PRM68
HEALTH ECONOMIC ANALYSIS OF PNEUMOCOCCAL VACCINATION – EXAMPLE FROM BULGARIA
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OBJECTIVES: To evaluate cost-effectiveness of pneumococcal vaccination of children with 10-valent (PHiD-CV) compared with 13-valent pneumococcal conjugate vaccine (PCV-13). **METHODS:** A Markov cohort model which simulates in a Bulgarian birth cohort the disease process of invasive disease (ID) (meningitis and bacteremia), community acquired pneumonia (CAP), and acute otitis media (AOM) over life-time caused by S. pneumoniae and non-typeable Haemophilus Influenzae (NTHi). The cohort model essentially considers the perspective of the health care payer. Bulgarian specific epidemiological and demographic data and data from other country sources were obtained for the model. Base case assumptions include estimates of pneumococcal and NTHi infection rates as well as vaccine efficacy based on published literature, 94% vaccine coverage, herd protection and a (3+1) vaccination schedule. One-way sensitivity analyses performed to assess the impact of changes in key model assumptions. **RESULTS:** PHiD-CV and PCV-13 are projected to prevent 29.4 and 29.9 cases of invasive diseases respectively and 437 and 434 bacteremia hospitalizations respectively . PHiD-CV in comparison with PCV-13 is projected to prevent additional 9393 cases of AOM, 426 myringotomies and 2801 GP visits. Vaccinating a birth cohort with PHiD-CV is expected to generate 41 more QALYs compared to PCV-13. The estimated total savings for health care system are 1.77 mil Euro. The PHiD-CV is dominant in comparison with PCV-13. Sensitivity analyses indicate that GP visits for AOM and efficacy vs. AOM due to Streptococcus Pneumonia non-Vaccine Types Sp nVT have biggest impact on results. **CONCLUSIONS:** Overall, PHiD-CV is expected to have betterI impact and under the given assumptions, PHiD-CV dominates PCV-13 because it also has a larger cost offsets.

PRM69
CORRELATING COST EFFECTIVENESS OUTPUT WITH PATIENT LEVEL DATA INPUT VIA THE IMS CORE DIABETES MODEL (CDM)
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OBJECTIVES: Analysing patient level data (PLD) within cost-effectiveness (CE) models offers the potential to better understand patient profiles associated with greatest health economic benefit. The objective of this study was to contrast the application of average treatment efficacy profiles compared to patient level treatment efficacy in assessing the CE of insulin glargine (IG) versus Neutral protamine Hagedorn (NPH) in Type 2 diabetes mellitus (T2DM) **METHODS:** This study used the IMS Core Diabetes Model (CDM), a validated and established diabetes model to evaluate the CE of switching to IG from NPH using published effectiveness data from a large population based cohort. Average HbA1c reduction after switching from NPH was -0.18% and weight gain was 0.5kg. Annual diabetes specific therapy cost was £573 (IG) versus £320 (NPH). A PLD extract was obtained from NHANES and the CE of IG versus NPH assessed applying (a) overall mean treatment effects (MTE) and (b) baseline HbA1c, BMI and sex adjusted treatment effects (ATE). Costs (2012 UK£) and benefits were discounted at 3.5%. **RESULTS:** For the MTE and ATE scenarios, the incremental cost effectiveness ratio (ICER) was £28,925 and £57,279 respectively. For MTE scenario, 765 (41.1%) of subjects were CE at the £20,000 willingness to pay (WTP) and 47 IG subjects (6.1%) were both cost saving with increased health benefit. Using ATE, 525 (28.2%) were CE at the £20,000 WTP threshold with 164 (31.2%) of IG subjects identified as both cost saving with increased health benefit. The odds ratio (OR) of being both cost saving with greater health benefit was significantly associated with age, OR=0.89(0.87-0.93) and baseline HbA1c, OR=6.11 (4.64-8.03). **CONCLUSIONS:** The identification of patient characteristics associated with greater potential for health gain and reduced cost is an important goal. The analysis of PLD alongside simulation model output provides an additional mechanism for informing health care decision-making.

PRM70
COMPARISON OF MARKOV AND DISCRETE EVENT SIMULATION MODELING TECHNIQUES WITH APPLICATION TO COST EFFECTIVENESS ANALYSES
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OBJECTIVES: To assess the bias introduced to absolute costs, absolute QALYs and the incremental cost effectiveness ratio (ICER) associated with Markov models, compared with discrete event simulation (DES) models. To investigate how such biases are a function of cycle length and half-cycle correction. **METHODS:** A hypothetical three health state model was constructed using both Markovian and DES approaches. Costs and utility were assigned to each health state and the ICERs between two treatment strategies were estimated. Six Markov models using different cycle lengths (1 month, 3 month, 1 year), and with and without half cycle correction were constructed. Differences in the absolute costs and QALYs generated between each Markov model were compared with the DES approach and the ICERs generated by each model were compared. **RESULTS:** Markov model simulation was shown to introduce biases in the absolute costs and QALYs when compared with a DES approach. The bias was related to the duration of the time cycle with the results converging to the DES values as the time cycle was reduced. The initial bias in cost fell from 14% to less than 1%; QALY bias was consistently below 1%. The ICERs show bias between 2.4% and 9.6% when using a 1 year cycle and between 0.6% - 5.4% when using a 1 month cycle. The half-cycle correction reduced absolute bias between 2% - 10%, the ICERs were not affected. The time cycle duration was the primary parameter in reducing bias. **CONCLUSIONS:** Markov models introduce bias due to the simplifying assumptions of fixed cycle length and half cycle correction; DES models do not suffer the same biases. It is suggested that when the ICERs produced are close to the Willingness to Pay threshold, Markov models should be analyzed with shorter cycle length or a DES approach adopted to ensure conclusions are robust.

PRM71
MODEL-BASED ECONOMIC EVALUATIONS IN ALZHEIMER'S DISEASE : A REVIEW OF MODELING METHODS
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OBJECTIVES: To review the modeling-based economic evaluations (MB2E) of acetylcholinesterase inhibitors (ACE) and memantine (MEM) used in the field of Alzheimer's disease (AD). **METHODS:** A systematic literature search was carried out based on several electronic databases such as Medline or the Cochrane Library up to November 2012. Modeling frameworks used to depict the natural history of AD and incorporation of treatment effects were qualitatively described and compared. **RESULTS:** More than thirty MB2E were identified with several local adaptations based on ten original modeling frameworks. First published MB2E were either Markov state-transitions models or partition failure time survival models while most recent MB2E relied on discrete events simulations. The hallmark of the disease, the cognitive dimension, was first introduced to model the disease progression mainly based on the Mini Mental State Examination (MMSE) scale. The two other fundamental-functional and behavioral-dimensions were taken into account as a second step. Models relied on distinct clinical milestones and risk equations to extrapolate intermediate clinical endpoints from clinical trials (mainly on cognition and function) into long-term final endpoints. These latter were delay in severity, loss of patient autonomy, institutionalization, burden of care and quality-adjusted life years. Differences occurred as well on the way inter-patient heterogeneity was incorporated with a trend towards more micro-simulations technics. Eventually, predictors and inter-relations between the several dimensions of the natural history of the disease seemed not to be fully captured in the model structures with challenging needs to assess the resulting potential biases. **CONCLUSIONS:** Advanced modeling methods in the field of AD were being introduced to better capture the continuous, progressive and multivariate natural history of AD. Further work is warranted given the emerging early diagnosis technics, neuropathological biomarkers and targeting therapies.

PRM72
THE COST-EFFECTIVENESS OF SEQUENTIAL FIRST- AND SECOND-LINE TREATMENTS IN METASTATIC RENAL CELL CARCINOMA USING REAL-WORLD DATA AND A PATIENT-LEVEL SIMULATION MODEL
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OBJECTIVES: Previous cost-effectiveness analyses of targeted therapies in metastatic renal cell carcinoma (mRCC) have been based on randomised trials and evaluate just one single treatment-line. The aim of this study was to estimate the real-world cost-effectiveness of sequential first- and second-line treatments for patients with mRCC using a patient-level simulation (PLS) model. **METHODS:** Based on patient-level data from a Dutch population-based registry, a PLS model was developed that comprised entities (i.e. patients with mRCC), attributes assigned to the entities (i.e. prognostic factors), and events (i.e. second-line treatment or death). Patients were repeatedly simulated from the model and time-to-event was estimated using a lognormal distribution. A separate sampling process was used to determine which type of event occurred. Time to death following second-line treatment was modelled using a Weibull distribution. Lifetime health care costs were modelled using patient-level data from the registry. **RESULTS:** In current daily practice, 50% (341/686) of patients did not receive any targeted therapy and 42% (291/686) received sunitinib as first-line therapy. In the second line, 31% (33/107) were treated with sorafenib and 31% (33/107) with everolimus. Mean overall survival (OS) was 13.6 months and mean costs were €69,622 for all patients. In a strategy where all patients are treated according to clinical guidelines, mean OS was 15.2 months and costs were €91,059. This meant an increase in OS (1.6 months) and costs (€21,437) compared to current practice, with an incremental cost-effectiveness ratio of €159,107 per life-year gained. Probabilistic sensitivity analyses showed the robustness of these results. **CONCLUSIONS:** A complete disease model and real-world data are essential in estimating real-world cost-effectiveness. Our PLS model allows comparisons between treatment strategies spanning multiple treatment lines, which will ultimately help to reveal the optimal strategy. For example, guidelines-based treatment appears to increase both OS and costs compared to current daily practice.

PRM73
THE ROLE OF SIMULATION MODELING IN PLANNING LONG-TERM CLINICAL TRIALS IN TYPE 2 DIABETES
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OBJECTIVES: Long-term cardiovascular outcomes studies are routinely undertaken to demonstrate safety in all new diabetes therapies. Given that diabetes models are extensively validated to contemporary outcomes trials they offer the potential to inform on design of new trials. The objective of this study was to use an established diabetes model to explore the relationship between levels of glycaemic control, major adverse cardiovascular events (MACE) and sample size. **METHODS:** The IMS CORE Diabetes Model (CDM) a validated and widely used simulation model was initiated with patient level data (PLD) drawn from NHANES. The model was run with a five-year time horizon and the sample sizes required to detect a difference in MACE (defined as myocardial infarction, stroke or CV death) at the 5% level as a function of change in HbA1c evaluated. **RESULTS:** PLD from NHANES was available on 1853 subjects with mean (SD) age 63.6(12.1) years, 53% male, duration of diabetes 9.6(8.5) years, baseline HbA1c 7.4% (1.8), systolic