diabetic Foot Ulcers (DFU) and Pressure Ulcers (PU), means that a consistent level of care and understanding of best practice is needed to improve patient outcomes and maximise value for money. This study aimed to achieve consensus on a set of evidence-based statements on these issues from a range of clinical experts. METHODS: A literature search identified 827 articles. Inclusion/exclusion criteria were applied resulting in 145 articles providing 308 quotations in 4 categories: epidemiology, clinical effectiveness, quality of life, and economics. From this, 47 statements were developed. A modified Delphi methodology was used and a consensus threshold of 80% was set. Round I and II: Participants examined and voted yes/no for each statement. If the threshold was not met, comments informed changes. Round III: A meeting to discuss all statements. RESULTS: Round I: 38/47 statements confirmed, none rejected. 9 statements modified using comments and resubmitted. Round II: 5/9 remaining statements confirmed, none rejected, leaving 4. At the meeting, all 47 were confirmed. During examination of confirmed statements, some modifications were made; agreed by all members of the panel. A consensus document is being developed using the statements. CONCLUSIONS: The consensus document developed from this approach can help to address areas of uncertainty in the management of chronic wounds by Healthcare Professionals across a range of disciplines resulting in benefits both for patients and the healthcare system. The panel enjoyed the Delphi methodology, which was an efficient way of arriving at consensus for a large and varied group. Using a Delphi methodology to achieve a consensus on evidence-based statements generated from a literature review is an efficient and robust methodology for resolving uncertainty regarding the management of clinical conditions.
**PIN89: BURDEN OF RESPIRATORY SYNCYTIAL VIRUS (RSV) DISEASE IN ADULTS: FINAL ANALYSIS FROM A RETROSPECTIVE CHART REVIEW**

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**OBJECTIVES:** Data demonstrating the burden of RSV disease in adults are limited. This analysis aimed to quantify the healthcare burden of RSV infections in at-risk adult subpopulations. **METHODS:** A retrospective review of patient cases (Oct 2014–Oct 2016; USA) was conducted. Data for adults ≥18 years with confirmed RSV diagnosis were collected. Each hospital physician submitted up to three randomly selected patient cases via an online survey. Data collected included treatments received during hospital stay: treatment and burden after hospital stay was included for patients in an integrated delivery network (56%). **RESULTS:** This study comprised 379 patients, collected in 4 groups: 3 with identified risk factors: underlying chronic lung disease (33%; Group A), immunocompromised (24%; Group B), elderly (≥65 years; 29%; Group C) and another without these risk factors (14%; Group D). Baseline characteristics for Groups A–D, were respectively: median age 62.5/56.5/70.0/41.0 years, male 54/57/55/60%, Caucasian 56/60/60/55%, asthma 25/8/6/0%, coronary artery disease 22/8/22/11%, and hypertension 25/8/26/13%. Mean length of hospital stay was 7.6/7.4/7.1/6.4 days by group, with 28/36/26/23% admitted to the intensive care unit (ICU) and 2.6/4.8/2.8/4.3% all-cause mortality within 60 days of hospitalisation. Hospital respiratory support treatments for Groups A–D, were respectively: supplemental oxygen 73/76/77/76%, bronchodilators 68/68/65/60%, invasive/non invasive mechanical ventilation 12/16/13/11%, and supportive care 8/6/11/8%. 58/61/59/51% received antibiotics (mean 4.5–5.8 days, 25% had confirmed bacterial coinfection). Other hospital treatments included corticosteroids 57/39/43/40% and ribavirin 30/40/26/38%. Most patients required follow-up visits with 6/7/9/2% requiring skilled nursing, either at home or in long-term care. **CONCLUSIONS:** Hospitalised adults with RSV place a large burden on healthcare resources, due in part to long hospital stays, ICU admission, required concomitant treatments and follow-up care. Burden of RSV could potentially be reduced by effective vaccination and antiviral treatments. In addition, specific RSV virologic diagnosis may also help to curtail unnecessary antibiotic use.

**PIN90: ANTIBIOTIC PRESCRIBING PATTERN IN ACUTE UPPER RESPIRATORY TRACT INFECTIONS IN DUBAI**

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**OBJECTIVES:** NICE clinical guidelines recommend no or delayed use of antibiotics in upper respiratory tract infections (URTI), while immediate use is only recommended in severe cases or where there is risk of developing complications. The primary objective of this study was to understand the antibiotic prescribing pattern during acute episodes of URTI. The secondary objective was to study the resource use during acute episodes of URTI. **METHODS:** A retrospective database analysis was conducted using Dubai Claims Database. All outpatient claims between Jan 2014 to Mar 2017 with a diagnosis for an URTI, specifically acute otitis media, pharyngitis/tonsillitis and common cold, were extracted. All episodes of URTI were identified as a 15 day period from the date of index URTI diagnosis. The index URTI diagnosis date for each episode was identified such that there were no claims for an URTI during prior 15 days. The unit of analyses was the number of URTI episodes. **RESULTS:** A total of 2,286,563 URTI episodes were identified, of which majority were for pharyngitis (42.2%) followed by common cold (32.2%), tonsillitis (19.7%) and acute otitis media (5.9%). Overall antibiotic was not used in 44.3% of the episodes, with highest for common cold (58.7%) and lowest for tonsillitis (29.9%). Of the remaining 55.7% of episodes where an antibiotic was prescribed, delayed prescribing (days 5-15 from diagnosis) was observed in 6.7% episodes. The average time to antibiotic from diagnosis was 1.7 days (SD 2.2, median 1.0). Use of multiple antibiotics was observed in 39.8% episodes. **CONCLUSIONS:** No use of antibiotics was observed in less than half of the acute URTI episodes. Episodes where antibiotics were prescribed, delaying its use was less common.

**PIN91: A FRESH LOOK AT THE PREDICTORS OF THE NUMBER OF HIV CASES IN TURKEY**

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**OBJECTIVES:** National health authorities in Turkey have emphasized that the country’s aim to fight against communicable diseases has surpassed the Millennium Development Goals for the year 2030. However, the reemergence of HIV cases needs to be revisited. Our study explores HIV case variation in Turkey from 1985 to 2013 and uses accessibility to health care and education, as well as well-being and poverty measures to determine predictors of HIV cases. **METHODS:** Data from the Turkish Public Health Institution-Ministry of Communicable...
Diseases and the Turkish Statistical Institute for the years 1985 to 2013 were used to measure the number of annual HIV cases and associated factors. The Generalized Poisson regression model was used to assess predictors of HIV cases. Physician density, number of hospital beds, number of mental and neurological hospitals, crude divorce rate, number of graduates from high school, crude suicide rate, and annual gross domestic product growth rate were determined as the model covariates. The Chi-square test was performed to statistically analyze the HIV cases’ associations with predictor variables. RESULTS: The Chi-Square test results’ likelihood ratio (X2=332.18, p<0.001) confirms the model’s overall significance. Factors significantly related to the number of HIV cases were physician density (p<0.01) and number of hospital beds (p<0.05) for the 29-year period in Turkey. CONCLUSIONS: The study results offer several policy insights for health policy makers to aid in Turkey’s increasing HIV epidemic. These study results confirm that health indicator accessibility is the best predictor of the number of HIV cases. The results confirm that Turkey has successfully improved access to health systems throughout the country. However, more can be done to fight the HIV epidemic; increasing public awareness, HIV testing, and counseling are advisable strategies. Furthermore, public campaigns, early diagnosis of high-risk groups, and improved data sharing and availability are additional ways to combat this disease.

PIN92: ANTIMALARIAL TREATMENT OUTCOMES IN ETHIOPIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVES: Ethiopia is among countries with a high malaria burden. There are several studies that assessed the efficacy of antimalarial agents in the country and we performed a systematic review and meta-analysis on this topic to obtain stronger evidence on treatment outcomes of malaria from the existing literatures in Ethiopia. METHODS: A systematic literature search using the Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) statement was conducted on studies from pubmed, google scholar, and science direct databases to identify published and unpublished literatures. RESULTS: Twenty-one studies were included in the final analysis with a total number of 3123 study participants. Treatment outcomes were assessed clinically and parasitologically using WHO guidelines. Adequate clinical and parasitological response was used to assess treatment success at the 28th day. Overall, a significant high treatment success of 92.9% (95% CI: 89.1-96.6), p<0.001, I2=98.39% was noticed. However, treatment success was higher in P. falciparum malaria patients treated with artemether-lumefantrine than chloroquine for P. vivax patients [98.1% (97.0-99.2), p<0.001, I2=72.55 versus 94.7% (92.6-96.2), p<0.001, I2=53.62%]. Seven studies reported the adverse drug reactions to antimalarial treatment; of 822 participants, 344 of them were exposed to adverse drug reactions with a pooled event rate of 39.8% (14.1-65.5), p=0.002. CONCLUSIONS: On the basis of this review, antimalarial treatment success was high (92.9%) and standard regimens showed good efficacy against P. falciparum (98.1%) and P. vivax (94.7%) infections in Ethiopia, but associated with high rates of adverse drug reactions. However, these ADRs were not serious enough to discontinue antimalarial treatment. Our results suggest that the current antimalarial medications are effective and safe, however, greater priority should be placed on the discovery of newer antimalarial drugs to achieve successful outcomes as resistance seems inevitable since cases of antimalarial drug resistance have been reported from other areas of the world.

PIN93: HOSPITAL PHARMACY MANAGEMENT OF ACCESS TO DIRECT-ACTING ANTIVIRALS FOR THE TREATMENT OF HEPATITIS C AND ITS CONTRIBUTION TO PUBLIC HEALTH AND ECONOMIC EFFICIENCY – A SINGLE-CENTER EXPERIENCE


OBJECTIVES: In February 2015 the Portuguese Ministry of Health (PMH) initiated a new policy granting universal access to direct-acting antivirals (DAA) for the treatment of hepatitis C virus (HCV) infection. The objective of this study was to project the long-term impact of this policy for all patients with authorized treatment at the Centro Hospitalar e Universitário de Coimbra until May 2017. METHODS: Age, gender, metavir, genotype, previous treatment experience and requested DAA were registered for all patients with authorized treatment between February 2015 and May 2017. A discrete-time Markov model was used to estimate the lifetime impact of the new policy on mortality, morbidity and related costs. Mortality endpoints considered were life expectancy and liver-related death. Morbidity was expressed in terms of cirrhosis cases, hepatocellular carcinoma (HCC) and liver transplant (LT). Costs were measured as direct medical costs to the Portuguese NHS. RESULTS: A total of 850 patients were included in this study. Average age of the population was 50.4 years, 76.8% were male. The majority of patients had genotype 1 (66.7%) and were treatment naïve (65.4%) and metavir F1 (35.3%). Ledipasvir/sofosbuvir as authorized treatment in 73.8% of the cases. On average, treatment with DAA is expected to increase life expectancy by 6.7 years/patient. We
estimate that in this population liver-related death can decrease by 305. Furthermore we anticipated that 472 cases of cirrhosis, 170 cases of HCC and 30 LT could be averted in the long run. This would result into a total saving in direct medical costs of 24.3 million euros, 6.1 million of which due to HCC and 6.0 million due to LT. CONCLUSIONS: Universal access to new generation direct-acting antivirals may contribute to unprecedented gains in patients outcomes and substantial reduce the long term costs for the Portuguese NHS.

PIN94: UNDERSTANDING THE BARRIERS TO VACCINE ACCESS AND UPTAKE IN EU5: ROTAVIRUS VACCINATION CASE STUDY

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OBJECTIVES: The aim of this study is to review existing barriers to access for rotavirus vaccines (RV) in 5 European countries (EUS): Spain, Italy, France, Germany and the United Kingdom (UK). METHODS: A structured literature search using online electronic databases was conducted to identify primary literature and national HTA recommendations guidelines. The search strategy was based on terms; rotavirus, economics and the European 5 countries: France, Germany, Italy Spain and the UK. Relevant literature published between 2007 and 2017 were included in the review. RESULTS: Eight publications were identified and included in the review. Three key factors were identified as existing barriers to vaccine access. Firstly, national policy recommendations around how rotavirus vaccines were introduced. In Italy, rotavirus is not considered an essential vaccine and recommendations are therefore made at a regional level, resulting in variance in vaccine uptake and coverage between regions. Secondly, the national system of vaccine administration: centralized systems (such as the UK) are expected to see greater access and uptake. However, such systems may also restrict access due to the reliance on the policy-makers' perception of disease burden. Finally, the occurrence of vaccine hesitancy (acceptability or refusal): lack of public awareness and insufficient communication on the benefits of vaccines can lead to refusals and negative perceptions from the general public. One study which conducts a confidence in immunisation survey, 41% of the French respondents considered vaccines unsafe compared to 12% of respondents in other nations. CONCLUSIONS: Variations in vaccine recommendation systems along with potentially false perceptions on their necessity from the general public and policy makers can constitute as barriers to access and uptake of vaccines in EU5. Vaccine coverage across the EU5 may be improved by common guidelines and schedules for vaccination between countries, along with greater public engagement and improved education on vaccination benefits.

PIN95: A RETROSPECTIVE ANALYSIS OF THE ROLE OF (ECONOMIC) EVIDENCE IN DECISION MAKING: THE INTRODUCTION OF HPV VACCINATION IN THE NETHERLANDS

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OBJECTIVES: To retrospectively investigate the decision-making process around the introduction of HPV vaccination in the Netherlands and to identify which actors were involved and what role (economic) evidence played in this process. METHODS: Using the introduction of HPV vaccination since 2006 in the Netherlands as a case study, a retrospective analysis based on existing policy documents was performed. Evidence used or asked for by various stakeholders in different stages of the policy process (prioritization, development and implementation) was identified. In total, 36 documents were analyzed and synthesized, for the period between August 2006 (when a first question by the parliament was raised on the possibility of introducing HPV vaccination) and September 2009 (when HPV vaccination was planned to be introduced in the national vaccination program). Documents were analyzed in NVIVO, using directed content analysis based on the decision-making framework of Burchett et all (2012). RESULTS: Our analysis demonstrates that a wide variety of stakeholders are involved in the process with a key role for the Minister of Health, the parliament and the Health Council. In 90% of the documents, the decision-making process itself was discussed, in 72% financial or economic issues were stipulated and in 64% evidence on vaccine characteristics were discussed. Economic evidence from economic evaluations was discussed most (50%) followed by evidence on funding sources for HPV vaccination (28%) and incremental costs related to the implementation of the vaccination in the Netherlands (16%). CONCLUSIONS: It can be concluded that next to the decision-making process itself economic evidence played an important role during the decision-making process on the introduction of HPV-vaccination, in particular the use of evidence resulting from economic evaluations.


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OBJECTIVES: The objective of this study was to compare the regulatory actions and characteristics of HIV ARV drugs approved by the FDA and the EMA in the period 1987-2015. METHODS: We obtained data from the FDA and EMA websites. We performed a descriptive analysis for all variables included in the analysis. We used Mann-Whitney U and chi-square tests. We set the statistical significance level at 0.05 a priori. RESULTS: The FDA granted orphan designation to 2 drugs (5.7%). There were 9 (25.7%) HIV ARV drugs with more strengths available in the US. There were 2 (5.7%) ARV drugs with more dosage forms in the EU, 3 (8.5%) with more dosage forms in the US, and 1 drug (3.5%) with different dosage forms in the EMA and the FDA. Differences in posology were found in 3 (8.5%) ARV drugs. The EMA approved more indications for 2 (5.7%) drugs. There were 16 (45.7%) ARV drugs with differences in age indications. There were 13 (37.2%) drugs indicated for adult patients only in the US. However, 15 (42.9%) were indicated for adult patients only in the EU. There were 21 (57.1%) ARV HIV drugs with the same boxed warnings in both agencies; 9 (25.7%) with boxed warnings in the FDA but not in the EMA; and 1 (3.5%) with boxed warning in the EMA but not in the FDA. CONCLUSIONS: This study found significant differences in FDA and EMA approvals and the characteristics of the HIV ARV drugs approved by both agencies. The majority of the HIV ARV drugs were first submitted to and approved by the FDA. The FDA had a significantly shorter review time (p<0.0001) than the EMA. The ARV drugs approved in the US and the EU have some differences in route, dosage form, strength, boxed warnings, therapeutic indications, and posology.

PIN97: DETERMINANTS OF HERPES ZOSTER VACCINE ACCEPTABILITY AMONG OLDER PEOPLE IN THE UK

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OBJECTIVES: Barriers to adult immunisation persist as rates for Herpes Zoster (HZ) vaccine among eligible individuals in the UK have decreased. The aim was to identify factors associated with the uptake of HZ vaccination and to gauge their importance to vaccination uptake. METHODS: In this non-interventional multicentre, primary healthcare-based study, cases and controls were individuals who were the last cohort (79 years old) eligible for the HZ vaccination campaign in 2014-2015 eligible for the HZ vaccination campaign in 2014-2015 to eradicate the risk of influencing future HZ vaccination decisions. Data were collected using an anonymised self-administered questionnaire completed by responders. The Health Belief Model (HBM) provided the theoretical framework for the development of the questionnaire, which included demographic and socio-economic characteristics, health status, knowledge, influences, experiences and attitudes to HZ and the HZ vaccination. Multivariable logistic regression was used to identify factors associated with participants’ decision to receive the HZ vaccine. RESULTS: Among the 2,530 eligible individuals contacted, 536 (21.2%) responded to the questionnaire. HZ vaccination uptake was 64.2%. Overall, 44% of variance in behaviour was accounted for by the model including all factors, 32% by the model using HBM constructs by scale, and only 14% was accounted for by demographics and socio-economics. Perceived barrier (OR=0.7, p-value=0.034), perceived control of disease (OR=0.7, p-value=0.004), and HZ history (OR=0.2, p-value<.0001) significantly decreased likelihood of vaccination. CONCLUSIONS: Longitudinally, HZ vaccination acceptability would be improved by efficient vaccination campaigns and communication interventions with in-depth understanding of psychosocial factors that drive or hinder vaccination.

PIN98: PATTERN OF ANTI-INFECTIVE DRUGS USE IN A TERTIARY HEALTHCARE FACILITY IN NIGERIA

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OBJECTIVES: Given the increasing need to promote rational use of drugs, the World Health Organization (WHO) encourages regular drug utilization evaluation (DUE) in healthcare facilities to provide insight into patterns, quality, and determinants of drug use. This study profiled anti-infectives to understand their extent of use. METHODS: The study was a cross sectional retrospective analysis of patients prescription records from June to December 2016, based on WHO’s recommended drug use indicators. Data were analyzed using descriptive statistics. RESULTS: Of the 624.0 patients prescription records studied, 329.0 (55.0%) were females. The mean age was 42.0±4.6 years while the mean number of drugs per prescription was 2.94±0.6 against the reference value of 1.6. Out of 1833.0 drugs prescribed, 646.0 (32.2%) were anti-infectives. The number of drugs prescribed by generic was 975.0 (53.2%) against the 100.0% benchmark recommended by WHO. This comprised of antibacterial drugs 475.0 (73.5%) against a standard reference of 20.0 – 26.8, antivirals 4.0 (0.6%), antifungal drugs 16 (2.5%), antiprotozoal 120.0 (18.6%), and anthelmintics 31.0 (4.8%). Of the anti-infectives prescribed, quinolones were the most prescribed 213.0 (44.8%) followed by amoxicillin+Clavulanic acid 52.0 (11.0%). The most prescribed quinolone was ciprofloxacin 146.0 (30.7%) followed by ofloxacin 65.0 (13.7%). The most prescribed antiprotozoal agent was metronidazole 91.0 (75.8%). The
anti-infectives prescribed as injectables were 188.0 (29.1%). CONCLUSIONS: The high use of anti-infectives was an indication of high prevalence of infections and irrational use of drugs. Other indications for irrationality in drug use include poor generic prescribing, higher number of drugs per prescription, and high proportion of injectables. They predispose patients to high cost of medicines and non-adherence considering catastrophic spending in developing countries driven by rise in pharmaceutical expenditures. This baseline study has provided fundamental data for further studies in promoting the rational use of anti-infectives in Nigeria.

PIN99: A RETROSPECTIVE STUDY ON THE ANTIRETROVIRAL DRUG DISPENSING AND ADHERENCE OF THE HUNGARIAN HIV INFECTED POPULATION

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BACKGROUND: The HEARTS (HIV Epidemiology and AntiRetroviral Treatment Study) is a non-interventional retrospective claims database study of patients receiving healthcare services for their HIV infection between 2005 and 2015 in Hungary (n=1772), who were identified from the National Health Insurance Fund Administration databases based on multiple criteria including International Classification of Diseases and International Classification of Procedures in Medicine codes, and medication purchase data. The first results about the epidemiology of HIV patients was published earlier. During the entire period, a total of 1,496 (84.4%) of the prevalent patients received antiretroviral (ARV) treatment. OBJECTIVES: In this part of the study, our aim was to investigate the changes of ARV drug dispensing over time at active substance and drug class level, to determine the therapeutic adherence of patients and to examine the persistence of active substances as third agents of combination therapies, especially darunavir (DRV). METHODS: The method of the ARV drug utilization analysis is based on days of treatment estimation. RESULTS: Between 2005 and 2015 the most commonly dispensed protease inhibitors (PI) were ritonavir (alone or as pharmacokinetic booster) (35%) and DRV (28%), whilst the patients most often used lamivudine (62%), tenofovir (56%) and zidovudin+lamivudine (41%) as their dual nucleoside reverse transcriptase inhibitor (NRTI) backbone. The adherence of the treated prevalent population was fair (≥80%) as defined by the PDC (proportion of days covered) ratio. Considering the third agent consumption of the adherent patient population, amongst PI’s persistence of DRV was the highest. Assuming 60-day gaps, the 1-year and 5-year persistence was 87% and 51%, respectively, and the median was 1851 days. CONCLUSIONS: Due to the development of ARV therapies and understanding their mechanism of action and keeping in mind the perspective of patients, we conclude that the tolerability and simplification of treatment administration could be major aspects of treatment success in real-world settings.

PIN100: PRESCRIBING PATTERN OF ANTIBIOTICS FOR ACINETOBACTER INFECTION IN A TERTIARY CARE HOSPITAL

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OBJECTIVES: The objective of this study was to assess the resistance pattern and drug utilization pattern of a patient undergoing treatment for acinetobacter infection. METHODS: A cross sectional, observational, retrospective study, done over a period of 6 months. The data collected was analysed to understand the pattern with respect to patient demographics, prescription patterns, comorbidities as risk factors to infection, and resistance patterns. RESULTS: The study showed that male patients were at a greater risk of A.baumanii infections within age distribution of 41-60 years and 61-80 years. Bacteria was found to be resistant to almost all categories of drugs. The length of stay of a patient with A.baumanni infection was 23.51±27.97 days. Empirical antibiotic therapy was prescribed to most patients and drugs ticlocycline and cefixime were used in 47(97.9%) patients. The least prescribed antibiotic was Piperacillin – Tazobactam in 25 (42.9%) patients. Cefoperazone-sulbactam was also found to be active against the bacterium. CONCLUSIONS: This study concluded that male patients were at a greater risk of A.baumanii infections. Ticlocycline and Cefixime were the most prominently used antibiotics. The strain in this study was resistant to almost all cephalosporins except Cefoperazone-Sulbactam which had activity in 57.14% of the samples tested.

PIN101: ECONOMIC BURDEN OF VACCINE PREVENTABLE INFECTIOUS DISEASES AMONG ELDERLY PATIENTS IN DUTCH HOSPITALS

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OBJECTIVES: Our immune system becomes less responsive to infections with age and therefore an increase in transmissible diseases is observed among elderly people aged 60+. These infections may trigger the manifestation of a real underlying chronic disease such as cardio-vascular or respiratory that may often lead to hospitalization of long duration with a high cost. Our study aimed to investigate the cost of primary and secondary diagnosis of vaccine preventable diseases causing hospital admissions in patients of 60 years and older in the Netherlands, to understand the magnitude of potential cost savings. METHODS: The Dutch Hospital Dataset was used to retrieve the number of diagnoses and hospitalisations over the most updated period (2009-2014). Expenditures were derived from governmental websites, and costs were based on references prices commonly used in the Netherlands. RESULTS: Vaccine-preventable infections account for 4% of total hospital cost for people aged 60+ years. Primary diagnosis accounts for 40%, however, 60% is through secondary diagnosis. A high increase in hospitalizations is observed over time among secondary diagnoses (+120%), coupled to an increase in number of bed days (+32%), while the average hospital stay dramatically decreases (-44%). This could argue that care is becoming either more effective, or less extensive. The number of beds available is slightly reduced as well (-4%), which is alarming as the demographic projections of the elderly population show increases of 6% in the age category of 60+ years during the coming decennia, potentially leading to a higher stress of the healthcare infrastructure, and a subsequent increase of costs. CONCLUSIONS: The number of hospitalizations and associated costs of primary and secondary diagnosis of vaccine preventable diseases are increasing, and could potentially increase more due to the impending ‘double ageing’. Decision makers should consider using already available vaccines to prevent some of these costs.

PIN102: HEALTHCARE RESOURCE USE AND ECONOMIC BURDEN ATTRIBUTABLE TO RESPIRATORY SYNCYTIAL VIRUS IN THE UNITED STATES

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OBJECTIVES: Despite several studies that have estimated economic impact of Respiratory Syncytial Virus (RSV), limited data are available on healthcare costs attributable to RSV. The aim of this study was to quantity age specific RSV related costs on the US healthcare system. METHODS: This retrospective case-control study identified RSV patients in the Truven Health MarketScan® Commercial Claims and Encounters database from August 31th 2012 to August 1st 2013, using the primary diagnosis for RSV specific ICD 9 codes (0.79.6, 466.11 or 480.1). RSV patients (cases) and non-RSV patients (controls) were matched 1:1 for age, gender, region, healthcare plan and index date. Stratified analyses were conducted by age groups. RSV related costs were assessed based on incremental differences in resource use and costs between cases and controls. RESULTS: The unadjusted average costs attributable to RSV were higher in elderly than in adults and children: elderly: US$15,050 to $26,151 and children & adults: $1,727$ to $8,796. Among children, unadjusted costs attributable to RSV were higher in children aged 5-17 years ($8,796). RSV patients had a higher healthcare resource use (hospital stays, ER/UC visits, ambulatory visits and outpatient visits) than controls (non-RSV patients) in all age groups (all P<0.01), particularly in the elderly age groups (0.4 to 0.5 more ER/UC visits, 0.7 to 2.7 more ambulatory visits, 12.1 to 18.6 more outpatient visits and 9.5 to 14.6 more prescriptions than elderly in the control groups). CONCLUSIONS: Our findings showed a substantial annual healthcare costs and resource use due to RSV in the US. These data can be used in cost effective analyses and are useful for policy maker to guide future RSV vaccination programs and other effective interventions and therapies.

PIN103: IMPACT OF SEASONAL INFECTIONS ON OVERCROWDING IN A PAEDIATRIC DEPARTMENT OF A FRENCH HOSPITAL IN MARSEILLE: A RETROSPECTIVE ANALYSIS

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OBJECTIVES: The objective of this study was to assess the impact of seasonal infections on overcrowding in one university paediatric department of a French hospital. METHODS: This study was a retrospective analysis using electronic records provided by a French hospital (Hôpital Nord, Marseille). All admissions of children aged less than 5 years in the paediatric department of the hospital occurring between 1 January 2012 and 31 December 2016 were analysed. The paediatric department was considered overcrowded in a given week if the bed occupancy rate exceeded 85%, threshold derived from the literature. Children admitted for bronchiolitis or gastro-enteritis were identified using ICD-10 codes selected based on the department coding practice. Proportions of cases with bronchiolitis and gastro-enteritis admitted in the department were calculated during overcrowding periods. RESULTS: The paediatric department recorded 1021 to 1321 admissions per year, 30% to 50% of which were cases of gastroenteritis (8.3% [2012] to 17.2% [2016]) or bronchiolitis (22.3% [2013] to 32.7% [2016]). Over the
5 years, there were 20 weeks of overcrowding (1 to 7 weeks per year), 18 of which occurred during periods from October to April (predominantly December and January). Bronchiolitis and gastroenteritis were associated with 52.7% and 10.6% of admissions respectively during overcrowding periods. During overcrowding weeks, the proportion of bronchiolitis and gastroenteritis patients transferred to the paediatric surgery department increased from 4.8% to 16.0%. **CONCLUSIONS:** During winter, the paediatric department of the studied hospital handled a large influx of patients with bronchiolitis and gastro-enteritis, leading to overcrowding situations that can cause disruption and degradation of the quality of care.

**PIN104: BUDGET IMPACT ANALYSIS OF TREATMENTS FOR HEPATITIS C VIRUS: WHAT'S NEW?**

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**OBJECTIVES:** While novel drugs (DAAs) for Hepatitis C Virus (HCV) care are more effective than interferon-based therapies used in the past, they represent a significant economic absorption for healthcare providers, particularly within the Italian setting, characterised by continuous spending review actions. The present study aimed at estimating the budget impact of the recently introduced treatments (Velpatasvir, a pan-genotypic regimen, and Zepatier), for a more accurate healthcare planning and decision making in the HCV setting. **METHODS:** A three-year budget impact analysis (BIA) was developed, taking into consideration the National Healthcare Service point of view, considering the overall HCV and HIV/HCV population. Patients' previous medical history, degree of liver fibrosis, genotypes, achievement of sustained virological response (SVR) and direct healthcare total costs were the model input variables. Data were collected from scientific evidence, regional and national legislation, administrative information and consumption data of two Hospitals (Valle Olona and Fatebenefratelli Sacco), and expert opinions. **RESULTS:** From a national perspective (population at point of care= 393,102), on the basis of current reimbursement criteria (F3-F4), at the 36 month-horizon, the introduction of the novel therapies could lead economic savings (-7%). Enlarging the reimbursement criteria to F0-F2, at the first year, patients achieving a SVR condition increase (+25%), although an initial investment is necessary (that mean an increase of costs of 0.33%), recovered within 24 months, generating economic benefits for the NHS (-16% in second year and -20% in third year). **CONCLUSIONS:** The proposed healthcare planning tool are useful in order to provide clinicians and policy makers a consistent economic forecast to allocate HCV patients. An investment in new HCV drugs would reduce the national healthcare expenditure, especially concentrating all the eligible patients (including F0-F2 individuals, with the consequent avoidance of Interferon-based combinations), within the same drug regimen could be considered a cost-effective strategy.

**PIN105: ADAPTING THE UNITED STATES’ ANTIMICROBIAL STEWARDSHIP PROGRAMME GUIDELINES TO BUILD AN ECONOMIC EVALUATION FRAMEWORK FOR CHINESE HOSPITALS**

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**OBJECTIVES:** Antimicrobial stewardship programmes (AmSPs) are widely reported to support appropriate antibiotic use and help control antibiotic resistance. However, the value of AmSPs has not been fully studied and there is a lack of established AmSP value evaluation framework in China. This study aimed to develop a China-specific AmSP evaluation framework by referring to the existing U.S. guidelines and supplementing with the unique characteristics of Chinese AmSPs. **METHODS:** Experts from geographically representative Chinese hospitals were interviewed face-to-face between August-October 2016 using the questionnaire developed based on the U.S. Center for Disease Control and Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection guidelines. An evaluation model framework adapted to the Chinese healthcare system was developed based on the US guidelines and survey responses. **RESULTS:** The interviewed experts were infectious disease specialists (n=6) or hospital/pharmacy directors (n=3) from 9 tertiary/Grade A hospitals with active AmSPs (average implementing time=3 years) in Beijing, Shanghai, Guangzhou, and Chengdu. Most components from the U.S. guidelines were incorporated into the Chinese framework with 3 main categories: resource needs (personnel, equipment), related clinical outcomes (antimicrobial resistant rate, mortality), and health economic impact (length of stay, defined daily dose). Main differences from U.S. include: 1) limited/no pharmacist involvement in routine participation in intravenous-to-oral switch programs, antibiotic dose modifications/discontinuations; 2) inclusion of more economic outcome endpoints of AmSPs (e.g., ICU use, reduced intravenous days due to early switch, hospital onset infection rate, and restricted antimicrobial drugs use); and 3) taking a hospital business case perspective by adding a return-on-investment calculation. **CONCLUSIONS:** This study is the first step to develop a comprehensive AmSP evaluation framework for Chinese hospitals. It will help Chinese hospital decision-makers measure the costs and benefits associated with their specific AmSP and gain a better understanding of their value, thus creating an enhanced engagement in implementing AmSPs.
PIN106: INFLUENZA VACCINATION AMONG PREGNANT WOMEN: EXPLORATORY ANALYSIS FROM THE 2012-2015 NATIONAL HEALTH INTERVIEW SURVEY

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OBJECTIVES: The issue of suboptimal flu vaccine coverage during pregnancy has been previously addressed by studies conducted with internet panel survey and several active surveillance systems. However, most of them suffered from insufficient statistical comparison due to lacking complex probabilistic sampling design. Our study aimed to explore the determinants and coverage of influenza vaccination among pregnant women using a national representative sample of the United States. METHODS: This study was conducted with the 2012-2015 National Health Interview Survey (NHIS). The Andersen Behavioral Model of Health Services Use was applied as the conceptual framework to explore potential factors that may influence the flu vaccination rate. A series of individual determinants, categorized into predisposing, enabling and need factors, were compared using logistic regressions between women who received flu shot before/during pregnancy and those who did not. All analyses were adjusted for complex survey designs and sample weights using SAS 9.4 (SAS Institute, Cary NC). RESULTS: Among an estimated 4.8 million pregnant women, an average of 35% women received influenza vaccination before/during pregnancy. The odds of receiving a flu shot before/during pregnancy was lower among non-Caucasian ethnicity groups (odds ratio (OR) [95% confidence interval (CI)], African American, 0.777 [0.550-1.098]; others, 0.636 [0.429-0.942]), women without usual source of health care (OR, 0.647 [0.442-0.945]), and women with heavier alcohol consumption (OR, 0.601 [0.403-0.894]). In contrast, higher education and family income were positively correlated with influenza vaccination, with an OR of 1.763, [1.290-2.409] (>= bachelor’s degree versus <= high school) and 2.038 [1.368-3.035] (ratio of family income to the poverty threshold category >4 versus <1), respectively. CONCLUSIONS: No usual source of health care, poverty, lower education level and alcohol drinking behavior appeared to be negatively associated with influenza vaccination during pregnancy. Policy makers may consider developing interventions to improve the vaccination rate among these subgroups.

PIN107: KNOWLEDGE OF LEPTOSPIROSIS AMONG MALAYSIAN WET MARKET SELLERS

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OBJECTIVES: The study aimed to assess the knowledge level of leptospirosis among Malaysian wet market sellers and investigated the differences, association, and predictors of independent variables with measured knowledge. METHODS: In this cross-sectional study, post ethics approval, wet market sellers (≥ 18 years old) in Klang and Shah Alam, Selangor, Malaysia, were given reliable and validated self-administered questionnaires determined by Rasch analysis that consisted of socio-demographic, medical and source of knowledge (n = 11 items), and knowledge (n = 26 items) of leptospirosis covering causes, signs, symptoms, complications, treatment, prevention and risk factors of leptospirosis (“correct”, “incorrect” or “don’t know” answers scored “2”, “0” and “1” mark(s), respectively). The collected data from January until March 2015 were statistically analysed using SPSS version 20. RESULTS: A total of 140 wet market sellers were recruited in this study. The mean (SD) age of the respondents was 36.37 years old. The mean (SD) number of years working at wet market was 8.72 (6.94) years. Majority of the respondents had moderate knowledge with percentage score of 51.4 (moderate: score < 72 %). There were statistical significant differences in the mean scores of the knowledge of leptospirosis with gender, marital status, ethnicity, highest completed level of education, type of occupation, and whether they had ever heard of leptospirosis (independent samples t-test and ANOVA). There were significant associations between knowledge and highest completed level of education, occupation, and ever heard of leptospirosis (chi-square test for independence). Two predictors that made statistically significant contribution to knowledge score were the highest completed level of education, and ever heard of leptospirosis that had a negative relationship with knowledge score while the other had positive relationship (multiple linear regressions). CONCLUSIONS: Malaysian wet market sellers possessed moderate knowledge level of leptospirosis, with significant differences and relationship with independent study variables, hence warrant leptospirosis education programme.

PIN108: MATERNAL SCREENING AND TREATMENT FOR GROUP B STREPTOCOCCUS (GBS) ARE ASSOCIATED WITH NON-ADHERENCE TO GUIDELINES, FALSE-NEGATIVE RESULTS AND HIGH MANAGEMENT COSTS IN THE UNITED KINGDOM, ITALY, FRANCE, SPAIN AND GERMANY

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OBJECTIVES: Group B streptococcus (GBS) rectovaginal carriage during late pregnancy and birth is associated with neonatal GBS disease which is life threatening and survivors may have long lasting sequelae. GBS screening of pregnant women and subsequent intrapartum antibiotic prophylaxis (IAP) has proved effective at reducing GBS early onset disease (EOD) in areas where it is universally applied. Despite the recommendation of these preventative measures, the incidence of neonatal GBS, particularly late-onset disease (LOD), is increasing. We therefore conducted a literature review to assess the adherence to guidelines and treatment, which is concerning given the costs associated with management. An alternative strategy, such as vaccination, could reduce GBS incidence and associated costs.

RESULTS: Maternal GBS screening and IAP remains inadequate across Europe in both non-adherence to guidelines and treatment, which is concerning given the costs associated with management. We also analyzed a vaccination strategy for high risk children. RESULTS: Similar to the first assessment in 2008, universal vaccination of rotavirus again seems cost-effective from the societal perspective, resulting in an incremental cost effectiveness ratio of €18,672 per QALY. Vaccinating a birth cohort of 170,510 infants results in reductions of 30,891 rotavirus episodes, of which 21,434 are mild, 5,785 moderate and 3,671 severe. A total of 4 lives are saved. In addition, targeted vaccination was deemed dominant over the no vaccination strategy. We conclude that universal and targeted vaccination are both effective and cost-effective, with herd immunity effects seems justified as relevant reductions in disease burden. RESULTS: Adherence to screening guidelines is high in France (89–96%) and low in Germany (23%). Assessment of whether the mothers of GBS positive infants had been screened during pregnancy revealed that in France and Italy 9% and 20% were unscreened. In the UK, IAP is provided on a risk factor basis yet mothers without risk factors accounted for 33% of GBS-positive neonates. Many women in these countries are eligible for IAP but do not receive IAP (range 11% [Germany] to 36% [Italy]). Non-adherence to screening guidelines may be due to increased costs when screening is not reimbursed, and non-adherence to treatment guidelines due to failure to document GBS-positive status, caesarean births and antibiotic resistance. Neonatal GBS is associated with a high economic and social burden, with management of LOD neonates costing over three times as much as healthy neonates. CONCLUSIONS: Maternal GBS screening and IAP remains inadequate across Europe in both non-adherence to guidelines and treatment, which is concerning given the costs associated with management. An alternative strategy, such as vaccination, could reduce GBS incidence and associated costs.

PIN109: DECIDING ON UNIVERSAL ROTAVIRUS VACCINATION IN THE NETHERLANDS - AGAIN

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OBJECTIVES: Since 2006 vaccines against rotavirus-induced gastroenteritis are available in Europe. Many European countries offer these vaccines to their infant population. In the Netherlands, the implementation of rotavirus (RV) vaccination is still under discussion due to various reasons and is currently under consideration in the Chamber for Vaccines Assessments “BeoordelingsKamer Vaccins” (BKV). The BKV combines the assessments of both the Dutch Health Council and Care Institute. For the BKV, cost-effectiveness presents one aspect of consideration. This study aimed to provide a cost-effectiveness analysis of the pentavalent vaccine based on the newest incidence data, which seemed lower than assumed. METHODS: An age-structured, discrete time-event, deterministic cohort model has been developed to evaluate the cost-effectiveness of adding RotaTeq® to the Dutch National Immunization Program. Model inputs were based on a previously published and generally accepted model of rotavirus vaccination. We also analyzed a vaccination strategy for high-risk children. RESULTS: Similar to the first assessment in 2008, universal vaccination of rotavirus again seems cost-effective from the societal perspective, resulting in an incremental cost effectiveness ratio of €18,672 per QALY. Vaccinating a birth cohort of 170,510 infants results in reductions of 30,891 rotavirus episodes, of which 21,434 are mild, 5,785 moderate and 3,671 severe. A total of 4 lives are saved. In addition, targeted vaccination was deemed dominant over the no vaccination strategy. The inclusion of at least moderate herd immunity effects seems justified as relevant reductions in disease in non-vaccinated populations have been observed in several countries were rotavirus vaccination has been introduced. CONCLUSIONS: We conclude that universal and targeted vaccination are both effective and cost-effective strategies for reducing rotavirus incidence in the Netherlands within the context of a national program.

PIN110: DIFFICULTIES IN VACCINE INTRODUCTION IN A LARGE-AREA COUNTRY: MENINGOCOCCAL VACCINATION IN RUSSIA

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OBJECTIVES: Country experts’ opinions have a huge impact on the identification of the strategy of the health economics analysis, which is crucial before the introduction of any intervention. The determination of a unique strategy seems to be very challenging in a large area country where the epidemiology differs a lot and the disease does not have a huge burden but leads to the severe sequelae. The objective of the study is to determine the importance of the introduction of the vaccination against meningococcal infection into the National Immunization Program (NIP) in Russia. METHODS: 18 regional vaccination experts from 14 Russian areas were interviewed. The on-line survey created in google forms was used to obtain information. The experts were asked about the importance of the vaccination against meningococcal infection in their region by ranking it from 1 (not needed) to 5 (most needed), the type of the vaccine to be used and the optimal age group for introduction. RESULTS: The opinions of
18 experts on the importance of the meningococcal vaccination were diverse and distributed between not needed (3 experts) to most needed (2 experts). More than a half of experts (55.6%) opted for the introduction of two vaccines (conjugated-ACWY, recombinant MenB vaccine) simultaneously. Although the majority believes in 10-13 years of age (55.6%) as the most suitable time period for immunization, others consider that the vaccination should be implemented for younger or older children first. CONCLUSIONS: There is no unanimous opinion on the universal strategy of meningococcal vaccination implementation into the Russian NIP. A few regions with high demand should be selected for a pilot project where health economics analysis should be conducted and further the vaccine introduced prior to the national implementation.

PIN111: HEPATOPROTective EFFECT OF HERBAL REMEDY WITH ANti-TUBERCULOSIS TREATMENT

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S.D. Asfendiyarov Kazakh National Medical University, Almaty, Republic of Kazakhstan Introduction: Tuberculosis is one of the leading causes of death among infectious diseases in developing and undeveloped countries. According to the WHO Western Pacific Region fact sheet on tuberculosis. Hepatotoxicity, a common adverse effect of antituberculosis drugs, varies from asymptomatic elevation of liver enzymes to fulminant hepatic failure. Methods: The study protocol was approved by the Ethics Committee on Human Rights related research. Results. From the total of 55 patients, there no significant differences in the distribution of the demographic characteristics. Antituberculosis drug-induced hepatotoxicity (ATDH) was seen in 17 (18.8%) out of 90 patients. Average age of the ATDH case was 35.65 ± 10.8 (CL 95% 18-81) sex ratio was 22.5% in men, 16% in women. During pre and post-treatment liver biochemical analyzes criteria such as AST, ALT, total bilirubin, and protein were not statistical significant between groups which are treated with Silymarin. However, in control group had a statistically significant difference total bilirubin and protein between post- and post-treatment liver biochemical analyzes criteria such as AST, ALT. Anti-tuberculosis drugs are used in combination, except in latent tuberculosis or chemoprophylaxis. The rate of hepatotoxicity is much higher in developing countries like India (8%–30%) compared to that in advanced countries. Therefore, we selected patients who have tuberculosis to study the hepatotoxic effect of antituberculosis drugs and hepatoprotective action of Silymarin. The serum ALT, AST of the control group (group I) and the Silymarin group (group II, III) show significant difference when compared with baseline values. This showed that Silymarin has significant desired actions. Conclusions Silymarin reduced the incidence of antiTB-DILI. The benefit of Silymarin may be explained from superoxide dismutase restoration. Larger clinical trials are required to confirm the result of our small study. References 1. WHO. Global tuberculosis report 2014

PIN112: VALUE OF TREATING ALL LIVER FIBROSIS STAGES TO REACH ELIMINATION OF DIAGNOSED CHRONIC HEPATITIS C: A MODELLING APPROACH IN FRANCE

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OBJECTIVES: With the increased efficacy and tolerability of all-or oral direct-acting antivirals (DAAs) against hepatitis C virus (HCV) infection, there is a growing will to treat all patients. Our objective is to determine the optimal and budget-feasible treatment path towards diagnosed HCV elimination in France. METHODS: Using a sequential multi-cohort model, the diagnosed HCV population in France, 68% of the 150,000 prevalent cases, was projected over a 20-year horizon from the payer perspective. Treatment effectiveness was based on clinical trial data of second-generation pangenotypic DAAs. Treatment course was assumed to cost 30,000€. A declining treatment budget was considered from 600M€ in 2017 to 500M€ in 2018 and 400M€ beyond. Two treatment scenarios were compared: the recently adopted policy in France of generalized treatment which treats proportionally all fibrosis stages, and a top-down strategy which treats the most serious fibrosis stages first and the less serious stages last according to the budget constraint. RESULTS: Our model-based analysis demonstrates that the elimination of diagnosed HCV is budget-feasible and could be reached in 2024 with the current universal treatment policy: 103,927 treated patients, 776 liver transplant, 4,445 liver-related deaths and 787,895 QALYs for a global budget of 3,7B€ over the 20 years. However, it is dominated by the top-down strategy, resulting in 4,661 less patients treated, 1,718 more liver-related deaths, 18,935 QALY lost, and 434M€ more healthcare spending. The undiagnosed population in 2024 is still of 45,964 patients. CONCLUSIONS: Widespread access to DAAs is an important milestone to reach WHO elimination goal in 2030 but the more severe patients still need to be prioritized from public health and efficiency perspectives. Full elimination of HCV requires increased investments for screening and treatment, and greater awareness and urgency to treat.
PIN113: EVALUATION OF MEASLES VACCINATION COVERAGE IN AUSTRIA

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OBJECTIVES: Monitoring the measles vaccination coverage is important towards the WHO goal to eradicate measles until 2020. In Austria, small outbreaks still occur occasionally. The aim is a coverage of 95% with two doses for all adults and children of age 2 and above. METHODS: As a basis, we used an agent-based model of the Austrian population that simulates from 1998 until 2015, where each person is represented by an agent. The model includes ageing, births, deaths, emigration, and immigration, and is based on data from Statistics Austria and Eurostat. Vaccination data from different sources since the introduction of the national immunization program in 1998 were combined: the administered vaccinations including the age of children, the delivered doses without age-specific information, and sales data from the private market. The resulting vaccination numbers were distributed among the model population according to the recommended immunization scheme in each year. The initial coverage of age groups born before 1998 is estimated based on the 1998 vaccination data. RESULTS: The model showed reliable results for children born 1997 and later. In 2015, more than 95% of 6 year olds are vaccinated once. However, 2-5 years olds only have a coverage of 92%. The coverage for two doses was 85% and 82% respectively. Additionally, it turns out that a third of young adults born before 1997 are missing a second dose. CONCLUSIONS: The model is able to give insights into the situation on measles coverage in Austria and to inform decision makers about the most important issues. Coverage for small children can be presented in a high quality while coverage for teenagers and young adults underlie a greater uncertainty due to immigrants with unknown vaccination status and vaccinations of persons with an undocumented age.

PIN114: INTER-STATE VARIABILITY OF ADULT VACCINATION COVERAGE IN THE UNITED STATES: CAN WE EXPLAIN IT?

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OBJECTIVES: Despite routine recommendations, adult uptake of influenza, pneumococcal, pertussis, and zoster vaccines in the United States is low. To inform development of evidence-based vaccination interventions, this study sought to evaluate inter-state variability and better understand local factors influencing adult vaccination coverage. METHODS: Logistic regression models were employed to estimate state-level adult vaccination coverage adjusted for individual-level characteristics using Behavioral Risk Factor Surveillance System data. States were ranked according to the sum of each state’s calculated z-score for each vaccine’s model-adjusted coverage, providing a composite metric across all four vaccines. Further considering the states ranked at the extremes, we then conducted a targeted review of state immunization websites and published literature to describe facilitators/barriers and interventions targeting adult vaccination, using the Social Ecological Model as a guiding theoretical framework to categorize interventions by level of influence on vaccination. RESULTS: Based on calculated z-scores, New Jersey, Florida, Illinois, Mississippi, and New York were ranked as low coverage states, while Minnesota, Washington, Colorado, Vermont, and New Mexico were ranked as high coverage states. All interventions reported on state immunization websites were implemented at the institutional or policy level, with immunization information systems most frequently reported (n=10 states). Only a subset of states reported quality improvement programs (n=6) and standing order interventions (n=4). Other common interventions were school immunization laws and state-purchased vaccines. All interventions from the literature (n=12 interventions) targeted improving vaccination at the institutional, interpersonal, or intrapersonal level. Data on state-specific vaccination facilitators/barriers were not identified. CONCLUSIONS: There is substantial inter-state variability in adult vaccination coverage in the United States. Existing data provide very limited insight on local facilitators/barriers or interventions impacting adult vaccination. Further efforts to bridge this information gap are critical towards developing targeted interventions to increase coverage. Collection of qualitative data from local stakeholders may provide further insights.

PIN115: A SURVEY ON THE SOCIETY’S AWARENESS LEVEL ON AIDS IN TURKEY

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OBJECTIVES: The survey aims to measure the society's awareness level on AIDS in Turkey. METHODS: Data were collected through a questionnaire on AIDS carried out with face-to-face interview method. A short and clear questionnaire was prepared and it was aimed to reach more people in the society. A total of 21,377 people were
reached and information on the society's awareness level on AIDS was collected.**RESULTS:** The mean age was 32.9 and 51.8% of the participants were female and 47.4% were male. 63.3% of respondents stated that they have a lot of information; 22.7% stated that they have little information and 14.1% stated that they have no information about HIV. 74.3% of respondents stated that HIV is transmitted through blood; 10.2% stated that it is transmitted through handshake; 33.8% stated that it is transmitted through kissing; 77.5% stated that it is transmitted through unprotected sex. 25% said that AIDS patients can continue their normal lives after taking the necessary treatment; 32.6% said that they cannot continue their normal life and 42.4% said that they do not know much about it. 53.4% of respondents stated that HIV testing can only be done in hospitals; 39.9% stated that it can be done in primary health care institutions and 6.7% stated that it can be done in all health care institutions. 49.7% of the respondents stated that their identity should be kept secret and that it is not right to submit their identity to the hospital when they have an HIV test. **CONCLUSIONS:** Although the prevalence of AIDS in Turkey is low compared to other countries, it shows an increasing trend according to the estimations made. However, since the disease is not accepted by the society in terms of culture and religion, the transfer of information on the disease has always been limited.

**PIN116: MAPPING OF SKIN AND SOFT TISSUE INFECTIONS WORLDWIDE: AN APPROACH FROM LITERATURE REVIEW**

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**OBJECTIVES:** The aim of this study was to conduct a global mapping of skin and soft tissue infections (SSTIs), to describe its clinical classification (bacterial, viral, parasitic, dermatomycoses and other infestations), as well as the geographical area of occurrence and climate (tropical, subtropical, desert, cold, temperate and others). **METHODS:** A systematic literature search was conducted (18/05/2017) through the PubMed database to identify the available evidence on SSTIs related to climate and humidity conditions. Five search strategies were designed taking into consideration terms located by MeSH vocabulary. Two additional filters were applied to search results (1. abstract availability; 2. title + abstract screening, in order to identify reports of SSTIs). The identified studies were evaluated by two independent reviewers to assess their inclusion in this project. **RESULTS:** All search strategies resulted in 1,122 references after duplicates removal. Subsequent filtration excluded 447 of them, resulting in 675 references for analysis. Global results showed that almost 20% of evidence was specific for Central America, Caribbean and Latin America areas (Brazil and Colombia accounted about 60%), followed by Africa (13%; highlighting Nigeria, Cameroon and Ethiopia). More than 50% of publications were focused on reporting a wide casuistry of parasitic SSTIs, followed by dermatomycoses (18%) and bacterial infections (16%). Parasitic SSTIs recorded were related to leishmaniasis in 60% of cases, dermatomycoses showed high variability of cases and bacterial SSTIs were mostly related to staphylococci and streptococci, accounting for 48% of references (i.e. abscess, furunculosis, cellulitis and impetigo/pyoderma). Studies located in tropical and subtropical climates exceeded 40% of total, followed by temperate (18%) and desert (15%). Maps with global and specific results for SSTIs and climates will be disclosed. **CONCLUSIONS:** The greatest burden of disease occurs in tropical and subtropical climates (mostly in Central America, Caribbean, Latin America and Africa areas), which are resource-limited settings with endemic populations of SSTIs.

**PIN117: PROCESSES AND REQUIREMENTS FOR HEALTH ECONOMIC ASSESSMENT OF ANTIBIOTICS FOR HTA PURPOSES: TIME FOR A PARADIGM SHIFT?**

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**OBJECTIVES:** Regulatory incentives for development of antibiotics have increased the number approved by EMA allowing them to come to market based on adapted evidence requirements, challenging the generation of evidence required for health technology assessment (HTA) reimbursement decision making purposes and impeding patient access to effective treatments. We aimed to assess the potential mis-alignment between regulatory approval requirements and HTA requirements for antibiotics in Europe. **METHODS:** A targeted review was conducted to identify the appraisal processes and health economic assessment requirements as well as incentive schemes for antibiotics (NICE, SMC, AWMSG, TLV and HAS). To understand the relationship between EMA approvals and HTA body appraisals, a search via the EMA website was performed to identify all antibiotics that were approved since 2013 followed by a search via the HTA body website to identify those that were eventually appraised. Finally, a review of the HTA appraisal challenges with the health economic assessment was performed. **RESULTS:** All but NICE appraise innovative antibiotics. Of those, only HAS instituted adapted appraisal criteria for antibiotics. Since 2013, a total of 8 antibiotics were approved by EMA. The SMO appraised all antibiotics on this list (n=8), followed by HAS (n=5), AWMSG (n=4) and TLV (n=3). The appraisals cited the following challenges with the health economic assessment: difficulty in establishing added therapeutic effectiveness due to non-inferiority design, small sample size and uncertainty around treatment effects, short treatment duration hindering lifetime horizon, and choice of
comparators. None incorporated the impact of treatment on resistance and spill-over effects. **CONCLUSIONS:** HTA processes in Europe need to be adapted for innovative antibiotics to support the regulatory incentives for their development and to accelerate patient access. As a start, traditional requirements for health economic assessment methodology, which does not capture the public health value of antibiotics, should be adapted specifically for antibiotics.

**PIN118: ARE WE PREP-ARED FOR DIFFERENCES BETWEEN NICE AND SMC DECISION MAKING?**

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**OBJECTIVES:** Recently, emtricitabine/tenofovir disoproxil for pre-exposure prophylaxis (PrEP) of HIV has been approved by NHS Scotland after appraisal by the SMC. However, following an evidence review by NICE it has been decided that further study is required before emtricitabine/tenofovir disoproxil can be approved for use in England. A case study was performed to evaluate this recent disparity between NHS England and NHS Scotland. **METHODS:** A comparative evaluation was performed to assess differences in decision making between each agency regarding emtricitabine/tenofovir disoproxil. The methods and findings of Evidence Summary ESNM78 from NICE and the SMC technology appraisal (No. 1225/17) were compared qualitatively. The NICE evidence summary did not offer formal guidance or include economic analysis. **RESULTS:** NICE evaluated data from four clinical trials of emtricitabine/tenofovir disoproxil, compared with the SMC which focused on two of the studies. Both bodies considered the drug combination to be clinically effective, with NICE reporting a reduced relative risk (of acquiring HIV infection) between 44% and 86% compared with placebo or no prophylaxis. The SMC performed an economic analysis, which estimated an annual cost of £4,316 per patient (£4.27m overall annual cost). However, the NICE evidence summary did not consider it possible to provide estimated usage based on the available data, citing prioritisation and eligibility criteria as factors influencing uptake. **CONCLUSIONS:** This decision makes Scotland the first country in the UK to adopt emtricitabine/tenofovir disoproxil for PrEP of HIV, while further research is considered necessary in England. This research is necessary to ascertain variables such as: uptake, adherence, sexual behaviour, and drug resistance. Differing epidemiology may explain the difference in approach. The example of emtricitabine/tenofovir disoproxil for PrEP of HIV hints at SMC divergence from simply following NICE recommendations and evidence requirements, indicating a growing influence of the SMC as a self-contained centre for technology appraisal.

**PIN119: THE EARLY BIRD CATCHES THE WORM: MEASURING THE POTENTIAL VALUE OF MESENCHYMAL STEM CELLS THERAPY FOR SEPTIC SHOCK USING THE EARLY HEALTH ECONOMIC EVALUATION**

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**OBJECTIVES:** Septic shock remains the leading cause of morbidity and mortality worldwide. Clinical evidence to date suggests that administering Mesenchymal Stem Cells (MSC) can improve survival in the event of septic shock. This study was conducted to assess the cost-effectiveness of the MSC therapy compared to usual care for patients with septic shock in an early stage from a payer’s perspective. **METHODS:** We conducted a headroom analysis and performed a value of information (VOI) analysis. We built a Markov model to simulate costs and outcomes of sepsis patients aged 65 years and older over a 20-years period according to their locations of care. Input parameters were obtained from the Phase I MSC trial, the published literature and expert opinions. An annual discount rate of 3% was applied for both costs and outcomes. All costs are presented in 2016 Canadian Dollars. **RESULTS:** The MSC therapy was associated with improved survival (0.33 years) and quality-adjusted life years (QALY) (0.190) compared to usual care. The headroom of the MSC therapy increased from $1,895 with a willingness to pay (WTP) threshold of $10,000/QALY gained to $18,952 with a WTP of $100,000 per QALY gained. The VOI analysis suggested that there was value for further research. The value for the efficacy of the MSC therapy, the cost of MSC therapy, and background in-hospital mortality were significant with Expected Value of Partially Perfect Information (EVPPPI) of $60,000, $50,000 and $48,000, respectively. **CONCLUSIONS:** Early health economic evaluation can be used to support product investment decision-making in an era of cost-constrained health systems. Results from this study show that future research should be focused on the efficacy of the MSC therapy, the cost of MSC therapy, and background in-hospital mortality.

**PIN120: A DYNAMIC DECISION ANALYSIS PROCESS FOR EVALUATING PANDEMIC INFLUENZA INTERVENTION STRATEGIES**

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**OBJECTIVES:** Public health authorities (PHA) experience challenges during outbreaks of pandemic influenza. There are (1) a high public attention and pressure for fast and effective actions, (2) uncertainty regarding development and potential impact of the pandemic, (3) complexity of the decisions on selecting interventions – this involves considering multitude of criteria and interests of stakeholders. Therefore we suggest a dynamic decision analysis process, which supports comprehensiveness, transparency, and consistency in decisions regarding interventions. **METHODS:** The process design was informed by scenario analysis, multi-criteria decision analysis methodology, and adapted to the Swedish context. The process was then validated in a pilot decision conference (DC) conducted at the PHA of Sweden. The process consists of elicitation and evaluation. Elicitation comprises developing scenarios, intervention strategies, and a multi-criteria model (MCM) against which the strategies are evaluated. In the evaluation process the strategies are scored, criteria weighted, and the results analyzed. **RESULTS:** In the pilot DC we considered a mild pandemic scenario, similar to the influenza pandemic of 2009. Three intervention strategies were evaluated, based on four interventions; vaccination (VAC), antiviral treatment (AVT), antiviral prophylaxis (AVP), school closure (SC). Strategy (1) included AVT to everyone with influenza-like illness (ILI), VAC to risk-groups, (2) AVT and AVP to risk-groups, SC, and VAC to everyone, and (3) AVT to everyone with ILI, AVP to risk-groups, and VAC to everyone. Guided by the process the seven participants outlined the MCM through a post-it session, evaluated the strategies against the criteria, and expressed criteria weights. Finally the results were aggregated and visualized. The analysis showed that strategy (1) was the most preferred. **CONCLUSIONS:** The process supports a dynamic, comprehensive, and transparent decision-making. An integrated decision-support toolset will be developed in forthcoming research along with contextualising and validating the process with Sweden related stakeholders.

**PIN121: THE ITALIAN ANSWER TO PREP TOPIC: EVIDENCE FROM A MULTI-CENTRE HTA STUDY**

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**OBJECTIVES:** The aim of the study was the multi-dimensional evaluation (HTA) of PrEP (TDF/FTC Pre-exposure prophylaxis) Italian adoption, compared with the traditional prevention strategies for high-risk HIV-negative individuals. **METHODS:** An HTA study comparing PrEP (utilized as an “add-on” or a “substitute” strategy) with a baseline scenario (use of condoms among men who have sex with men and sero-discordant couples, and of Needle Syringe Programmes among injection drugs users) was developed within 25 Infectious Disease Departments. **RESULTS:** Considering 16,577 high-risk individuals, PrEP’s introduction would lead to: i) a reduction in patients safety (-0.74 vs 0.00, p<0.05); ii) an effectiveness dependent on treatment adherence; iii) a perceived incremental staff workflow (-1.24 vs 0.00, p<0.05), requiring additional clinicians, with investment in medical supplies/equipment and training courses (€3,575); iv) an improvement in patients’ quality of life and satisfaction (1.50 vs 0.00, p<0.05). The economic analysis assumed both the NHS and the patient’s perspective, considering both branded and generic drugs costs (-70%). If PrEP is used as an “add-on” strategy, directly distributed and paid by the NHS, considering branded drugs, NHS investments would be +40%, while NHS economic benefits (-63%) are found if PrEP is purchased by citizens (individuals’ investment:+2,248%). As for generic drugs, the NHS would benefit from an advantage (-37%) and a shrink of the patients’ out-of-pocket expenditure emerged (+682%). If PrEP is introduced as a “substitute” strategy, the economic burden would be higher, both for the NHS (+212%) and the citizens’ (+3,423%). Even considering the generic drug, the NHS and patients face a relevant economic challenge, equal to +73% and +1,077% respectively. **CONCLUSIONS:** PrEP improvements in HIV prevention (as an “add-on” strategy) generate safety and economic concerns, but results show that the best cost-containing strategy would be the use of generic molecules. All possible scenarios should be considered in the decision-making process.

**PIN122: KNOWLEDGE AND ATTITUDES ABOUT EBOLA VIRUS AMONG COMMUNITY RESIDENTS IN THE US: A CROSS-SECTIONAL STUDY**

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**OBJECTIVES:** In 2014, while majority of Ebola virus cases were detected in West Africa, the CDC reported four cases in the US. This study was conducted to assess knowledge and attitudes about Ebola virus among community residents in USA. **METHODS:** A cross-sectional survey study was conducted in Winchester, Virginia from August 2016 to December 2016. The survey was distributed to patients in the waiting area of a clinic or pharmacy. The survey was comprised of questions on: demographics (4), knowledge (9) and attitudes (3). Out of the nine knowledge related questions, participants with a score of four or higher were considered to have good knowledge of Ebola.
Descriptive and inferential statistics (t-test and logistic regression) were employed using SPSS v23. A p-value of <0.05 was considered significant. **RESULTS:** A total of 375 participants completed the questionnaire. Internet served as the main source of Ebola information (72%). 11% of our participants had good knowledge of Ebola virus. People who received graduate degree/professional degree/PhD were more likely to have a good knowledge of Ebola compared to those who had a high-school degree (OR=6.62, p<0.01). A majority of the participants strongly agreed that Ebola virus is a serious condition (p<0.001) and communities should actively participate in controlling the risk of Ebola (p<0.001). **CONCLUSIONS:** Knowledge about Ebola virus was poor among the study participants. A large percentage of individuals surveyed feel their community should be engaged in controlling the spread of Ebola virus. Educating the community can bolster engagement and encourage proper preparedness, a crucial step in preventing the spread of Ebola.

**PIN123:** REQUIREMENTS FOR A NOVEL INHALED COMBINATION TO IMPROVE MANAGEMENT OF PSEUDOMONAS AERUGINOSA INFECTIONS IN CYSTIC FIBROSIS PATIENTS - A PAYER PERSPECTIVE


**OBJECTIVES:** Chronic infection with Pseudomonas aeruginosa (PA) is the primary cause of pulmonary deterioration in cystic fibrosis. The objective was to understand from a payer perspective the unmet needs, the value drivers and evidence requirements for a novel inhaled “add on” product for CF patients. With the acquisition cost of antibiotics generally low, understanding the potential willingness to pay for new innovative treatments could help guide future development, particularly in view of current efforts to develop new and effective antimicrobials. **METHODS:** 40 qualitative telephone interviews with payers across the EU5 and USA were conducted, utilising a discussion guide and pre-prepared list of potential attributes to explore unmet need, value drivers (scored on a 1-5 analogue scale), willingness to pay for an additional product, key evidence requirements and optimum positioning (e.g.acute, chronic or eradication setting). **RESULTS:** There is a high burden and cost due to chronic PA infection. The reported value drivers for an innovative additional treatment were, in descending order: reducing exacerbations, hospitalisations, the use of inhaled aminoglycosides, improving lung function, slowing the decline in function, and addressing future antimicrobial resistance. Targeting the chronic setting was considered optimal, from a practical and evidence perspective. Delivery and ease of use was important for use in this chronic setting, so a combined inhaler was required. A reduction in inhaled aminoglycoside use and associated side effects enhanced value. There was a willingness to pay for an additional product that demonstrated a reduction in exacerbations, long term antibiotic use, resource and drug costs as well as addressing the growing threat of resistance in Pseudomonas aeruginosa infections. **CONCLUSIONS:** There is a significant need for additional treatments to improve the long term management of chronic P.aeruginosa infections in patients with CF. Such a treatment should focus on a reduction in exacerbations, hospitalisations and antimicrobial resistance.

**SENSORY SYSTEMS DISORDERS - Clinical Outcomes Studies**

**PSS1:** COMPARING THE EFFICACY, SAFETY, AND EFFICIENCY OUTCOMES BETWEEN LENSX FEMTOSECOND LASER-ASSISTED CATARACT SURGERY AND PHACOEMULSIFICATION CATARACT SURGERY: A META-ANALYSIS

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**OBJECTIVES:** There has been increased interest in femtosecond laser-assisted cataract surgery (FLACS) due to potential for improved efficacy, efficiency, and safety. The objective was to conduct a pairwise meta-analysis comparing LenSx FLACS to phacoemulsification cataract surgery (PCS) in patients undergoing cataract surgery. **METHODS:** A systematic literature review identified 29 clinical studies comparing LenSx to PCS from 2010 to August 2016. Commonly reported outcomes were identified which included best corrected visual acuity (BCVA; logMAR), endothelial cell density (ECD; cells/mm2), central corneal thickness (CCT; µm), phacoemulsification time (seconds), effective phacoemulsification time (EPT; seconds) and phacoemulsification energy (%). BCVA, ECD and CCT were reported as the mean difference between procedures in the change from baseline while the remaining outcomes were reported as the mean difference between procedures. The meta-analysis was performed using STATA and included random and fixed effects models for each outcome. Where possible, the LenSx pre-SoftFit and LenSx SoftFit systems were considered separately as SoftFit is a newer system. **RESULTS:** Seven studies reported
comparable outcomes. LenSx was associated with lower phacoemulsification energy versus PCS (-3.72; 95% CI [-5.01, -2.43]). EPT was statistically significantly lower for LenSx SoftFit compared to PCS (-2.59; 95% CI [-3.11, -2.08]). At one week post-surgery, change in CCT was lower with LenSx versus PCS (-1.62; 95% CI [-3.12, -0.11]). Phacoemulsification time was lower with LenSx versus PCS, but was not found to be statistically significantly different, though could be considered clinically relevant as the CI has minimal overlap with 0. High heterogeneity among studies, as evidenced by I-squared statistics, and variation in study design made it difficult to draw conclusions across remaining outcomes. **Conclusions:** The results suggest that LenSx performs better than PCS for outcomes including phacoemulsification energy, EPT and CCT at one week. This analysis highlights the need for consistent reporting across future FLACS studies.

**PSS2: A NETWORK META-ANALYSIS TO EVALUATE THE EFFICACY OF BRODALUMAB IN THE TREATMENT OF MODERATE-TO-SEVERE PSORIASIS**


**Objectives:** To compare the clinical efficacy of brodalumab, an anti-IL 17RA human monoclonal antibody, with approved biologic therapies and apremilast for the treatment of moderate-to-severe psoriasis. **Methods:** A PRISMA-compliant systematic literature review identified RCTs reporting induction phase Psoriasis Area Severity Index (PASI) responses for therapies at European Medicines Agency approved doses. The primary analysis examined the proportion of patients achieving PASI 50, 75, 90 or 100 responses using a random effects Bayesian multinomial likelihood model with probit link, without and with an adjustment for study-level placebo responses. A second analysis assessed the number of patients with Physician Global Assessment (PGA) scores of 0 or 1. Effects of alternative inclusion criteria, such as including unlicensed therapies and introducing restrictions based on disease severity, were explored in a series of sensitivity analyses. The NMA adhered to NICE Decision Support Unit recommended methods. **Results:** A total of 41 studies reporting PASI outcomes were included in the base case NMA. All active therapies were found to be significantly more efficacious than placebo at achieving all levels of PASI response. Based on PASI 100 response (complete clearance), the most efficacious therapies in the network were brodalumab and ixekizumab, followed by infliximab and secukinumab. Brodalumab was significantly more efficacious than adalimumab, apremilast, etanercept and ustekinumab. This ranking was consistent for PASI 50, 75 and 90 outcomes, as well as the PGA response analysis and all sensitivity analyses. **Conclusions:** Results of the NMA reflect the results from recent pivotal trials which found that high levels of complete clearance can be achieved with brodalumab. Based on currently available evidence, the induction-phase efficacy of brodalumab is similar to ixekizumab, secukinumab and infliximab and superior to other approved therapies, including adalimumab, apremilast, etanercept, and ustekinumab. Analysis of longer-term data is needed to understand the comparative efficacy of biological therapies beyond induction.

**PSS3: ASSESSING THE LONGER-TERM EFFICACY OF BIOLOGIC THERAPIES AND APREMILAST FOR PATIENTS WITH MODERATE-TO-SEVERE PSORIASIS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS**


**Objectives:** Patients with moderate-to-severe psoriasis require long-term treatment, yet few clinical trials compare outcomes beyond a short-term induction period. To our knowledge, no network meta-analysis (NMA) of longer-term data has been performed. This NMA aimed to compare longer-term outcomes of currently approved biological therapies and apremilast. **Methods:** A systematic review (2000 to August 2016) identified studies reporting Psoriasis Area Severity Index (PASI) 75, 90 and 100 responses. Feasibility of an NMA on maintenance phase PASI endpoints was assessed and sources of heterogeneity considered. Data appropriate for analysis were modelled using a Bayesian multinomial likelihood model with probit link. Wherever possible, study data corresponding to an intention-to-treat approach with non-responder imputation was used. **Results:** Twenty-two studies reporting outcomes at 40-60 weeks were included, but heterogeneity in study design led to use of a step-wise approach to the synthesis. Forty-five-week RCTs were included in the primary indirect comparison, which found brodalumab to be significantly more efficacious than secukinumab (Risk ratio: 1.32 [95% Credible Intervals: 1.06, 2.02]), ustekinumab (1.90 [1.26, 3.46]) and etanercept (3.31 [1.58, 7.00]) in terms of PASI 100 response. In secondary analyses, 18 additional studies and four more drugs were included in the network by comparing maintenance phase outcomes from active interventions to induction phase outcomes from placebo arms. For this it was assumed that, had placebo therapy been continued, no change in response would have been observed between end of induction and
maintenance. Results were consistent with the main analysis: brodalumab appeared to be most effective, followed by ixekizumab, secukinumab, ustekinumab, infliximab, adalimumab, etanercept and apremilast. CONCLUSIONS: Results of this NMA suggest that brodalumab is associated with the highest likelihood of maintained PASI response after a year of treatment. Further long-term active-comparator RCT data is required to better assess relative efficacy across the range of currently approved therapies.

**PSS4: DRUG UTILIZATION AND PHARMACOLOGICAL COSTS OF INTRAVITREAL INJECTED ANTIVEGFs IN MACULOPATHIES IN SAN RAFFAELE HOSPITAL**

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**OBJECTIVES:** To investigate drug utilization and drug-related costs of intravitreal injected anti-VEGF drugs in ophthalmology hospital setting, 2013 to 2015. **METHODS:** An observational cohort study based on secondary data from hospital pharmacy databases was performed. Patients with intravitreal anti-VEGFs for: wet age-related macular degeneration, diabetic macular edema, macular edema secondary to retinal vein occlusion, choroidal neovascularization secondary to pathologic myopia in the period 2013 to 2015 were included. Anti VEGF drugs reimbursed by the national healthcare system were ranibizumab and aflibercept. **RESULTS:** During 2013-2015, in San Raffaele hospital 2,117 patients started anti-VEGF therapies. Median duration of follow-up for these patients was 224 days (0-1448). Majority of patients was female and mean age was higher for age-related maculopathy (74.9±9.6). During follow up 138 patients changed medication. The 1,979 that have not changed it were followed for 12 months. A total of 2,279 eyes were treated. There was high prevalence of patients with single administration of drug, mainly in the pathologic myopia group. Patients treated on both eyes were most in diabetic maculopathy (39%); a large amount of patients treated bilaterally received a more intensive treatment on the higher-severity eye. Of the 1,979 patient-years examined, more than half of the spending on drugs (3.3Mil €) was absorbed by age-related macular degeneration, due to the higher prevalence and to the greater mean number of injection. **CONCLUSIONS:** Our study pointed out in Real World environment the followings: a high prevalence of patients who had a single administration of anti VEGF; a suboptimal adherence as compared with drug prescribing information; most of the drug expense was absorbed by age-related maculopathy; a difference in prevalence between the various diseases in terms of patients treated on the second eye; a difference in treatment intensity between the two eyes in cases of patients treated bilaterally.

**PSS5: BODY PIERCINGS: EPIDEMIOLOGICAL STUDY ON A REPRESENTATIVE SAMPLE OF 5,000 FRENCH SUBJECTS**

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**OBJECTIVES:** Body piercing (BP) is a common form of body modification as popular as tattooing. In the US, it was estimated(2012) that 49% of adults had an ear piercing, 7% a piercing on their torso, and 4% a facial piercing other than an ear piercing. We are not currently aware of any equivalent study in France based on robust methodology. **METHODS:** A national, cross-sectional study in France was conducted on the general population based on a representative sample of 5,000 French individuals older than 15 years chosen by the method of quotas. **RESULTS:** Nearly 12% of the French participants reported at least one or BP (8.4% of men (M) and 19.4% of women (W)). Of these, 49.8% had only one BP. The most common body parts for piercings were the external ear(42%), the navel(24.3%), the tongue(15%), the nose(11%). Among intimate piercings, 5.8% of M had a piercing on the gentitalias, with 4.4% reporting a testicle piercing, and 2% of women declared that they had piercing on the clitoris. Notably, 45.1% of French persons with a single BP had an ear piercing.The most commonly reported motivations included embellishment of the body(53.1%) and individuality(31.1%). Erotic motivations and sexuality were more commonly cited by M(4.7%) than by W(2.3%), p<0.05, and the same was true for body reappropriation (M6.5%vsW3.7%,p<0.05). 40.8% of persons with BP had skin problems with at least one of their BP. These problems resolved in 30.4% of cases, were recurrent for 8.2% of the respondents, and chronic and persistent for 2.2% of them. The complications included: infection(44%), scarring(37.9%), irritation(29.7%), and itching(15%). **CONCLUSIONS:** To the best of our knowledge, this is the largest epidemiological study on BP in France to date. The practice of BP appears stable, unlike tattooing that increases with time. This study also confirms that infectious complications are common after a piercing.

**PSS6: THE PRESCRIPTION PATTERN AND PREVALENCE OF PSORIASIS IN A TERTIARY CARE HOSPITAL**

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OBJECTIVES: The aim of the study was to analyses the prescription pattern and prevalence of psoriasis in a tertiary care hospital. METHODS: A prospective, observational, single centre study was carried out in the dermatology department for six month duration after obtained the written approval by an Institutional Review Board and from Head of Dermatology Department. Patients attending in the Dermatology department who diagnosed with psoriasis by the Dermatologist were enrolled in the study after obtaining written informed consent from the patient. RESULTS: 79 patients with complaints of psoriasis were examined. Males 57(72%) were more as compared with females 22(28%). In our study, it was found that the higher incidence of psoriasis lies in the age group between 51-60 years for both males and females, 61-70 years for males alone and 41-50 years for females alone. In case of type of psoriasis, the most frequent manifestation was chronic plaque psoriasis 48%, followed by palmoplantar psoriasis (30%), scalp psoriasis (10%), Guttate (9%) and the rare manifestation was flexural psoriasis (3%). The most common sites involved was upper limb 60 (75.94%), followed by lower limb 48(60.75%), abdomen (46.67%), scalp (35%), back (31.66%), and chest (3.33%) of patients. The study populations received the total of 168 drugs. Topical steroids and Anthihistamines were commonly prescribed classes of drugs that is, both 37.9% and the rarely prescribed class of drug was antimetabolites 2.5%. CONCLUSIONS: The study observed higher incidences of psoriasis in males and maximum seen in the age group between 51-60 years. Chronic plaque shows maximum frequency and topical steroids and Anthihistamines were broadly prescribed medications.

PSS7: ACNE VULGARIS: PREVALENCE, CLINICAL FORMS AND ITS MANAGEMENT IN PHARMACY STUDENTS FROM BAHAWALPUR, PAKISTAN

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OBJECTIVES: Acne is a common skin disorder, commonly prevalent in younger adults and characterized with papules, cysts and skin scar. Acne is often reported to result in psychological distress, low self-esteem and reduced quality of life. The prevalence and management of acne varies among countries according to gender, ethnicity and age group mostly due to hereditary causes, social behaviors, and environmental factors. The data on acne prevalence, distribution of clinical forms of acne in Pakistan is still limited. There is a need to its study prevalence, sociodemographic factors and gender preference associated with management of acne in local population. To determine prevalence and distribution of clinical forms of acne among students of pharmacy at Islamia University of Bahawalpur, Pakistan. Further, to explore a relationship between its prevalence sociodemographic factors, geographical location and life style. METHODS: A cross sectional study was conducted on students in Pharmacy department the Islamia University of Bahawalpur. A self-administered questionnaire was administered to a representative number of students representing the whole population. RESULTS: Overall, 83.45% were females aged 20-25 years. Individuals with oily skin type were most likely affected (62%) with acne while 80% of participants affected by some form of acne. In our sample mild (55.8 %), moderate (28.5 %) papular-pustular and severe comedonal (4%) were most prevent affecting mostly the face. Only 2.4% had sought doctors’ advice, and 18.4% tried some form of medical treatment, out of which 1 1.7% used topical treatment and 6.7% used oral treatment. CONCLUSIONS: Our study found that acne and its associated complications are highly prevalent in younger adults in Bahawalpur, Pakistan. While, only third of participants sought medical help, and lack of preference or knowledge to treat the illness. These findings emphasize the need of educating the local youth and improve their awareness about acne treatments.

PSS8: PROGNOSTIC AND TREATMENT EFFECT MODIFYING BASELINE FACTORS FOR VISUAL FUNCTIONING RESPONSE IN NON-INFECTION UVEITIS OF THE POSTERIOR SEGMENT TREATED WITH INTRAVITREAL SIROLIMUS

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OBJECTIVES: Studying prognostic and treatment effect modifying variables permits targeting interventions towards high-risk groups. We explored the prognostic effect of baseline characteristics on visual functioning response (VFR) and effect modification in subgroups differentiated by baseline characteristics of SAKURA Study 1 subjects with active non-infectious uveitis of the posterior segment (NIU-PS). METHODS: Phase 3 SAKURA Study 1 randomized 347 subjects 1:1:1 to intravitreal sirolimus doses of 44 μg, 440 μg, or 880 μg, administered on Days 1, 60, and 120. Based on principal component analysis, the most relevant visual function (VF) measures from the National Eye Institute Visual Function Questionnaire and best-corrected visual acuity variable were selected. Subjects were defined as a VF responder if their response at month 5 on any of the selected VF measures exceeded the threshold.
for minimal important difference. The effect of prognostic and treatment effect modifying categorical baseline variables on VFR was tested using univariate logistic regression. **RESULTS:** Baseline characteristics with positive prognostic value for VFR included non-panuveitis (P=0.003), unilaterality (P=0.028), non-white (P=0.020), and idiopathic etiology (P=0.032). VFR rate difference between the 440 µg and 44 µg group was 18.3% in the non-panuveitis versus -16.5% in the panuveitis subgroup (P=0.029), 33.4% in the unilateral versus -5.1% in the bilateral subgroup (P=0.018), and 14.5% in the non-white versus 1.1% in the white subgroup (P=0.011). **CONCLUSIONS:** This exploratory analysis revealed non-panuveitis, unilateral manifestation, idiopathic NIU-PS and non-white race to have positive prognostic value. The effect of sirolimus 440 µg on VFR differed in subgroups with positive compared to poor prognosis defined by race, anatomic location and laterality of NIU-PS.

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**SENSORY SYSTEMS DISORDERS - Cost Studies**

**PSS9: BUDGET IMPACT ANALYSIS OF ENSTILAR® FOR THE TREATMENT OF PSORIASIS IN ITALY**

**La&nti EP.** Orlando VL, MA Provider Srl, Milano, Italy

**OBJECTIVES:** The objective of this study was to perform a Budget Impact Analysis (BIA) assessing the introduction of Enstilar® for the treatment of psoriasis into the Italian market. Enstilar® is a fixed combination foam (calcipotriene and betamethasone dipropionate) approved for the treatment of psoriasis vulgaris in adult patients. The Standard of Care is Dovobet® Gel, indicated for the topical treatment of mild to moderate psoriasis. **METHODS:** BIA compared two different scenarios: Scenario 1 without the fixed combination foam vs. Scenario 2 with the introduction of Enstilar®. Population data were obtained from IMS database and OsMed report 2015. The time horizon was 3 years from the introduction of Enstilar®. Total number of patients was the same for the two Scenarios, because the model allows the switch of patients from current treatments: Dovobet® Gel, mono-component therapies, topical corticosteroids and systemic therapies (DMARDs and Biologics). The perspective of the Italian National Healthcare Service was considered. **RESULTS:** The study showed that the introduction of Enstilar®, thanks to its incremental efficacy and shorter therapy cycle compared to other topical agents (4 weeks with Enstilar® compared to 8 weeks with Dovobet® Gel), generates savings for the Italian NHS equal to 4,926,537 €, 5,076,094 € and 6,465,717 € respectively in year 1, 2 and 3 over the total expenditure of 215,254,963 €, 224,089,975 € and 232,924,987 € related to the year 1, 2 and 3 in the first scenario. **CONCLUSIONS:** The present study indicates that the introduction of Enstilar® improves the adherence to the therapy thanks to its rapid onset of action and generates significant savings for the Italian NHS. Indeed, because of its incremental efficacy, Enstilar may reduce or delay the use – sometimes inappropriate – of systemic therapies.

**PSS10: TITLE: THE IMPACT OF THE RADS ASSESSMENT: CAN FEWER INJECTIONS WITH INTRAVITREAL AFLIBERCEPT TRANSLATE TO LOWER OVERALL TREATMENT BURDEN AND COSTS IN WAMD WHEN COMPARED WITH INTRAVITREAL RANIBIZUMAB?**

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**OBJECTIVES:** Intravitreal aflibercept (IVT-AFL) and ranibizumab have proven to be effective in treating neovascular age-related macular degeneration. Despite their effectiveness, debate is ongoing on how to maximize treatment outcomes while optimizing resource use. The Danish Council for the Use of Expensive Medicines (RADS) has concluded that, in the Danish setting, 17% fewer IVT-AFL injections than ranibizumab injections are required to reach similar treatment outcomes during first year of treatment. This study assessed, from the Danish perspective, the impact on non-drug costs associated with different frequency for injections with IVT-AFL and ranibizumab. **METHODS:** We performed an analysis applying the RADS guidelines. The analysis focused on healthcare resource use & direct healthcare costs. Administration costs in the hospital were estimated using national tariffs. Costs for preparation of medication from vials were taken into account. **RESULTS:** The 17% lower number of required injections for IVT-AFL translates to 6 injections for IVT-AFL in the first year compared to 7 injections for ranibizumab. The lower number of visits resulted in total costs of 8267 DKK for patients treated with IVT-AFL and 9530 DKK for ranibizumab treated patients. Costs for preparation of vials added 64 DKK for IVT-AFL in the first year. Costs for patients’ transport to the hospital were 3570 DKK for IVT-AFL compared to 4164 DKK for ranibizumab. Total non-drug cost savings for IVT-AFL treatment were 1794 DKK per patient in the first year. **CONCLUSIONS:** For the same outcome, IVT-AFL was associated with a reduced treatment burden, fewer injections, and less use of resources in Denmark. The reduction in resource utilization resulted in lower non-drug costs compared to ranibizumab, a potential savings of 1794 DKK per patient treated. Impact on resource utilization with IVT-AFL may be considered in addition to the savings in drug costs of one fewer injection.
**PSS11: COST-EFFECTIVENESS COMPARISON BETWEEN BIOBRANE AND SUPRATHEL FOR PARTIAL THICKNESS BURN TREATMENT FOR AUSTRIA**

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**OBJECTIVES:** The current treatment of partial-thickness burns includes the wound coverage with many different materials and techniques. One is a polylactide-based temporary skin substitute (Suprathel), another consists of porcine collagen type I and is a bi-layer, semi-permeable biosynthetic wound dressing (Biobrane). Given limited resources and the up rise of evidence based decision making, there is little guidance about the costs, the cost-consequences and the cost-effectiveness of different coverage options of burn injuries. This study is comparing Biobrane and Suprathel for the cost situation in Austria in partial-thickness burn patients with a TBSA of 15%. **METHODS:** A literature review identified relevant publications about both covering methods and the health states in question. Those health states include successful healing, duration of healing, infected and non-infected delayed healing and necessity of surgery, pain, and number of dressing changes. Where applicable these health states were combined with cost data from Austria for the development of a decision tree model using Tree Age®. The model computed a point estimate for the C/E ratio for the treatment alternatives. In addition, the statistical error of the C/E and incremental cost-effectiveness ratio (ICER) was assessed by a probabilistic sensitivity analysis (PSA). **RESULTS:** The incremental cost-benefit ratio for Suprathel in comparison with Biobrane was negative for Austria. One way sensitivity analysis confirmed the robustness of the model. Thus, the use of Suprathel consumed less resources than the use of Biobrane. Drivers were the lower effort for additional dressings with Suprathel, less analgesia, less use of the operation room and a shorter length of stay. **CONCLUSIONS:** It could be demonstrated that Suprathel was cost-effective over Biobrane, given an Austrian grid of in-hospital costs. The study was limited due to the fact that only few micro costing data available for burns injuries in both countries. Thus, further research will be needed to confirm this result.

**PSS12: COST COMPARISON OF LICENSED INTRAVITREAL THERAPIES FOR DIABETIC MACULAR EDEMA THAT RESPONDS INSUFFICIENTLY TO INTRAVITREAL ANTI-VEGF – A GERMAN 3 YEAR COST MODEL**

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**OBJECTIVES:** In treating center-involving diabetic macular edema (DME), there are patients that will require intensive and still respond insufficiently to intravitreal anti-VEGF compounds. In such cases, therapeutic options include a switch to corticosteroid implants, which include the longer-acting fluocinolone acetonide (FAc) implant or the shorter-acting dexamethasone implant. A systematic literature review (SLR) was conducted to assess the effectiveness of treatments after initiation of anti-VEGF treatment and also to assess their associated costs. **METHODS:** A systematic literature review (SLR) of randomised controlled trials (RCT) was performed using Medline and Embase. A short term cost-cost model was built in MS Excel with a 3 year time horizon, which enabled the comparison of DME treatments i.e., ranibizumab (Lucentis®), aflibercept (Eylea®), FAc implant (ILUVIEN®) and dexamethasone implant (OZURDEX®). Costs included drug and procedure (injection and optical coherence tomography (OCT)) costs as well as the cost of managing adverse events (i.e. cataract surgery, endophthalmitis, IOP-lowering drops and surgeries). **RESULTS:** A total of 23 publications (including 16 RCTs) were identified. No study had a clearly defined population after first-line anti-VEGF treatment, thus no effectiveness comparison was conducted. In the 3-year period, total DME treatment costs for Germany were: €17,540, ranibizumab; €15,894, aflibercept; €10.822, FAc implant; and, €12.363, dexamethasone implant. For all treatment regimens drug costs were the predominant cost component, followed by injection costs (with variations dependent on the specific drug) and then OCT costs. Uni- and multivariate sensitivity analyses revealed costs were robust to changes of model inputs. **CONCLUSIONS:** In summary, the short term cost-cost comparison demonstrates that steroidal implants can provide significant cost savings versus intravitreal anti-VEGF treatment for center-involving DME. Single application of the long-lasting FAc implant was most cost-efficient of the intravitreal injections therapies currently approved for DME.

**PSS13: THE ECONOMIC AND HUMANISTIC BURDEN OF PATIENTS ON TREATMENT FOR NEOVASCULAR AGE-RELATED MACULAR DEGENERATION**

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**OBJECTIVES:** To investigate the economic and humanistic burden of neovascular age-related macular degeneration
(nAMD) among the treated adult population compared to a matched-cohort of adults without nAMD. **METHODS:** A retrospective, cross-sectional analysis of the combined 2010, 2011 and 2013 National Health and Wellness Surveys from France, Germany, Italy, Spain, and UK was conducted. A greedy-matching algorithm matched adults of ≥50 years of age with a self-reported diagnosis of nAMD and who reported current receipt of treatment for the disease to controls (never experienced nAMD) by demographics, health characteristics, and study year (ratio 1:4). Generalized linear models were conducted to compare the nAMD respondents and matched controls, adjusting for alcohol consumption, which remained statistically different between groups after matching. Economic outcomes included self-reported healthcare use and activity impairment. Humanistic outcomes included health related quality of life (HRQoL) and self-reported health. RESULTS: Average patient (age: 45.8 years and TBSA: 10%) showed an estimated mean cost of €25,697 (n: 75; median: €11,932; interquartile range: €5,607 – €32,879). The most important cost determinants were ICU stay (€10,615) and hospital stay (€8,104); pharmacologic cost (NXB) was only €2,740. Subgroups analysis showed that total cost was determined by age, TBSA and deep of burn. Cost was lower when age ≤60 (78.7%) than >60: 20,407 € vs. 45,202 €; or if TBSA ≥10%: 57,245 € vs 9,923 €; or depth of burn (second degree (82.7%): 17,904 € vs. third degree: 33.3%) than <10%: 57,245 vs €9,923; or age > 60, third degree burn or TBSA ≥10% showed an estimated mean cost of €25,697 (n: 75; median: €11,932 €; interquartile range: €5,607 – €32,879 €). The most important cost determinants were ICU stay (€10,615) and hospital stay (€8,104); pharmacologic cost (NXB) was only €2,740. Subgroups analysis showed that total cost was determined by age, TBSA and deep of burn. Cost was lower when age ≤60 (78.7%) than >60: 20,407 € vs. 45,202 €; or if TBSA ≥10% (33.3%) than <10%: 57,245 vs €9,923; or depth of burn (second degree (82.7%): €17,904 vs. third degree: €62,865). Cost was higher in women (25.3%): 31,721 € vs. 23,653 €.

**CONCLUSIONS:** The burden of nAMD on healthcare use remains significant in terms of healthcare resource utilization. nAMD burden on HRQoL manifested as lower PCS scores, utility scores, and impaired overall activity, despite patients receiving treatment. There is a need for nAMD therapies that reduce the burden of healthcare resource utilization.

**PSS14: ECONOMIC BURDEN OF BURN INJURIES TREATED WITH AN ENZYMATIC DEBRIDING AGENT IN SPAIN**

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**OBJECTIVES:** Burn care is considered expensive care by the payers; so, the objective is to analyze the direct cost of burn care in patients treated with a novel enzymatic (bromelain) debridging agent (Nexobrid, NXB) in a reference hospital in Spain and to identify the cost determinants. **METHODS:** Resource use of all patients with deep burns, treated from Dec 2014 to Dec 2016, was analyzed retrospectively from the hospital perspective, until 3 months post injury. Only direct costs were included. Subgroups analyses were carried out to examine differences between them (age, sex, percentage total body surface area (TBSA) burned, type of burn). **RESULTS:** Average patient (age: 45.8 years and TBSA: 10%) showed an estimated mean cost of €25,697 (n: 75; median: €11,932 €; interquartile range: €5,607 – €32,879 €). The most important cost determinants were ICU stay (€10,615) and hospital stay (€8,104); pharmacologic cost (NXB) was only €2,740. Subgroups analysis showed that total cost was determined by age, TBSA and deep of burn. Cost was lower when age ≤60 (78.7%) than >60: 20,407 € vs. 45,202 €; or if TBSA ≥10% (33.3%) than <10%: €57,245 vs. €9,923; or depth of burn (second degree (82.7%): €17,904 vs. third degree: €62,865). Cost was higher in women (25.3%): €31,721 € vs. 23,653 €. **CONCLUSIONS:** 72.5% of the total direct cost of treatment of burns depends on ICU and hospital stay; pharmacological cost of NXB is only 10% of total. Women with age ≥ 60, third degree burn or TBSA ≥10% showed a higher cost than the average.

**PSS15: ECONOMIC EVALUATION FOR THE TREATMENT OF ACUTE BACTERIAL SKIN AND SKIN STRUCTURE INFECTIONS (ABSSSI) FROM THE NHS PERSPECTIVE: A SPENDING PREDICTOR MODEL FOR ITALY, ROMANIA AND SPAIN.**

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**OBJECTIVES:** Dalbavancin is a new innovative long-acting antimicrobial treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSI) that allows clinicians to endorse an early discharge (ED) approach. Aim of this study was to develop a spending predictor model for evaluating the direct costs associated with the management of ABSSSI from a National Fayer perspective of Italy, Romania and Spain, in terms of hospitalization and drug costs for the treatment of ABSSSI comparing the standard of care (SOC) vs long-acting treatment dalbavancin. **METHODS:** A decision Tree model was developed to evaluate the clinical pathways of the ABSSSI patients in hospital. The SOC scenario was compared with a scenario using dalbavancin where patients have the possibility of being early
discharged from hospital. The epidemiological and cost parameter were extrapolated from national administrative databases (hospital information system) and systematic literature review related to each country. Drug, hospitalization, specialist service, administration and adverse event costs were considered. Probabilistic Sensitivity Analysis and One-Way sensitivity Analysis were performed. RESULTS: The model estimated a total annual number of patients with ABSSSI of 48,800 in Italy, Romania and Spain. The introduction of dalbavancin could reduce the length of stay of an average of 4.1 days per patient (Base-case 11.5 vs 7.4 days). This effect could increase drug costs about +34.7%, and decrease other costs of -35.1%. Overall, dalbavancin reduced the economic burden of ABSSSI of 0.4% from the National Payer perspective with consistent results among Countries. The PSA e OWA demonstrated the robustness of the results. CONCLUSIONS: Preliminary results highlight that the introduction of dalbavancin into ABSSSI clinical pathways could generate a significant reduction in term of length of stay with no incremental costs from the NHS perspective, moreover creating the opportunity for hospital’s efficiency increasing and reduced patients exposure to hospital acquired infections.

PSS16: COST-EFFECTIVENESS OF APREMILAST FOR THE TREATMENT OF MODERATE TO SEVERE PSORIASIS IN GREECE

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OBJECTIVES: To assess the cost-effectiveness of placing apremilast before biologics in adult patients with moderate to severe plaque psoriasis, who have failed to respond to, have a contradiction to, or are intolerant to other systemic treatments, from a Greek payer perspective. METHODS: A 10-year Markov transition model with monthly cycle duration was used. The analysis compared an apremilast-prior-to-biologics drug sequence vs a biologic-only sequence. Sequential biologics were etanercept, adalimumab, ustekinumab and infliximab for both treatment strategies. Patients failing infliximab received best supportive care as last line of treatment. Response to treatment was defined as a 75% reduction in Psoriasis Area and Severity Index (PASI) score at the end of the trial periods, obtained from a meta-analysis. Non-responders moved to the next treatment line. Long-term treatment withdrawal and all-cause mortality rates were retrieved from the literature and national published databases, respectively. Utility gains by PASI response were estimated using a published regression equation. Following a payer perspective, direct costs pertaining to drug acquisition, administration, and monitoring were considered (€, 2017). An annual discount rate of 3.5% was applied for both cost and health outcomes. RESULTS: Placing apremilast before biologics was found to be a dominant strategy (less costly and more effective). The apremilast-prior-to-biologics drug sequence was estimated to generate 0.01 additional quality-adjusted life-years (QALYs), compared with the biologic-only sequence (6.74 vs 6.73) and cost-savings of €778 (€75,582 vs €76,360), respectively. One-way sensitivity analysis confirmed apremilast sequence’s cost-effective profile. At the defined willingness-to-pay threshold of €34,000 per QALY gained, probabilistic sensitivity analysis showed that the apremilast-prior-to-biologics sequence was estimated to have a 90% probability of being cost-effective relative to the biologic-only sequence. CONCLUSIONS: Placing apremilast before biologics was found to be a dominant strategy for the treatment of moderate to severe plaque psoriasis in the Greek healthcare setting.

PSS17: COST-PER-RESPONDER OF FIXED COMBINATION CALCIPOTRIOL + BETAMETHASONE DIPROPIONATE AEROSOL FOAM VS OINTMENT IN PATIENTS WITH PSORIASIS VULGARIS IN THE UK

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OBJECTIVES: Innovative reformulation of active pharmaceutical ingredients used to treat psoriasis can produce significant improvements in clinical and patient-reported outcomes. The efficacy and safety of fixed-combination 0.005% calcipotriol plus 0.064% betamethasone dipropionate (Cal/BD) topical therapy in the treatment of patients with psoriasis vulgaris has been established. The aim of this study was to perform a short-term cost-per-responder analysis of Cal/BD aerosol foam versus Cal/BD ointment in the management of adult patients with psoriasis vulgaris of the body (trunk and limbs). METHODS: Treatment response was defined as a ≥ 75% reduction in Psoriasis Area Severity Index (PASI-75). Data for response rates were taken from the LEO90100-035 clinical trial (NCT01536886) which compared Cal/BD aerosol foam vs Cal/BD ointment. Drug acquisition costs (in 2017 UK pounds) were according to the British National Formulary (per June 2017). Drug costs only were considered, from the UK payer perspective, based upon dosing regimens from the clinical trial. Cost-per-responder at treatment Week 4 was calculated for Cal/BD aerosol foam vs Cal/BD ointment. RESULTS: Mean 4-week treatment costs per patient were £83.59 for Cal/BD foam, and £80.95, £80.95, and £75.34, for Cal/BD ointment 30 g, 60 g, and 120 g packs, respectively. At Week 4, 50.4% of patients had achieved PASI-75 with Cal/BD foam, compared with 40.7% of patients with Cal/BD ointment. The average cost per PASI-75 responder at Week 4 was £165.86 for Cal/BD aerosol foam, and £198.89, £198.89, and £185.10, for Cal/BD ointment (30 g, 60 g, and 120 g packs, respectively).
**PSS19: COST EFFECTIVENESS ANALYSIS OF THE USE OF ENSTILAR® COMPARED TO DOVOBET® GEL IN THE TREATMENT OF PSORIASIS IN ITALY**

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**OBJECTIVES:** The aim of this study was to determine the cost-effectiveness of Enstilar® compared to the Standard of Care in treating patients with psoriasis vulgaris. Enstilar® is a fixed combination foam (calcipotriene and betamethasone dipropionate) approved for the treatment of psoriasis vulgaris in adult patients. The Standard of Care is Dovobet® Gel, indicated for the topical treatment of mild to moderate psoriasis. **METHODS:** A decision-tree model was used to compare costs and effects of Enstilar® and Dovobet® Gel using the Italian National Healthcare Service perspective. The time horizon used in this simulation is one year, it was deemed sufficient to evaluate cost and results of both therapies. Efficacy and length of treatment cycle for the two therapies were determined using a head to head study. The utility is expressed in terms of QALYs for the two health states considered (patients respond to treatment or not) and was derived from published data. Results are presented in terms of incremental cost per quality-adjusted life years gained. Probabilistic sensitivity analysis was conducted using Monte Carlo simulation. **RESULTS:** The Incremental Cost-Effectiveness Ratio (ICER) for Enstilar® compared to Dovobet® Gel is -117.75 €. Indeed, the introduction of Enstilar® reduces the cost per cycle (83.86 € compared to 91.86 € with Dovobet® Gel) and increase the efficacy (PGA of 38.3% with Enstilar® Vs 22.5% with Dovobet® Gel). The sensitivity analysis confirmed these results showing an average ICER of -106.92€ with a standard deviation of 217.35€. **CONCLUSIONS:** The present study indicates that Enstilar® is Dominant compared to the standard of care (Dovobet® Gel). The sensitivity analysis demonstrates that in the 72% of the 1,000 simulations conducted Enstilar® is still dominant and that in the 88% of the simulations the ICER falls below the maximum acceptable ceiling ratio, fixed equal to the Dovobet® Gel cost per cycle.

**PSS20: HTA ANALYSIS OF INTRAOCULAR LENSES AFTER CATARACT SURGERY: HYDROPHOBIC VS. HYDROPHILIC LENSES - HEALTH TECHNOLOGY ASSESSMENT IN SLOVAK HEALTHCARE ENVIRONMENT.**

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**OBJECTIVES:** to explore the cost-effectiveness in patients with cataract who undergo an IOL exchange, either hydrophobic or hydrophilic, from the perspective of payers. **DESIGN:** Health economy model, using Cost-Effectiveness Analysis (CEA), complemented by Budget-Impact Analysis (BIA) on public health insurance coverage in Slovakia. **DATA SOURCES:** Based on modeling, lifelong treatment costs were obtained for patients after the cataract surgery with implanted lenses (whether hydrophobic or hydrophilic). Real-world data from General Health Insurance, Inc. were used for costs associated with diagnosis, complications, treatment and management of patients with cataract (average age of 70 years old, life time horizon). **METHODS:** Markov Model (life time horizon) for cataract patient management was developed. Outcomes observed were decreased by number of complications. An analysis of cost-effectiveness and budget impact was put into place, when both technologies were introduced into the system of reimbursement from public health insurance funds and their mutual cost effectiveness. Payer’s perspective and direct healthcare costs, associated with cataract surgery and complications were considered in CEA and BIA for diagnosis subgroups. Discount rate of 5% was used for costs as well as outcomes. Sensitivity analysis for major complications was implemented. **RESULTS:** Highest lifetime costs were recorded when a hydrophobic IOL was implanted during cataract surgery. These costs are estimated to € 514.20 (undiscounted), respectively € 268.80 (discounted). If the hydrophobic IOL is implanted, the lifetime costs are estimated to 380.01 € (undiscounted), respectively € 198.16 (discounted). Net saving costs (BIA) associated with hydrophobic IOL for one year cohort of patients in Slovakia are 1.12 mil. €. **CONCLUSIONS:** When a hydrophobic IOL is implanted during a cataract surgery then from the payer’s perspective to investigate the costs of public health insurance to deal with later complications of cataract surgery and other “secondary effects” (complications) following the Nd: YAG capsulotomy.

**PSS21: COST-EFFECTIVENESS OF A 0.2 MG/DAY FLUCINOLONE ACETONIDE (FAC) IMPLANT IN THE TREATMENT CHRONIC DIABETIC MACULAR OEDEMA (DMO) IN THE UK**

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Compared with ointment, the extra cost per additional PASI-75 responder for Cal/BD foam was substantially lower, between £27 and £85. **CONCLUSIONS:** Cal/BD aerosol foam is more cost effective than Cal/BD ointment in patients with psoriasis vulgaris.
OBJECTIVES: A single injection of the FAc implant (ILUVIEN(r)) continuously releases 0.2 µg per day of FAc for up to 36 months. It is indicated in Europe for the treatment of chronic DMO that is insufficiently responsive to available therapies, and NICE restricted its use in the UK to pseudophakic eyes. In order to assess the cost-effectiveness in patients with a phakic lens and a cataract, a new model was developed. METHODS: A Markov model was developed to predict costs and QALYs over 15 years in patients treated with FAc implant, compared to usual care, consisting of laser photocoagulation and anti-VEGFs. The model captured changes in best-corrected visual acuity level, DMO status, lens status and treatment phase in both eyes. Transition probabilities were obtained from multinomial models estimated from the FAME clinical trial. Patient baseline characteristics, resource utilisation and treatment patterns were obtained from real-world data, collected in the Iluvien Clinical Evaluation-Uk (ICE-UK) study and the literature. Costs were evaluated from the UK National Health Service perspective and included treatment acquisition and administration, disease monitoring, adverse events management and cost of blindness. RESULTS: The FAc strategy was more expensive compared to usual care, with differences of £1,597 and £1,647 per patient with pseudophakic and phakic study eyes, and produced more QALYs (+0.18 and +0.09 per patient, respectively). Predicted numbers of anti-VEGF injections avoided in these eyes in the 12 months after FAc administration were 6.27 and 6.69. Incremental cost-effectiveness ratios (ICER) were estimated at £8,653 and £17,740/QALY gained. Sensitivity analyses showed that the ICER was sensitive to usual care costs, vision-related utility decrements and transition probabilities. The probabilities of FAc being cost-effective were 78% and 51.5% at a threshold of £20,000 per QALY gained, respectively. CONCLUSIONS: The FAc implant is cost-effective in patients with chronic DMO irrespective of lens status.

PSS22: SECUKINUMAB SIGNIFICANTLY REDUCES WORK IMPAIRMENT AND INDIRECT COSTS COMPARED TO USTEKINUMAB AND ETANERCEPT IN THE UNITED KINGDOM

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OBJECTIVES: The severity of psoriasis can impact work productivity. Whether differential treatment efficacy translates into differential indirect cost-savings is unknown. We compared indirect costs associated with secukinumab, ustekinumab and etanercept, were used to assess the impact of psoriasis on work, and were applied to FIXTURE, a study comparing secukinumab and etanercept. Efficacy at 16 and 52 weeks was measured by Psoriasis Area and Severity Index (PASI) improvements from baseline: less than 50% (PASI < 50), 50%-74% (PASI 50-74), 75%-89% (PASI 75-89), and at least 90% (PASI ≥ 90). Work impairment by PASI response was used to estimate weekly and annual mean work hours lost due to psoriasis. PASI response distributions were assumed consistent across employed and non-employed patients in both studies. Average hours lost across both groups were calculated for all treatments. Annual indirect costs were based on UK Office for National Statistics average earnings data. RESULTS: In CLEAR, 502 patients (67%) were employed at baseline. At week 52, percentages of weekly work impairment/mean hours lost decreased with higher PASI: PASI < 50: 26.3%/8.77 hours; PASI 50-74: 16.4%/5.46 hours; PASI 75-89: 10.4%/3.46 hours; and PASI ≥ 90: 6.9%/2.30 hours. Weighted mean weekly/annual work hours lost were significantly lower for secukinumab than for ustekinumab (1.93/100.69 vs. 2.35/122.72; P = 0.0001). Consistent results were obtained for secukinumab versus etanercept (2.44/127.15 versus 3.27/170.48; P = 0.0001). Average annual indirect cost-savings with secukinumab were £346.26 versus ustekinumab and £681.13 versus etanercept. Results at 16 weeks were similar (P = 0.0001). CONCLUSIONS: Secukinumab significantly reduces work impairment and associated indirect costs of psoriasis, when compared with ustekinumab and etanercept, as early as week 16 and up to week 52.

PSS23: EVIDENCE MAP OF INDIRECT COSTS IN PSORIASIS AND PSORIATIC ARTHRITIS SINCE 1960

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OBJECTIVES: To create an evidence map of studies reporting the indirect costs associated with psoriasis and psoriatic arthritis, and the geographical settings in which these studies were conducted. METHODS: We searched the heoro.com database (www.heoro.com) for abstracts reporting indirect costs in psoriasis or psoriatic arthritis published between 1960 and 1st June 2017. We analysed the abstracts identified by the search to determine the range of geographical locations, disease types, interventions and study methodologies. We presented the findings as an evidence map. RESULTS: We found a total of 57 abstracts. Of these, 14 reported indirect costs, including productivity losses, from the USA, six from Germany, five each from Italy and the UK, three each from Canada and the Netherlands, and eight were reviews of the international literature. Forty-one abstracts assessed indirect costs associated with plaque psoriasis and 19 with psoriatic arthritis. Twenty nine abstracts reported on observational cost of illness studies or those with patient-reported productivity assessments, nine included indirect costs in an economic
model, seven assessed indirect costs as part of a clinical trial and 12 were reviews of the literature. Interventions studied included targeted therapies, in particular adalimumab (8 abstracts), etanercept (8), ustekinumab (5) and infliximab (3), phototherapy (6), corticosteroids (4) and cyclosporine (2), although no specific treatment was cited in 28 abstracts. Two papers were published before 2000, 16 between 2000 and 2009, and 39 between 2010 and 2017. CONCLUSIONS: As with many diseases, there is a relative lack of published data on indirect costs of psoriasis and psoriatic arthritis, and 53% of studies reporting indirect cost data were from four jurisdictions: the US, Germany, the UK and Italy.

**SENSORY SYSTEMS DISORDERS - Patient-Reported Outcomes & Patient Preference Studies**

**PSS24: TREATMENT PERSISTENCE IN PSORIASIS PATIENTS INITIATED ON APREMILAST, ORAL SYSTEMICS, OR BIOLOGIC THERAPIES**

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**OBJECTIVES:** Previous studies have shown a positive association between treatment satisfaction and persistence. There is a paucity of real-world data regarding persistence associated with the use of apremilast, conventional systemic therapies and biologics in the treatment of psoriasis. The objective of this study was to compare treatment persistence among psoriasis (PSO) patients initiating apremilast, conventional systemic therapies or subcutaneous biologic therapy in US claims data. **METHODS:** This descriptive, observational, retrospective cohort study was conducted using MarketScan Commercial and Medicare Supplemental Databases (2013-2016). Adults with ≥2 diagnosis codes for psoriasis (ICD-9:696.1; ICD-10:40.0) who initiated apremilast, other oral therapy, or biologic therapy were selected. The first prescription date was defined as the index date and patients were required to be continuously enrolled for ≥12 months pre- and ≥12 months post-index. Persistence was measured as the time from initiation to discontinuation, defined as the end of days’ supply prior to at least a 60-day gap without medication. At 12 months post-index the percentage of patients persisting on drug was assessed. **RESULTS:** In total, 972 patients initiating apremilast, 2,934 patients initiating other oral therapy, and 2,303 initiating biologic therapy met the inclusion criteria and had similar baseline characteristics. Mean enrolment follow-up time post-index was 499 days for apremilast, 591 days for other oral therapy, and 590 for biologic therapy. At 12 months post-index, persistence to initiated drug was 37.3% for apremilast, 20.4% for other oral therapy (p<0.001 vs apremilast), and 38.2% for biologic therapy (p=0.600 vs apremilast). Further sub-analyses showed a statistically significant, higher persistence for patients on apremilast compared to etanercept, (apremilast: 37.3% vs etanercept: 31.9%, p=0.022), while the persistence rates for patients on apremilast and adalimumab were similar (adalimumab: 40.2% vs apremilast: 37.3%, p=0.123). **CONCLUSIONS:** Patient persistence on apremilast therapy is significantly higher compared to conventional systemic therapies and not significantly different compared to biologic therapies.

**PSS25: SUN PROTECTION KNOWLEDGE AND BEHAVIOUR AMONG UNIVERSITY STUDENTS IN HUNGARY**

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**OBJECTIVES:** The aim of the study was to measure the knowledge about melanoma malignum and the UV-protection behaviour among university students. **METHODS:** We conducted a quantitative, cross-sectional study among students of five faculties at the University of Pécs by using non-random sampling (n=291). The self-edited questionnaire contained the following question groups: socio-demographic data, skin type, the number of previous sunburns, sunbathing habits, usage of solarium, usage of sunscreens, self-checking, knowledge about UV-protection and melanoma. Descriptive statistics and Chi-square test were used with 95% probability level (p<0.05). We used the SPSS statistics program. **RESULTS:** 61.9% of the students have had sunburns more than three times in their lives. Significantly more people belonging to the skin types I-II use physical protection (p=0.007), 27.1% of the sample use sunscreens regularly (whilst sunbathing). Women (p=0.001), people who have never had sunburns in their lives (p=0.045), students of the Medical School (p=0.016) use sunscreens with a sun protection factor 16 or higher. 90.4% of the students do not know the risks of skin cancer. 38.1% of the sample know in which cases they need to visit a doctor because of a birthmark, primarily women (p=0.004), medical students (p=0.002), and students at third-fourth grades (p=0.010). They referred to commercials as their main sources of information (76.3%). **CONCLUSIONS:** Physical and chemical sun protection among university students is not adequate to the desired extent. Students’ knowledge is insufficient especially of the ones studying at lower grades and at non-medical faculties. Evoking the pieces of information regularly at public education would be as important as forming the appropriate habits within the educational frameworks.
**PSS26: A PATH ANALYSIS OF EFFECTS OF PATIENTS’ UNDERLYING CONDITIONS, TREATMENT SATISFACTION AND ADHEREANCE ON QUALITY OF LIFE AMONG KOREA GLAUCOMA PATIENTS: RESULTS FROM KOREA GLAUCOMA OUTCOMES RESEARCH**

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**OBJECTIVES:** This aimed to determine factors that presumptively contribute to quality of life and assess total, direct, and indirect effects that exist between the determinants using path analysis. **METHODS:** The data included in this analysis was derived from Korea Glaucoma outcome research, a cross-sectional, observational study where a total of 1,050 glaucoma outpatients with≤2-year of eye-drop use were recruited at 15 eye clinics from March to November, 2013. Among the total, 213 patients were excluded due to missing data for path analysis. Including factors and their hypothetical pathways to quality of life were based on literature review and consultation with specialists in ophthalmology. In this model, age, gender, co-morbidity, education were included as underlying conditions and treatment patterns was defined by daily number of instillation of prescribed eye-drops. Treatment satisfaction and adherence were estimated using Treatment Satisfaction Questionnaire for Medication (side effect satisfaction, effectiveness satisfaction, convenience satisfaction, global satisfaction) and pill count, respectively. Quality of life was assessed by EQ-5D and EQ-VAS. AMOS was used to perform path analysis. **RESULTS:** For EQ-5D, male showed total effects(βtotal=0.102, P=0.0026) including both direct(βdirect=0.076, P=0.0095) and indirect effect(βindirect=0.0253, P=0.0020) which was mediated by side effect satisfaction and global satisfaction. Also, higher education(βdirect=0.197, P=0.0020), global satisfaction(βdirect=0.075, P=0.0414) and side effect satisfaction(βdirect=0.095, P=0.0076) were found to have direct effects on EQ-5D. For EQ-VAS, higher education had significant total effects(βtotal=0.153, P=0.0020) accounting for direct effect(βdirect=0.131, P=0.0030) and indirect effects(βindirect=0.0223, P=0.0531) through global satisfaction. In addition, male(βdirect=0.0274, P=0.0165) had indirect effect which was mediated by global satisfaction. Co-morbidity(βdirect=0.096, P=0.0090), effectiveness satisfaction(βdirect=0.094, P=0.0302), global satisfaction(βdirect=0.144, P=0.0020), and convenience satisfaction(βdirect=0.076, P=0.0390) showed direct effects on EQ-VAS. Interestingly, convenience was found to be negatively influenced by male, higher education and increased daily number of instillation of prescribed eye-drops in the pathways. **CONCLUSIONS:** This analysis revealed the magnitude of determinants and their pathways to quality of life. These findings are critical to develop effective interventions for improving quality of life while glaucoma treatment.

**PSS27: ARE GENERIC HEALTH STATE UTILITY INSTRUMENTS SUFFICIENTLY SENSITIVE TO CAPTURE CHANGES IN HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH VISUAL DISORDERS?**

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**OBJECTIVES:** When assessing new therapies, health technology assessment (HTA) bodies express a preference for generic instruments to measure health state utility values (HSUVs), such as the EuroQol 5-Dimensions (EQ-5D), over disease-specific measures and direct elicitation methods. We performed a targeted literature review to identify studies considering generic or disease-specific HSUV instruments in patients with chronic ophthalmologic conditions, to assess and compare their ability to accurately reflect changes in vision-related quality of life (QoL). **METHODS:** MEDLINE, Embase, the Cochrane Library, major ophthalmology congresses from the past 5 years, HTA websites and HSUV registries were searched. Articles were screened by one reviewer; all included articles and 10% of excluded articles were checked by a second reviewer. Primary research articles, cost-effectiveness studies, reviews and editorials reporting or discussing HSUVs in chronic ophthalmologic diseases were included. **RESULTS:** Studies assessing the correlation between HSUV instruments and measures of visual acuity and function generally found generic instruments to be less responsive than disease-specific instruments. In particular, generic measures were less sensitive in patients with mild or severe (rather than moderate) disease. The EQ-5D was frequently found to be less sensitive than other generic instruments, including the Health Utilities Index (2 and 3) and Short-Form 6-Dimensions, as tested in multiple conditions. Several studies therefore reported difficulties mapping vision-related QoL instruments to the EQ-5D. Direct elicitation methods, such as time trade-off, were reported to correlate more closely with visual parameters than indirect methods. **CONCLUSIONS:** Although generic HSUV measures are generally preferred by HTA bodies worldwide, they are inadequately responsive to changes in vision-related QoL. Use of generic measures may therefore underestimate the benefits of new therapies for ophthalmologic disorders undergoing cost-utility assessment. Disease-specific instruments or direct elicitation are more sensitive than generic measures, and may therefore be preferable for cost-utility assessment in chronic ophthalmologic conditions.
**PSS28: DEVELOPMENT OF A NEW PATIENT-REPORTED OUTCOME INSTRUMENT TO EVALUATE TREATMENTS FOR STRETCHMARKS: THE BODY-Q STRETCHMARK SCALE**

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**OBJECTIVES:** Stretchmarks are common permanent dermal lesions that can cause psychosocial distress. A number of treatment modalities are available, with the majority targeted towards increasing collagen production. A recent systematic review confirmed that current treatments lack high quality evidence (1). The aim of this study was to develop and field-test a new PROM that measures appearance of stretchmarks, to provide a means to incorporate the patient perspective into future treatment studies. **METHODS:** We previously described the development of the BODY-Q conceptual framework, which involved a literature review, 63 patient interviews, 22 cognitive interviews and input from 9 experts, and the international field-test study that involved 403 weight loss and 331 body contouring patients (2). To develop the stretchmarks scale, we re-examined appearance codes from the original set of 63 interview transcripts. The scale was field-tested in an international study. Rasch Measurement Theory (RMT) analysis was used to refine the scale and examine measurement properties. **RESULTS:** The stretchmarks scale was completed by 253 Canadians and 400 Danish patients (82% female, mean age 44.8 (SD=10.4)). The sample include 414 bariatric surgery and 239 body contouring patients. The data fit the Rasch model (p=0.56). Items (eg, length, width, amount, location, up close) mapped out a well targeted clinical hierarchy. All items had ordered thresholds and good item fit. There was no evidence of DIF (bias) by country, age or gender. The scale evidenced reliability, i.e., Person Separation Index=0.94, Cronbach's alpha=0.97. **CONCLUSIONS:** This scale could be used to measure the impact of innovative treatments of stretchmarks. Hague A, Bayat A. Therapeutic targets in the management of striae distensa: a systematic review. J Am Acad Derm. 2017 May 24. Klassen AF, et al. The BODY-Q: A PRO instrument for weight loss and body contouring treatments. Plast Reconstr Surg Glob Open. 2016 3:e679.

**PSS29: THE RELATIONSHIP OF QUALITY OF LIFE AND COMPLETE PSORIASIS CLEARANCE OVER TIME – ANALYSES FROM BRODALUMAB TRIAL DATASETS**

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**OBJECTIVES:** We analysed the DLQI and PASI scores from the pivotal active-comparator brodalumab studies AMAGINE-2 and AMAGINE-3, in order to better understand the dynamic relationship of quality of life (QoL) and complete psoriasis clearance (defined as 100% reduction in PASI score or PASI 100) over time. **METHODS:** Pooling data from the two identically-designed pivotal trials, we defined two groups of subjects receiving constant brodalumab (n=339) or constant ustekinumab (n=590) over the extended 52 week study period. Subjects' attainment of PASI 100 (“complete clearance”) and DLQI score 0 or 1 (“no impact of disease on QoL”) was described throughout this period, and their time to first attainment was calculated and compared. Analyses were separated according to study drug (ustekinumab or brodalumab) to assess whether treatment had any impact on the relationship of DLQI and complete clearance. **RESULTS:** At week 52, 51% and 55% of brodalumab patients maintained PASI 100 or DLQI 0/1 respectively, and 43% maintained both. For ustekinumab patients, the corresponding percentages were 28% and 40% for PASI 100 and DLQI 0/1, and 24% had both. Over time, DLQI 0/1 tended to occur earlier than PASI 100, although the two followed a similar pathway generally. The median times to attainment of PASI 100 and DLQI 0/1 were 98 days and 56 days respectively for brodalumab patients, compared to 168 and 86 days for ustekinumab patients. The difference by treatment in time to attainment was statistically significant for both outcomes. **CONCLUSIONS:** Patient DLQI score improved with biologic treatment along a timeframe comparable to PASI 100, although a DLQI score of 0/1 was generally achieved before PASI 100 was achieved. The more efficacious biologic, brodalumab, was associated with quicker and higher rates of attainment of complete clearance as well as DLQI 0/1 compared to ustekinumab.

**PSS30: PATIENT PREFERENCES IN THE TREATMENT OF PERIODONTAL DISEASE: MULTI-DIMENSIONALITY AND VALIDITY**

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**OBJECTIVES:** Parodontopathies refer to all inflammatory diseases of the tooth retaining apparatus. Various treatments are available for therapy. So far, it is unclear which patient-relevant endpoints determine the benefit of treatments. The aim of the study is to document the relative importance of patient-relevant endpoints for therapies in
periodontal disease. In addition, it will be examined to what extent changing decision criteria influence the validity of Discrete Choice Experiments (DCE). METHODS: Two randomized online-supported DCEs with different decision models were performed. For each model, six patient-relevant endpoints were considered as attributes for morbidity and side effects of the therapy. "Tooth loosening/tooth loss" was presented as a multi-dimensional attribute with varying severity and the number of teeth concerned. The data were analyzed by Random Parameter Logit (RPL) model and Latent Class (LC) model. RESULTS: Data from N=627 participants (Model1:N=309, Model2:N=318) were evaluated. The results of the RPL-model show in both DCEs that decisions were significantly influenced from "tooth loosening/tooth loss" (Model1:Koef.:0.827; Model2:Koef.:0.885). In the two questionnaire versions, the attributes "tooth loosening/tooth loss", "gum bleeding", "pain in everyday life" and "pain by the therapy" occupied the front ranks and influenced the patients benefit most. Significant standard deviations (p<0.01) for "tooth loosening/tooth loss", "pain" and "performing the treatment" were indicative of heterogeneity in the sample. CONCLUSIONS: The study analyzed patients' preferences in the treatment of periodontal disease. From the perspective of patients, avoidance of tooth loosening/tooth loss and pain are the most important criteria in the treatment. It was also shown that the side effects as well as the performance of the therapy influence the evaluation of the patients to a lesser degree. The LC model revealed preference differences in the subgroups. In both DCEs, one class whose decisions were mainly influenced by the "tooth loosening/tooth loss" was identified. In each other class "pain" was more important.

PSS31: MIXED METHODS EVALUATION OF AN ITCH NUMERIC RATING SCALE AMONG ADULT AND ADOLESCENT PATIENTS WITH ATOPIC DERMATITIS

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OBJECTIVES: To explore the relevance of itch to adults and adolescents with atopic dermatitis (AD) and assess validity of the Itch Numerical Rating Scale (NRS). METHODS: A mixed-methods study consisting of concept elicitation (CE) interviews, 2-week daily diary, and cognitive interviews (CI) of adults and adolescents (≥12 years) with AD. The Itch NRS asked about “worst itching” in the past 24 hours on an 11-point scale (0 [no itch] – 10 [worst itch imaginable]). The qualitative and quantitative data were analyzed. RESULTS: Itch was the most common symptom reported in AD. All participants (N=44) confirmed relevance of itch as a concept; 43/44 agreed on the wording, understanding of the response scale, and correctly referred to the 24-hour recall period when discussing their responses. Of the 15 participants probed, 13 incorrectly reported their “average” itch with several describing their chosen response as the severity of their itch compared to their worst-ever itch. These findings align with participants’ suggestion that “worst itch” be defined (eg, “rate your itching severity by circling the number that best describes your worst level of itching…”). Quantitative diary data demonstrated acceptable psychometric performance. Participants utilized the majority of the response scale on ≥1 days, with an even distribution across response options. Day 7 (test) versus Day 14 (retest) reliability was high, with an observed intraclass correlation coefficient=0.94 among stable participants. Concurrent validity was acceptable, with strong correlations (0.55–0.76) observed with other diary AD symptom measures. There were no major overall differences between adults and adolescents. CONCLUSIONS: Adults and adolescents noted that the Itch NRS was easy to understand and relevant to their AD experiences, with clear alignment between item wording and language used by participants. Psychometrically, the Itch NRS was a valid and reliable measure of itch that applied to both adults and adolescents.

PSS32: VALIDITY AND INTERPRETATION OF A SKIN PAIN NUMERIC RATING SCALE AMONG ADULTS AND ADOLESCENTS WITH ATOPIC DERMATITIS

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OBJECTIVES: To explore the relevance of skin pain in adults and adolescents with atopic dermatitis (AD) and assess validity of the Skin Pain Numerical Rating Scale (SP-NRS). METHODS: A mixed-methods study consisting of concept elicitation (CE) interviews, 2-week daily diary, and cognitive interviews (CI) was conducted with adults and adolescents (≥12 years) with AD. The SP-NRS queries "worst skin pain" in the past 24 hours on an 11-point scale (0 [no pain] – 10 [worst pain imaginable]). Qualitative and quantitative data were analyzed. RESULTS: Among 43 CE
OBJECTIVES: To develop a patient-reported questionnaire, measuring the severity of Chronic Pruritus (CP) and its impact on health-related quality of life (HRQoL). METHODS: A three-step approach was followed: (1) a Conceptual Framework (CF) was developed using a systematic literature review and experts’ interviews, to render the relevant domains for severity and HRQoL; (2) the CF was updated following Focus Groups with 19 patients suffering from CP (underlying skin condition: psoriasis, atopic dermatitis, scalp seborrheic dermatitis, urticaria or sine materia in elderly people); participants’ verbatim were textually reported into transcripts, which were analyzed using qualitative content analyses to understand how patients suffering from Chronic Pruritus perceived the severity of CP and its impact on health-related quality of life (HRQoL); (3) a pool of items was generated for each domain of interest, and their comprehensibility was tested during cognitive debriefing with patients (semi-structured interviews; n=21 additional patients). RESULTS: 155 articles were reviewed to develop the preliminary CF addressing 16 domains of HRQoL and 7 of severity, which was clinically validated by 2 medical experts. Patients’ verbatim showed some relevant differences on severity, between clinical and patients’ perspectives in terms of (i) intensity of itch, (ii) duration and (iii) extension. Moreover, sub-domains of interest for HRQoL were revealed: sleep and fatigue, coping and anticipation, sexual life, emotions and cognitions, concentration, daily activities, cognitions attributed to others, social relations, and time spent. A preliminary version of the questionnaire was drafted and refined after cognitive debriefing sessions. The final version includes 50 items. CONCLUSIONS: A first version of this patient-reported questionnaire was developed following international guidelines and namely, using patients’ interviews. This questionnaire will measure the severity of CP and its impact on HRQoL in a comprehensive and clinically sound manner.

PSS34: THE PATIENT-REPORTED DISEASE BURDEN IN ADULTS WITH ATOPIC DERMATITIS: A CROSS-SECTIONAL STUDY IN CANADA AND EUROPE

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OBJECTIVES: To compare the patient-reported burden associated with atopic dermatitis (AD) across severity levels in adults in Canada and Europe. METHODS: This cross-sectional study from clinical practices included adults (18–65 years) diagnosed with AD by dermatologists, general practitioners, or allergologists. Subjects who provided informed consent were categorized as mild (n=369; 37.1%), moderate (n=348; 34.8%), or severe (n=277; 27.9%) AD based on Investigator’s Global Assessment, and completed a questionnaire that evaluated itch (pruritus numerical rating scale [NRS]), PO-SCORAD visual analog scale [VAS]), pain NRS, sleep (PO-SCORAD VAS); quality-of-life (QoL; Dermatology Life Quality Index [DLQI]), and anxiety/depression (Hospital Anxiety and Depression Scale [HADS]).
Subjects were also stratified by inadequate efficacy/intolerance/contraindication to cyclosporine (Post-cyclo; n=33 [2 mild, 11 moderate, 20 severe]) and any systemic immunomodulatory agent (Post-IMM; n=57 [8 mild, 17 moderate, 32 severe]) and compared with the severe group. **RESULTS:** Demographics were similar across severity groups (38.5%–47.7% male; mean age 36.6–38.4 years), but Post-cyclo and Post-IMM populations were significantly older, 44.8 and 43.5 years, respectively (P<0.05). Compared with moderate and mild AD, subjects with severe AD had significantly more comorbid atopic conditions (P<0.001); greater itch severity as indicated by significantly higher mean pruritus NRS and PO-SCORAD itch VAS scores (P<0.001); worse sleep (P<0.001 on PO-SCORAD sleep VAS); more pain (P<0.001 on pain NRS); and higher levels of anxiety and depression (P<0.001 on HADS subsccales). Mean±SD DLQI score among severe patients (16.4±6.8) was consistent with a very large effect on QoL and was significantly higher than moderate (10.6±6.3; P<0.001) and mild (5.4±5.0; P<0.001). The burden among Post-cyclo and Post-IMM subjects was generally similar to that of subjects with severe AD. **CONCLUSIONS:** Adults with AD reported a substantial burden across multiple domains that appeared to be significantly higher in those with severe disease and in Post-cyclo/Post-IMM subjects.

**PSS35: GENERATING PATIENT INSIGHTS IN DRY EYE DISEASE WITH A SOCIAL MEDIA LISTENING STUDY**

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**OBJECTIVES:** To understand evolving trends in social media on dry eye disease (DED) and generate valuable insights on patients’ perceptions of disease burden, diagnosis, treatment, unmet needs and quality of life (QoL). **METHODS:** Data for the time period (Dec 2016 – Feb 2017) was downloaded through social media data aggregator using MeSH terms based on predefined search criteria. Social media discussions specific to DED on channels such as Twitter, Blogs, Forums and Newswires were evaluated to identify discussion themes, stakeholders and sentiment. Post data anonymization, text algorithms and manual curation was used to analyse and map psychological aspects expressed by stakeholders to understand impact on patients’ QoL and state-of-mind. **RESULTS:** A total of 2,641 posts were considered for analysis. Twitter was primary source of information, contributing to 61% of total posts. Discussions were primarily on treatment options, causes and symptoms of DED. The analysis provided key insights into patients’ experiences, patient journey and unmet needs. While the study suggests a need to increase awareness about DED among patients, lack of standard diagnostic tools, treatment options and specialists emerged as key unmet needs. Poor QoL is also highlighted by patients with significant impact on daily activities, work and commute. Further exploration of QoL also revealed a huge gap in patient emotional needs. Fear, anger and sadness were expressed by 20%, 18% and 30% posts respectively. Additionally, 1% of patient posts also indicated suicidal tendency. **CONCLUSIONS:** Real world data from social media is an effective way to generate patient insights to inform decision-making and strategy in early drug development. Findings from social media analysis and patient preference studies can be leveraged to bring the patient perspective into clinical development and access plans. It will be interesting to see how HTA bodies and payers evaluate these patient insights, for consideration into early scientific advice.

**PSS36: IXEKIZUMAB TREATMENT IMPROVES ITCHING AND HEALTH-RELATED QUALITY (HRQOL) OF LIFE IN PSORIASIS PATIENTS IN LATIN AMERICA**

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**OBJECTIVES:** Ixekizumab (IXE) is a high affinity anti-IL-17A antibody shown to be highly effective in reducing psoriasis plaques and improving health-related quality of life (HRQoL) over a 12 week induction period in moderate-to-severe psoriasis (PsO) patients. This study assessed the impact of IXE compared to etanercept (ETN) and placebo (PBO) on itch and HRQoL after 12 weeks. **METHODS:** In this phase 3, multicenter, double-blind, active-comparator, PBO-controlled trial, patients were randomized to receive subcutaneous PBO (N=193), ETN (50 mg, twice weekly; N=382), or 80 mg IXE as 1 injection every 2 weeks (IXE Q2W; N=385) or every 4 weeks (IXE Q4W; N=386) for up to 12 weeks following an initial 160-mg starting dose. (At Week 12, all patients received open-label IXE Q4W through Week 60.) In all Latin American patients (n=102), analyses were performed on itch (assessed by a 0-10 numeric rating scale [NRS]), Psoriasis Skin Appearance Botheromeness (PSAB, score range 0–30), and HRQoL (assessed by the Dermatology Life Quality Index [DLQI; score range 0–50]). Treatment comparisons were made using an ANCOVA model with missing values imputed by last observation carried forward. **RESULTS:** Patients treated with IXE had statistically significantly greater reductions in itch vs. ETN and PBO as early as week 1 (Q2W -3.1, Q4W -3.3, ETN -0.5, PBO -0.5); and improvements continued through week 12 (Q2W -5.8, Q4W -5.6, ETN -4.5, PBO -1.3; all p-values vs. PBO <.001). At week 12 IXE patients showed significant improvements in DLQI (Q2W -5.8, Q4W -
12.7, Q4W -11.7, ETN -11.0, PBO -2.2; p-values vs. PBO <0.001) and PSAB (Q2W -21.9, Q4W -21.3, ETN -15.0, PBO -4.7; p-values vs. ETN<0.01 and PBO <0.001). **CONCLUSIONS:** After 12 weeks IXE treatment led to significant improvements in itch as early as 1 week, and in HRQoL and PSAB compared to ETN and PBO in Latin American PsO patients.

**PSS37: ASSESSING THE DISEASE COURSE AND TREATMENT OF PSORIATIC ARTHRITIS (PSA) IN CANADA**

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**OBJECTIVES:** To describe disease course, severity level, and treatment of PsA patients in Canada. **METHODS:** Data were gathered from the Adelphi Real World 2015 Disease Specific Program. Rheumatologists (n=25) and dermatologists (n=5) completed patient record forms on consulting PsA patients. The same patients completed self-completion questionnaires voluntarily. Advanced therapy (AT) included patients receiving biologics and apremilast. **RESULTS:** Data were collected for 92 PsA patients; 53.3% were female, and mean age was 50.2 years. Patient-reported mean time since diagnosis was 2.45 years (n=66), although time from original symptom onset was 3.99 years (n=56). Advanced Therapy: 83 (88.5%) patients have received AT, 25 (27.2%) were considered AT naive, and 4 (4.3%) were on AT with specific line unknown. Among those on AT, 35 (55.6%) were on Anti-TNF, 21 (33.3%) were on non-Anti-TNF, and 7 (11.1%) were on apremilast. Only one patient has since discontinued AT. Additionally, 36 (53.7%) of these patients received at least one DMARD before commencing AT, mean duration, where known, was 14.4 months prior to AT (n=24). DMARD: Including those who subsequently progressed to AT, 49 (53.3%) patients received at least one DMARD; mean time since initiation was 27.9 months (n=36). Change in Disease Severity with current treatment: Levels of disease severity at diagnosis (n=92) were mild (25.0%), moderate (47.8%), and severe (27.2%). Current severity was mild (76.1%), moderate (22.8%) and severe (1.1%). Since initiation of current therapy (for patients on current therapy >3 months), 62 (84.9%) improved or remained mild, 9 (12.3%) remained moderate or severe, 2 (2.8%) deteriorated. **CONCLUSIONS:** Patients on AT were more likely to be severe on initiation of current treatment. Long delays between symptom onset and diagnosis highlight a significant gap in the identification and diagnosis of PsA in Canada. With current treatments available, PsA patients are able to achieve some degree of improvement in disease severity.

**PSS38: PSORIASIS (PSO) PATIENTS’ PROFILE AND IMPACT OF THE DISEASE ON PATIENTS’ QUALITY OF LIFE AND WORK PRODUCTIVITY IN A REAL-LIFE SETTING IN BRAZIL**

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**OBJECTIVES:** To describe psoriasis (PsO) patients’ profile and to evaluate the impact of the disease on patients’ quality of life and work productivity in a real-life setting in Brazil. **METHODS:** This analysis used data from the GfK Disease Atlas multinational, retrospective, cross-sectional syndicated survey. The study sample consisted of Brazilian patients who have or have ever had moderate to severe PsO and who were receiving a prescribed treatment at the time of the survey. **RESULTS:** The overall sample included 497 Brazilian patients, 50% were male, mean age of 45.4, 81%. Of the total sample, 22% had moderate to severe psoriasis [Psoriasis Area Severity Index (PASI > 10 or Body Surface Area (BSA) ≥ 3 or Dermatology Life Quality Index (DLQI) > 10)] with mean disease duration of 7.7 years. Psoriatic arthritis (18%), anxiety or depression (18%) and cardiovascular diseases, obesity or type II diabetes (13%) were the most prevalent comorbidities among PsO patients. Despite treatment, 18% of patients reported current disease exacerbating and 77% exacerbated in the past 12 months. At the moment of survey, 11% were being treated with biologic/biosimilar agents only, 4% with biologic and conventional systemic, 4% biologic and topical, 2% a combination of biologic, conventional systemic and topical agents. These patients had significant burden in terms of quality of life and work productivity, DLQI (mean score: 10.5); 12-Item Short-Form Health Survey (SF-12) - (Physical component summary: 47.4 and mental component summary: 41.6) and overall work impairment due to PsO: 42.2%, absenteeism (13.9%), presenteeism (35%). **CONCLUSIONS:** Results from this large real world survey revealed specific clinical aspects of psoriasis among Brazilian patients helping to address some medical needs in daily practice. Despite treatment, psoriasis places a substantial burden on patients’ life.

**PSS39: DAILY LIVING WITH EARLY RETINAL DISEASES: THE PATIENT PERSPECTIVE**
OBJECTIVES: To determine which daily activities are difficult to perform and important to patients who retain a good visual acuity in the early stages of neovascular age-related macular degeneration (nAMD) or diabetic macular oedema (DME). METHODS: Multinational, individual, structured interviews were conducted with consenting patients in Canada, France, UK and the USA to identify activities that patients find both important and difficult to engage in, despite good best-corrected visual acuity (BCVA) (defined as ≥64 letters on an Early Treatment Diabetic Retinopathy Study [ETDRS] chart). Patients were diagnosed with nAMD or DME for no longer than a year. The interview questionnaire was designed by the investigators, based on their own knowledge, data available in the literature, and advice from additional experts. Overall, 18 pre-defined activities pertaining to 4 categories (reading & writing, independent living, navigation & orientation, social interactions & occupation) were investigated. RESULTS: A total of 46 patients were interviewed; 26 with nAMD and 20 with DME. The average age was 72.1 ± 9.9 years. Patients had an average BCVA of 74 letters, and the majority were still driving. A majority of patients (74%) reported impairment in ≥1 activity due to their eye condition. Isolated cases reported impairment in up to 12 activities. Driving, adjusting to darkness, reading (print and on-screen), doing hobbies such as playing cards or creating artwork, and working with the hands were difficult for the greatest number of patients. Of these, driving, reading, and doing hobbies were rated as being the most important. CONCLUSIONS: Patients who maintain good BCVA with nAMD and DME were found to still experience difficulties in performing important activities in their daily lives (ie, driving, reading, and doing hobbies). This study suggests that endpoints other than BCVA may be needed to assess impairment from the patient perspective in the early stages of these diseases.

PSS40: ATOPIC DERMATITIS IS ASSOCIATED WITH POOR QUALITY OF LIFE IN ADULT PATIENTS.

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OBJECTIVES: Atopic dermatitis (AD) is a chronic skin disorder characterized as an inflammatory, relapsing, non-contagious... Patients with AD could experience a wide range of symptoms ranging from trivial problems to major handicaps that may affect their lives. METHODS: A self-administered questionnaire was designed and completed by adults AD patients. Data were collected from patients' members of the French Eczema associations or patients seen in four department of Dermatology in France. Validated tools for evaluating the burden (ABS-A) and QoL (DLQI and SF12) were administrated. The severity of AD was also evaluated using a modified version of Patient Oriented (PO)-SCORAD. The severity of the AD disease was classified as mild or moderate (score<25) [AD-MM] or severe(score>25) [AD-S] according of this same score. RESULTS: 1,024 subjects responded to the questionnaire, including 596 women (58.3%): the mean age of the patients was 39.7 for women and 46.5for men (p<0.001). 697 subjects were classed as [AD-MM] and 327 were classed as severe AD [AD-S]. 25.8% reported a familiar history of AD at 1st degree. On average, 56% of subjects reported to visit visited a dermatologist on a regular basis to monitor their AD (28.3%[AD-MM]) to 74%:[AD-S]). The DLQI score obtained for patients was significantly higher than for [AD-MM] 6.4[6.0;6.9] vs. 16.2[15.5;16.8], p<0.001. No differences in the physical dimension of SF12 were observed. In contrast, the mental dimension was degraded in both groups, and showed a significantly more impact in [AD-S] patients compared to [AD-MM] patients: 35.9[34.9;36.8] vs.42.4[41.6;43.1], p<0.001. The burden evaluated by ABS-A increased with the severity of AD: AD-MM=18 [16.7;19.3] vs. AD-S=43.4[41.6; 45.2],p<0.001. CONCLUSIONS: These results show that the QoL of adults suffering from AD is significantly more impacted in severe AD patients than in moderate and mild patients. The tangible impact of atopic dermatitis on the QoL must be taken into account in order to improve therapeutic care.

PSS41: SKIN PAIN IN PSORIASIS

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OBJECTIVES: Although it is now widely accepted that itching occurs in cases of psoriasis, skin pain is often neglected despite being readily reported by patients. Accordingly, we wished to measure the frequency and consequences of skin pain. METHODS: A sample of 5,000 individuals representative of the French population aged from 15 to 80 years was chosen using the usual method of quotas (gender, age, geographical location, and socio-professional category) and asked to respond to an internet-based questionnaire regarding these items. One subgroup of subjects suffering from psoriasis was identified, as well as another subgroup without any form of dermatosis (control group). The quality of life was measured with the DLQI in the subjects with psoriasis, and with the SF12 in
both subgroups. RESULTS: 244 individuals (of which 53% male) reported psoriasis, corresponding to a prevalence of 4.8%. The mean age was 47.8 ± 15 years, which was not significantly different from the control group. Both the physical and mental dimensions of the quality of life evaluated by SF12 were degraded in the patients with psoriasis (48.8 ± 8.7 vs. 51.6 ± 8 and 41.7 ± 9.7 vs. 45.4 ± 9.1, p<0.001, respectively). Skin pain was 5 times more common in the group with psoriasis than in the group without (33% vs. 6%, p<0.001). In subjects with psoriasis accompanied by painful skin, a significant degradation in the quality of life was observed, as measured by both the DLQI (13.59 vs. 7.66, p<0.001) and the physical dimension: 46.76 vs. 49.82, p<0.001) and the mental dimension (39.15 vs. 42.97, p<0.001) of the SF12. CONCLUSIONS: Skin pain is clearly overlooked in cases of psoriasis, even though it is present in one-third of patients and aggravates the effect of the condition on patients’ quality of life.

PSS42: ATOPIC DERMATITIS IN ADULTS: IMPACT ON SEXUALITY

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OBJECTIVES: Currently, only few studies have been conducted to evaluate the burden associated with atopic dermatitis, a chronic skin inflammatory disease in adult subjects and its impact on their sexuality. METHODS: A self-administered questionnaire was designed and completed by adults AD patients. Data were collected from patients members of the French Eczema associations or patients seen in four department of Dermatology in France. Validated tools for evaluating the burden (ABS-A) and QoL (DLQI and SF12) were administrated. The severity of AD was also evaluated using a modified version of Patient Oriented (PO)-SCORAD. The severity of the AD disease was classified according of this same score. RESULTS: 1,024 subjects responded to the questionnaire (women: 58.3%). 283 subjects had mild AD, 414 had moderate AD, and 327 had severe AD. 81.65% of the patients declared to be affected by AD on their sexuality behavior. 12% of the patients reported genital involvement. This proportion increased with the severity of AD: 2.8%, 9.4% and 22.02% respectively for mild, moderate and severe AD (p<0.001). 40.34% of patients with severe AD declared that AD affected their libido (compared to 17.26% and 4.11% for mild or moderate patients). The burden scores (ABS-A: 39.4±19.5 vs. 23.7±19.4 (p<0.001)) and QOL (DLQI: 8.9±7.1 vs. 4.5±7.2 and mental dimension of SF12: 36.5±9.1 vs. 40.9±10.2) were significantly (p<0.001) more impacted in patients with genital involvement. Finally, 59% of the patients with genital involvement declared that this localization was the most distressing manifestation of their condition. CONCLUSIONS: These results show a major impact of AD on Patients’ sexuality and libido. The QOL and the burden are significantly more deteriorated in patients with genital involvement compared to patients without this symptom. Our results on a large sample show that involvement of the genital areas is relatively common. Physicians should take into account this symptom to improve patients care.

PSS43: PATIENT CHARACTERISTICS AND DISEASE BURDEN OF PSORIASIS IN MEXICO: A REAL-WORLD PHYSICIAN AND PATIENT SURVEY

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OBJECTIVES: The burden of psoriasis (PsO) is known to be high but data in Mexico remain scarce. This study aimed to describe PsO patients' characteristics and determine the burden of PsO in Mexico. METHODS: Data came from the multinational, cross-sectional GfK Disease Atlas real-world evidence program, collected between September 2015 and January 2016. Eligible patients currently or previously had moderate-to-severe psoriasis, as determined by the dermatologist, and were treated with prescription. Disease severity (Psoriasis Area Severity Index [PASI]) and Body Surface Area (BSA) was assessed by the dermatologist. Patients self-reported their quality of life from the Short-form 12 (SF-12), EuroQol five dimensions (EQ-5D), and Dermatology Life Quality Index (DLQI) questionnaires, and their work productivity and activity impairment from the Work Productivity Activity Impairment (WPAI) Questionnaire. RESULTS: The Mexican sample included 40 dermatologists and 248 PsO patients; 55% of patients were male and 83% had plaque PsO. The BSA percentage and mean PASI score were 9.9% and 3.3, respectively. Overall mean disease duration was 9.3 years, and the mean number of PsO consultations in the last year was 4.8. Furthermore, 23% had a concomitant diagnosis of either cardiovascular disease, psoriatic arthritis, obesity, and/or Type II Diabetes. Almost half (48%) of patients reported scaling or redness/inflamed skin symptoms. Only 5% (n=12) reported currently exacerbating, and 77% reported exacerbating in the last year. Almost half (52%; n=128) used topical agents only, and very few patients (7%; n=17) were on biologic/biosimilar agents only. Approximately 20% received conventional and topical agents. SF-12 physical and mental were 46.9 and 45.7, respectively, and the mean
DLQI and EQ-5D scores were 7.1 and 0.9, respectively. From the WPAI, 9.4% of patients reported absenteeism, 28.7% presenteeism, and 31% activity impairment. **CONCLUSIONS:** Results from this real-world survey show that despite current treatment, there remains a high disease burden with PsO in Mexico.

**PSS44: PREFERENCES OF THE GENERAL POPULATION TO AVOID ORAL HEALTH OUTCOMES: RESULTS OF A BAYESIAN DISCRETE CHOICE EXPERIMENT**

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**OBJECTIVES:** Paucity of data on quality of life associated with oral health conditions and concerns over using generic measures has led to alternative approaches being used to value prevention of oral health problems. The purpose of this study was to obtain willingness-to-pay (WTP) values for preventing oral ill-health to inform economic modelling, using a discrete choice experiment (DCE). **METHODS:** The first stage of the DCE was to identify attributes and levels associated with specific oral health problems (tooth decay and gum disease). This was informed by health states expected to be included in an oral health economic model and a focussed literature review. Pretesting was conducted, followed by two surveys administered online to UK general population panel. The DCE study included a cost attribute to estimate respondents' WTP to avoid specific oral health problems. A Bayesian D-efficient design was employed using estimates from first survey as informative priors in the final statistical design. **RESULTS:** Attributes were defined according to the type of tooth affected (molar, pre-molar, anterior), gum disease and cost. The levels within tooth attributes were: no problem, decay without pain, decay with pain and tooth requiring removal. Coefficients and standard errors from the first survey (N=944), were used to inform the second survey (N=1047). Conditional logit model reflecting repeated observations from the same individuals was fitted to the data. The model was statistically significant. Avoiding problems in anterior teeth was most highly valued followed by premolar and molar teeth. Avoiding decay with pain in an anterior tooth generated the highest WTP (mean £245; 95% CI £216 to 272) followed by removal of anterior tooth (mean £203; £169 to £235). **CONCLUSIONS:** Results demonstrate that people have stronger preferences to avoid problems with anterior teeth compared to pre-molars and molars. Prevention of gum problems are also highly valued by respondents.

**PSS45: PREFERENCES OF PARENTS TO AVOID ORAL HEALTH OUTCOMES IN CHILDREN: RESULTS OF A DISCRETE CHOICE EXPERIMENT**

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**OBJECTIVES:** Economic evaluation of oral health interventions requires a valuation of potential health outcomes. This is challenging for interventions targeted at children due to a lack of measures of oral health outcome for children. We propose direct elicitation of oral health states by parents of children. We aim to obtain willingness-to-pay (WTP) values for preventing oral ill-health in children to inform economic modelling, using a discrete choice experiment (DCE). **METHODS:** We characterised oral health problems using type of tooth and severity in decay. This was informed by economic model planning, clinical advice and a focussed literature review. Pretesting was conducted, followed by two surveys administered online to UK general population panel. The DCE study included a cost attribute to estimate respondents' WTP to avoid specific oral health problems. A Bayesian D-efficient design was employed using estimates from the first survey (N=257), were used to inform the second survey (N=1050). Conditional logit model was fitted to the data. Avoiding problems in permanent teeth was valued much higher than baby teeth by the parents. They were willing to pay more to prevent tooth decay in baby teeth than avoiding baby tooth loss. Avoiding decay with pain in the child's permanent tooth generated the highest WTP (mean £417; 95% CI £373 to £465) followed by removal of permanent tooth (mean £415; £373 to £459). Avoiding decay with pain in baby tooth obtained a WTP of £107 (95% CI: £70 to £141). **CONCLUSIONS:** Results demonstrate that parents have stronger preferences to avoid problems with permanent compared to baby teeth.

**PSS46: BARRIERS TO MANAGEMENT OF DIABETIC EYE DISEASES IN TURKEY: DR BAROMETER SURVEY**

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**CONCLUSIONS:** Results from this real-world survey show that despite current treatment, there remains a high disease burden with PsO in Mexico.
OBJECTIVES: The Diabetic Retinopathy (DR) aims to assess the awareness of, and access and barriers to diabetes management, including screening for Diabetic Eye Diseases (DED). METHODS: DR Barometer Study was implemented in 41 countries. 426 adult with diabetes and 175 health care professionals (14 diabetes specialists, 46 ophthalmologists, 64 primary care providers, 51 others) were surveyed in Turkey. The patient survey consisted of 46 questions divided into four sections covering awareness and knowledge, current care for diabetes and eye complications, screening and treatment of DR and Diabetic Macular Edema, and quality of life. The provider survey comprised 43 questions covering characteristics of the practice. RESULTS: Patients and providers who participated in the study were self-selected. Most of patients (45%) were aged between 18 and 39 years. 42% of respondents were in paid employment. 47% of respondents reported that they had no complications of diabetes. Of those who did have complications reported vision loss (23%), neuropathy (19%), kidney disease (13%), cardiovascular disease or stroke (13%), and foot ulcers (3%). 82% of these respondents reported issues in their daily activities: difficulty in driving (36%), working or keeping a job (33%), social interactions (31%). Providers reported the biggest barrier to eye exams as long waiting time for an appointment (34%). Waiting time for ophthalmologist exam was usually less than one week in 53% of practices. Barriers that were related to the healthcare system were primarily focused on the limited access to diabetes specialists (34%) or the cost, and proximity of care (27%). Ophthalmologists reported that the greatest challenges for improving patient outcomes in DED were late diagnosis (86%), ineffective screening services (54%), and limited access to patient education on DR and DME (43%). CONCLUSIONS: Even in this engaged study population, there are many remaining barriers for care. Knowing that diabetes-related vision loss is now preventable, addressing barriers to eye screening is an important policy issue and potential calls for action are needed.

PSS47: QUANTITATIVE ASSESSMENT OF OPHTHALMOLOGIST PRESCRIBING PATTERNS FOR SEVERE VERNAL KERATOCONJUNCTIVITIS (VKC) TO INFORM PAYER DECISION MAKING IN THE EU

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OBJECTIVES: VKC is a rare, chronic form of ocular allergy that can cause severe visual complications. It predominantly affects children and adolescents. Prevalence is estimated to be ≈3/10,000 individuals with higher rates in young males and hot dry climates. VKC is characterized by symptoms like severe itching, photophobia, foreign body sensation, mucous discharge and blurring of vision. Like many orphan diseases, there is a need for better understanding real world disease management. This research aims to explore the burden of illness of VKC and treatment patterns in severe VKC, to better inform payer decision making. METHODS: A survey targeting 60 ophthalmologists from several EU countries treating severe VKC was undertaken. The survey covered the differences in treatment approach and use of non-licensed use of ciclosporin eye drops to treat severe VKC. RESULTS: Physicians identified several problems with prolonged use of corticosteroids, including development of glaucoma (11% of patients), and highlighted limitations of antihistamines in severe VKC. If not treated adequately, patients with severe, persistent VKC may develop corneal ulcers and chronic eye disease throughout adulthood which can threaten vision, reducing visual acuity in ~27% of patients, and may require surgical intervention. In the light of this ciclosporin is often used to treat severe VKC; off-label branded ciclosporin (in up to 87% of cases, where licensed) and hospital formulations (~13%) are frequently used. 20% of physicians reported encountering frequent reimbursement restrictions for severe and very severe VKC. CONCLUSIONS: The survey highlighted an unmet need for licensed therapies for severe VKC Antihistamines and corticosteroids are not considered to be viable maintenance therapies for severe VKC. Given these limitations and the absence of licensed options, hospital-compounded formulations and off-label products of ciclosporin are currently prescribed, despite inconsistencies in formulation and downsides related to non-licensed use in severe VKC.

PSS48: DOSE INCREASE BEYOND LABELLED DOSE OF BIOLOGIC TREATMENTS IN PSORIASIS PATIENTS: A REAL-WORLD STUDY IN SWEDEN

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OBJECTIVES: Previous research shows dose increase beyond labelled dose (DIBLD) of biologic treatments is commonly observed in psoriasis. However, this has not been studied in Sweden. This study estimated the occurrence of DIBLD of biologic treatments including anti-TNFs (adalimumab; etanercept) and ustekinumab in patients with moderate to severe psoriasis in Sweden. METHODS: The study included adult psoriasis patients beginning maintenance phase of treatment with adalimumab, etanercept, or ustekinumab between 1 January 2013 and 31 December 2015 with at least 2 prescriptions during study follow-up. Patients’ psoriasis diagnoses were identified in the Swedish National Patient Registry and corresponding drug dispensing data in the Swedish Prescribed Drug
OBJECTIVES: The research aim was to compare antifungal drugs for topical treatment of onychomycosis listed in British National Formulary 70 (BNF, 2016) and Ukrainian National Formulary 8thedition (UNF, 2016). METHODS: data and comparative analysis of preparations included in the formularies. RESULTS: Topical antifungal drugs for onychomycosis are represented in the chapters “Fungal skin infections” of BNF and “Topical antifungal preparations” of UNF. These preparations are mostly recommended for skin, but some of them may be also used for nails. It must be noted that analysis of antifungals listed in UNF was a little complicated due to the lack of clear delimitations in the indications. BNF recommends 10 preparations to treat nails in different dosage forms: 1 powder, 1 spray, 2 creams, 6 lacquers and paints. UNF recommends only 8 preparations, most of them are semi-solids (87.5%: gels – 37.5%, creams – 50%) and only 1 cutaneous solution (12.5%). Imidazoles are the widest group of the analyzed preparations (50% in BNF, 100% in UNF). The preparations, except of lacquers/paints, are generally recommended for transungual application that involves nail removal. The distinct difference in the lists is absence of preparations specially developed for nails in UNF; however, antifungal nail lacquers have been registered in Ukraine. Conversely, BNF recommends 6 such preparations: paint with tioconazole, lacquers with amorolfine (4) and paint with boric, salicylic and tannic acids. CONCLUSIONS: The obtained results revealed that topical antifungals specially developed for nails are not included into UNF, whereas BNF does recommend them. There is a need for review of topical antifungal preparations and inclusion of lacquers/paints into UNF for good treatment.

PSS51: ANALYSIS OF THE INDIVIDUAL ECONOMIC BURDEN (BORNE-COST BY THE PATIENTS) IN ADULT PATIENTS WITH ATOPIC DERMATITIS.
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OBJECTIVES: Atopic dermatitis (AD) is a chronic skin inflammatory disorder with potential impact on the patients’ QoL. Few studies analyzed the burden of the disease, especially the economic burden. In AD, we sought to analyze the borne-cost by the Patients (BCP) that is defined as the amount that a household must pay after deducting any reimbursements provided by governmental agencies (in charge of health insurance). METHODS: A self-administered questionnaire was designed and completed by adults AD patients. Data were collected from patients’ members of the French Eczema associations or patients seen in four department of Dermatology in France. The severity of AD was also evaluated using a modified version of Patient Oriented (PO)-SCORAD. The severity of the AD disease was classified as moderate[AD-M] or severe [AD-S] according to this same score. Specific questions related to the medical and non-medical resources consumed by the patients over the past 12 months were proposed. RESULTS: 1,024 subjects responded; 67.7% were professionally active. The BCP was €462.15 [398.9; 525.2] for AD-S patients and 247.40 € [206.7; 288.1] for AD-M patients. Emollients were the most frequent patients expenditures: AD-S: 93%: BCP: 254 € and AD-M: 82.5%: BCP: 93 €. Clothing was the he main non-medical expenses: AD-S: 27%: BCP: 162 € and AD-M: 19%: BCP: 91 €. Finally, the proportion of patients purchasing AD-related hygiene products was: AD-S: 85%: BCP: 103 €, and AD-M: 71%: BCP: 63 €. CONCLUSIONS: These results show that the CBP of adults suffering from AD is significantly higher for patients with severe-AD than for patients with moderate-AD. While emollients represent the most significant category of expenditure, the expenses generated by clothing (requirement cotton quality ‘high, necessity to changing clothes frequently in part due to frequent applications of emollients and topical-treatments) are significant. Our results on a large sample show that the economic burden of AD is significant, which should be taken into account to improve patients’ care. Larger studies specifically focused on the BCP should be conducted in a next future.

PSS52: EPIDEMIOLOGY OF PSORIASIS IN COLOMBIA: A GOVERNMENTAL DATABASE ANALYSIS

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OBJECTIVES: There is lack of epidemiological information regarding psoriasis in Colombia. We performed an epidemiological analysis of the disease in Colombia based on Health Benefits Information System (RIPS) data, which is a healthcare governmental database, estimating geographical distribution, health insurance providers, gender, age and overall prevalence for years 2010-2015. METHODS: We extracted patient data from RIPS database regarding the diagnosis with ICD-10 codes L400, L401, L404, L408 and L409. The extracted information allowed us to identify the patients with the diagnosis who used healthcare provider services in Colombia during the six-year period 2010 to 2015 considering both the presumptive and confirmed diagnosis in order to obtain useful information for the characterization of this population. RESULTS: We found that 19,735 people were diagnosed with psoriasis during the years 2010 to 2015, which would mean an average prevalence in this period of 4.2 cases per 10,000 people per year. The age group with the highest prevalence of psoriasis was people older than 60 years with a prevalence of 13.0 cases per 10,000 people per year. For “confirmed cases” only, average prevalence for men and women would be 1.8 and 1.5 cases per 10,000 people per year, respectively. We have also found that Antioquia was the region with greater prevalence in this period: 7.4 cases per 10,000 people per year. CONCLUSIONS: There seems to be an important underreporting of epidemiological information on RIPS database regarding psoriasis. Prevalence figures found in our study are significantly lower than those published in other studies around the world. However, the information generated is useful in our local context in order to create and implement health-related policies.

PSS53: SENSITIVE SKIN IN FRANCE: UPDATED EPIDEMIOLOGICAL DATA

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OBJECTIVES: An international consensus has now been established for the definition of sensitive skin [SS], as proposed by a group of experts assembled by the International Society for the Study of Itch. The only study on the prevalence of SS in France was conducted in 2004. METHODS: A national sample of 5,000 individuals representative of the French population was chosen by means of the usual method of quotas. The subjects participating in the study gave a response to an open question on the presence or absence of SS, and the appearance of burns, tingling, or irritation in the presence of various factors. The QoL was measured by the DLQI in subjects reporting SS and by the Sf12 in all subjects. RESULTS: Of the 5,000 participants (48.9% men). When asked
the question "Do you have SS?", 51.9% of men, 66.0% of women responded with "sensitive" or "very sensitive" (p<0.001). The participants reported an associated dermatosis in 65.88% of cases with very sensitive skin, 41.2% of cases with quite sensitive skin, 19.53% of cases with less sensitive skin. The QoL as measured by both the DLQI and the SF12, was significantly impaired. The DLQI scores were 10.4; 7.4; and 4.6, respectively, in subjects with very sensitive, quite sensitive, and less sensitive skin. In the results of the SF12, the mental dimension was significantly more affected by the reported sensitivity, with 39.9 for very sensitive skin, 43 for relatively sensitive skin, and 46.2 for less sensitive skin. CONCLUSIONS: In 2004, 44% of men and 59% of women answered "sensitive" or "very sensitive" to the same question. Several explanations for this increase can be given: 1) the concept of sensitive skin may have become more familiar to the population, 2) the sample size (4 times larger than the sample in 2004), 3) new or more aggressive environmental factors.

PSS54: HTA & MCDA IN THE TREATMENT OF MACULAR EDEMA

Ferrario L1, Foglia E1, Bandello F2, Ferri C2, Figini I3, Franzin M2, Gambaro G3, Introini U2, Staurenghi G4, Tadini P2, Zuppini T5, Tessari R5, Scarpa G6, Urban F26, Beltramini S7, Tobaldi RF7, Nicolò M7, Ancona C7, Moriconi S8, Nuti E9, Fusco F3, Croce D1, LIUC University, Castellanza, Italy, 2Scientific Institute San Raffaele, Milano, Italy, 3Valduce Hospital Como, Como, Italy, 4Hospital Authority L. Sacco, Milano, Italy, 5Sacro Cuore Negrar Hospital, Negrar, Italy, 6Ca Foscello Hospital, ULSS 9 Treviso, Treviso, Italy, 7San Martino Hospital, Genova, Italy, 8Asl Toscana Centro - Empoli, Empoli, Italy, 9Polliclinico Santa Maria alle Scotte, Siena, Italy

OBJECTIVES: The present study aimed at evaluating the implications related to the implementation of a multidimensional approach for the study of alternative technologies (Ranibizumab, Dexamethasone and Aflibercept), for treating diabetic macular edema, in 4 Italian Regional settings: Lombardia, Liguria, Toscana and Veneto. METHODS: 4 HTA reports, covering all the EUnetHTA Core Model dimensions, were developed by means of literature research, specific questionnaires, and self-reported interviews administration. A final appraisal phase was simulated by applying the MCDA approach in which a first prioritisation phase, conducted by 21 healthcare professionals, was followed by a final evaluation, evaluated by 12 professionals, attributing a 3-level rating score to each domain. One-way Anova tests were also performed in order to investigate the presence of statistically significant differences. RESULTS: No statistically differences emerged with regard to the prioritisation phases, except for the equity dimension (p-value=0.013) that was considered the most relevant aspect within the Toscana setting. All the other Regions reported a superior score for the safety dimensions. The 12 evaluators, despite their different professional titles and referring to various hospitals within 4 Regional settings, attributed similar scores to the HTA dimensions during the appraisal phase, demonstrating the robustness of the MCDA process. No statistically significant differences (p-value=0.05) emerged concerning the scores attributed to Ranibizumab, Aflibercept and Dexamethasone in the 4 Regions, except for Dexamethasone’s safety and efficacy dimensions (p-value=0.002). Lombardy evaluators provided more conservative scores as the HTA was conducted in the first part of the life cycle of the technology. CONCLUSIONS: The results reported high homogeneity in both the prioritisation and evaluation phases, demonstrating consistent behaviour among different professionals. The MCDA approach suggests that Dexamethasone could be considered the preferable treatment to adopt within the target population, having acquired higher scores than the comparators (p-value<0.001) in all the 4 Regions under assessment.

PSS55: PRIMARY TREATMENT PATTERNS AMONG GLAUCOMA PATIENTS IN KOREA FROM 2002 TO 2013 USING THE NATIONAL HEALTH INSURANCE SYSTEM CLAIMS DATA

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OBJECTIVES: Due to the rapidly increasing life-expectancy and changes in lifestyle behaviors in Korea, the prevalence of glaucoma has increased steadily in recent years. Evaluations in primary treatment strategy patterns for glaucoma are lacking in Korea and have merit in order to assess the quality of care for glaucoma patients. METHODS: The health claims data from the Korean National Health Insurance Service was used to identify glaucoma patients from 2002 to 2013. Glaucoma patients were divided into primary open angle glaucoma (POAG) and primary angle-closure glaucoma (PACG) patients, identified using the codes for the Tenth Revision of International Classification of Diseases. Hospital records for drug prescriptions, admissions, and surgical interventions were used to identify primary treatment strategies, which included medication, laser treatment, and surgery. The proportions of primary treatment strategies for each year and according to glaucoma subtypes were assessed. RESULTS: Among POAG patients, 56.2% of the patients did not receive any type of treatment, and 43.5% were managed by medications in 2002. Among PACG patients, 80.0% did not receive any type of treatment while 16.6% were managed by medications in 2002. With each passing year, the proportion of patients without any interventions decreased, with POAG and PACG patients receiving medications increasing to 75.4% and 55.5% in 2013, respectively. While 8.6% of PACG patients received glaucoma-related surgery, only 1.0% of POAG patients received surgery in 2013. Among newly diagnosed PACG patients in 2008 who received surgery, the majority of
patients (7.8% out of 8.0%) received surgery within the first year of diagnosis. **CONCLUSIONS:** The primary treatment strategy shifted from no intervention to medication and surgery between 2002 and 2013. Surgery was more prevalent for PACG patients compared to POAG patients, and most newly diagnosed PACG patients who received surgery did so within the first year.

**PSS56: A LONGITUDINAL PATTERN OF CARE FOR PROSTAGLANDIN PRESCRIPTION FOR GLAUCOMA IN KOREA**

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**OBJECTIVES:** While the prevalence of glaucoma has increased in recent years in Korea, evaluations in management patterns for glaucoma are lacking. We investigated prostaglandin prescription patterns in order to assess the quality of care for glaucoma patients. **METHODS:** Glaucoma patients were identified using the health claims data from the Korean National Health Insurance Service from 2002 to 2013. Using the Tenth Revision of International Classification of Diseases, glaucoma patients were divided into primary open angle glaucoma (POAG) and primary angle-closure glaucoma (PACG). Outpatient and hospitalization prescription records were used to identify and categorize prostaglandin drugs into latanoprost, travoprost, bimatoprost, and tafloprost. The proportions of each subtype of prostaglandin drug prescribed for each year and according to glaucoma subtypes were assessed. **RESULTS:** When all four types of prostaglandin drugs were first available in 2010, the proportions of prostaglandin drugs among POAG patients were 80.0% for latanoprost, 13.5% for travoprost, 3.0% for bimatoprost, and 3.5% for tafloprost. The proportions for PACG patients were 92.4%, 17.9%, 2.7%, and 6.0% for latanoprost, travoprost, bimatoprost, and tafloprost, respectively. In 2013, the proportion of latanoprost decreased to 63.4% while the proportion of tafloprost increased to 18.6% for POAG patients. Among PACG patients, the proportion of latanoprost decreased to 57.6% and the proportion of tafloprost increased to 14.4%. **CONCLUSIONS:** While the primary prostaglandin drug for both POAG and PACG remained unchanged in latanoprost from 2010 to 2013, the proportion of latanoprost decreased steadily during the 4-year period. On the other hand, the proportion of tafloprost increased rapidly for both POAG and PACG patients from 2010 to 2013.