for income was higher than that of health. In all cases, as often observed, hyperbolic discounting characterised by decreasing rate over increasing delay, was observed.

PRM60

GENERAL METHODOLOGICAL ISSUES IN COST-EFFECTIVENESS ANALYSIS INSPIRED BY THE ASSESSMENT OF DASATINIB, NILOTINIB AND IMATINIB FOR 1ST- LINE CHRONIC MYELOID LEUKAEMIA

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OBJECTIVES: In 2011-12, the cost-effectiveness of imatinib, dasatinib and nilotinib for 1st-line chronic myeloid leukaemia in the UK was evaluated by NICE. We discuss three methodological issues which strongly influence the estimated cost-effectiveness of these drugs. These issues are also important for the cost-effectiveness of many other drugs and medical devices. **METHODS:** We discuss the pros and cons of the following competing methods. 1) Estimation of overall survival: Method A: estimated as the cumulative duration of 1st-, 2nd- and 3rd-lines of treatments. Method B: estimated from the surrogate responses: complete cytogenetic response and major molecular response; 2) Cost-effectiveness of subsequent treatments: the cost-effectiveness of 1st-line drugs are substantially affected by the cost-effectiveness of subsequent drugs. Method A: traditional method of modelling estimated costs and QALYs of subsequent drugs. Alternatively, minimise impact of cost-effectiveness of subsequent treatments by either Method B: setting per patient costs and QALYs of subsequent treatments equal between treatment arms, or Method C: cap the cost-effectiveness ratio whilst on subsequent treatments at the willingness to pay threshold; 3) Future drug prices: This is an important issue given that the patent for imatinib will expire soon, in 2016, after which its price may fall substantially. Method A: use the current list prices of all drugs in the future, as required by NICE. Method B: assume constant drug prices until patent expiry, at which time assume a fixed price cut. Assuming a modest 25% price cut on patent expiry, the ICER for nilotinib vs. imatinib increases substantially, from £36,000 to £54,000 per QALY. **RESULTS:** The pros and cons of the various methods are discussed. **CONCLUSIONS:** This study informs important methodological issues which apply to many health technologies. The study ultimately contributes to more accurate assessments of the cost-effectiveness of health technologies, and hence whether a given technology should be publicly-funded.

PRM61

EXTERNAL VALIDATION OF A CARDIO-VASCULAR DISEASE MODEL

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OBJECTIVES: Cardiovascular disease is the leading cause of death in Germany. For a better communication of the individual risk profile, a group of researchers of the University of Marburg developed ARRIBA, a tool for a better communication between the general practitioners and the patient, that reports the individual 10-year probability of a cardiovascular event. To further enhance communication and to include lifetime risk and time-to-event estimates in this tool, we developed and validated a state-transition microsimultion model (STMM). The focus of this presentation is on the validation of our model. **METHODS:** Our STMM was validated against the results from a US observational multi-cohort study (Berry et al., 2012) This study included data from 18 cohort studies with a total of 257,384 subjects and estimated the lifetime risk of cardiovascular events. Our STMM was populated with 28 cohorts closely matching 7 risk profiles and 4 age groups of the observational study and was evaluated for the time period of data collection in the observational study. Projected outcomes were proportion experiencing myocardial infarction, stroke, cardiovascular death, or any cardiovascular event. These outcomes were compared to the observed outcomes. **RESULTS:** When comparing the lifetime risk of experiencing any cardiovascular event estimated by the model to the observed data, 15 and 14 of the 28 cohorts were within the 95% confidence intervals of the observed results for men and women, respectively. The other estimates were within two and a half times this range. Although the observational study was a useful source for validation, the validation process was challenging with respect to matching cohorts and outcomes. One issue is whether a validation to a US cohort study is suitable for a European model. **CONCLUSIONS:** External validation increased our confidence in the microsimulation model. When comparable European data become available the validation will be repeated.

PRM62

TIME-DEPENDENCY FOR TREATMENT SEQUENCES: A CASE-EXAMPLE IN EPILEPSY

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OBJECTIVES: The memory-less feature of Markov models can be a limiting factor when treatment-sequencing needs to be modeled and the transition probability in second- and subsequent-line treatments are not constant. Although tunnel-states are commonly used to model time-dependency, they can become unruly. Hence, patient simulation models and/ or sophisticated software packages such as R are required to model complex time dependency. An alternate method of using nested markov models was presented at a previous conference to model time-dependency in treatment sequence for a hypothetical model in Excel. This method is now applied to a published model in epilepsy and results are validated using real data. **METHODS:** The Wilby 2004 epilepsy model is used as a reference to derive model inputs and validate results. It is a probabilistic treatment sequencing decision model in epilepsy implemented using R. The nested markov method involves first disaggregating the model by treatment, then combining the net present values of each treatment into the treatment sequence by weighting proportional to the time spent in the sequence, lastly followed by further discounting to account for placement in the sequence. Results obtained using the nested markov methods are validated with those published in Wilby 2004. **RESULTS:** Quality-adjusted life-years obtained with the nested Markov modeling approach were similar and were within the confidence intervals of results obtained by Wilby 2004. **CONCLUSIONS:** Nested markov models can be a simple alternative to model time-dependency if transparency and less intense computational programming are required. It represents a straightforward and intuitive approach to modeling a fixed treatment sequence, however, it may not be suitable if the position in a sequence is inter-changeable, and treatment effectiveness depends on the position in a sequence (e.g. cancer therapies where disease progression impacts treatment effectiveness).

PRM63

LONG-TERM BURDEN OF ASTHMA IN CHILDREN WITH ALLERGIC RHINITIS/ CONJUNCTIVITIS

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OBJECTIVES: To assess the long-term burden of asthma in children with allergic rhinitis/conjunctivitis. **METHODS:** We reviewed the literature on incidence of asthma in patients with allergy. Furthermore we estimated long-term outcomes associated with allergic rhinitis/conjunctivitis in children using a Markov health state model. The model was populated using data from a long-term prospective follow-up, where asthma status was recorded up to 10 years in patients receiving only symptomatic treatment for allergy and asthma symptoms. The model was used to explore the impact of key drivers of long-term patient outcomes. Burden to patient was measured as the difference between net present value of QALYs and life-years. **RESULTS:** Allergic rhinitis/conjunctivitis in childhood is associated with a risk of developing asthma. The asthma risk is highest at younger age and decreases as the child reaches adolescence and adult age. Furthermore, allergic rhinitis is a risk factor for childhood allergic asthma to persist into middle age. The model analysis showed that in per one hundred 10-year old patients with hay fever, but no previous asthma: 57 will develop asthma over a 10 years horizon; In total 55 QALYs are lost over a 10 years horizon of which 67% is attributable to allergic asthma; and Additional 23 respectively 43 QALYs are lost when analyzing on a 15 respectively 20 years horizon even when assuming no additional cases occur after year 10. **CONCLUSIONS:** Childhood allergic rhinitis is a risk factor for developing allergic asthma in childhood/ preadolescence. Allergic asthma in turn has a pro-found effect on the long-term burden of allergic rhinitis/conjunctivitis. Literature suggests that childhood asthma may impact on quality of life also when the patient reaches middle age. Taken together this suggests a large potential for specific immunotherapy with disease-modifying properties to reduce the burden of allergy and allergic asthma.

PRM64

BAYESIAN MTC MODELS TO COMBINE EVIDENCE FROM DIFFERENT TRIAL DESIGNS

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OBJECTIVES: Bayesian mixed treatment comparison models (MTCs) provide a powerful methodology to obtain estimates of relative efficacy between alternative treatments when head to head evidence is not available or not sufficient. Most evaluations only consider evidence from randomized controlled trials (RCTs), while information from other trial designs is ignored. In this work we propose 3 methods to extend MTC models to systematically include evidence from different trial designs using an application in Rheumatoid Arthritis (RA). **METHODS:** A systematic literature review identified 13 RCTs and 3 observational trials assessing the treatment effects of five anti-TNF agents currently licensed in Europe. Naïve Pooling does not differentiate between designs, one simply pools across all studies. It is not possible to down-weight designs of lesser quality or to adjust for bias. Alternatively observational data can be analysed separately and the results used to inform the prior distribution for the RCT model. This allows for bias adjustments and controlling the influence on the overall effect. In addition to that, a 3-level hierarchical model allows the direct comparison of estimates on study type level to overall level. The method accounts for between trial design heterogeneity; overall estimates become more conservative when study type estimates differ. **RESULTS:** Including evidence from observational trials to estimate the relative efficacy between anti-TNF agents in RA has strengthened our belief in the effect estimates. Overall, the observational trial data found less difference between the agents than was suggested by RCT evidence only. **CONCLUSIONS:** Observational data is available for many disease areas providing additional information on treatment effectiveness. We think it is important for an informed decision making process to include all available evidence. The proposed techniques provide a framework for systematically including evidence from different trial designs in a MTC model.

PRM65

A MINIMAL INFORMATION DECISION-ANALYTIC APPROACH TO EARLY HTA OF DIAGNOSTIC TESTS

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OBJECTIVES: To demonstrate a simplified approach to cost-effectiveness analysis of new diagnostic tests based on minimal information and without developing a full decision-analytic modeling framework, which is often complex, time consuming and potentially inefficient. **METHODS:** Using a simplified decision-analytic approach to the complete pathway of care from diagnosis to subsequent treatment, cost-effectiveness of the new diagnostic test is expressed as a mathematical function of diagnostic accuracy, cost, burden, and the cost-effectiveness of treatment. This function only includes parameters available during early test development phases and does not require any simulation. Parameter uncertainty is accounted for by applying probabilistic sensitivity analysis. In a clinical example, the cost-effectiveness of magnetic resonance angiography (MRA) compared with digital subtraction angiography (DSA) for the detection of new intracranial aneurysms is assessed in patients with previous subarachnoid hemorrhage. **RESULTS:** The simplified approach produced cost-effectiveness results for MRA compared with DSA in line with our previous and similar, but much more comprehensive assessment. The comprehensive assessment resulted in a net monetary benefit (NMB) of $1,910 (95%CI −1,809 to 5,565) and probabilities of effectiveness and cost-effectiveness of 98% and 87%, respectively (Willingness-to-pay threshold $50,000 per QALY). Our simplified approach returned a NMB of $1,779 (95%CI 1,170 to 2,477) with corresponding probabilities of effectiveness and cost-effectiveness of 100% and 98%, respectively. Hence, the simplified approach would already have provided a clear indication of the potential benefits of replacing DSA with MRA. **CONCLUSIONS:** Given the abundance of new diagnostic tests an approximation of the cost-effectiveness of new tests at minimal costs is highly valuable. Our low-cost mathematical satisficing approach supports improved use of health care resources by indicating 1) which tests are promising; 2) which tests are not promising; and 3) which tests require more rigorous economic evaluations to obtain improved estimates of cost-effectiveness but at a higher use of health care resources.

PRM66

DISCRETE EVENT SIMULATION: MODELING SIMULTANEOUS COMPLICATIONS AND OUTCOMES

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OBJECTIVES: To present an effective and elegant model approach to deal with specific characteristics of complex modeling. **METHODS:** A discrete event simulation (DES) model with multiple complications and multiple outcomes that each can occur simultaneously was developed. In this DES model parameters, attributes and distributions were estimated based on patient population (patient-level DES model). Next to this, the DES model was constructed in such a way that it is particularly capable to deal with: different disease states, multiple complications, and multiple long-term outcomes. Our model was designed for comparing two radiation treatments (photon vs. proton) for head and neck cancer. In this model the following elements were included: different disease states (local recurrency, distance metastasis, and combinations), simultaneous complications (xerostomia, sticky saliva, dysphagia, and thyroid dysfunction), and multiple long-term outcomes (overall survival, quality of life, costs). Estimates were based on the patient population (n=1013) treated with radiation therapy for head and neck tumor and combined with literature based estimates. **RESULTS:** The following discrete events were scheduled by a so-called statechart (system of graphical specification): primary tumor, mortality, time-to-event, and disease states. These events are scheduled with transitions following distributions that depend on tumor and other patient characteristics. In addition, the model contains a module for the primary tumor prognosis, and separate, parallel modules/events for each important complication. Costs and values of health for the different states/complications and combined to cost-effectiveness are included. **CONCLUSIONS:** This elaborated DES model allows multiple complications and outcomes to be modeled in parallel and is suited to estimate the long-term effects. The global structure of our model can be interesting for modeling other diseases that are associated with complex treatment regimes and multiple complications. In addition, side effects in parallel to main effects can be modeled and multiple outcomes of new pharmaceuticals compared to current medication.

PRM67

THE USE OF HEALTH ECONOMIC MODELS IN HUNGARIAN HEALTH TECHNOLOGY ASSESSMENT

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OBJECTIVES: To identify the possible problems and trends regarding health economic modelling in Hungarian Health Technology Assessment. We were especially interested in the general quality of health economic models. **METHODS:** We analyzed the submissions which were based on a health economic model, which were assessed by the Hungarian HTA Office since 2004. We created a database in which we summed up our findings: the type of the model, the quality and robustness of the model, the type of disease which was modelled. We sorted the models by these criteria and searched for correlations. We attempted to set some indicators regarding the quality of models. We also analysed some methodological and procedural problems from multiple aspects related to modelling in Hungary. **RESULTS:** Our findings show that the use of health economic models is increasing and that most of the models are decision tree and Markov types. The submitted Markov models are from the subtype of Markov chain models with only a few exceptions. Primarily simulation models are only used in a small share of submissions (11%), especially in the cases of chronic diseases. Trends show that the proportion of Markov models which have probabilistic sensitivity analyses are also increasing (from 0% to nearly 30%). The submitted models became more detailed and they show a distinct improvement in methodology during the past 8 years. These factors indicate the general improvement of the quality of Hungarian health economic modelling. **CONCLUSIONS:** Although it is not compulsory in Hungary, more and more manufacturers present or submit health economic models to the Department of Health Technology Assessment. Based on our findings, several factors indicate that the submitted models are getting more detailed, and better of quality.

PRM68

COMPARATIVE COMPUTATION SPEED OF EXCEL, VISUAL BASIC FOR APPLICATIONS, R, AND JAVA IN EXECUTION OF A MICROSIMULATION MODEL WITH PROBABILISTIC SENSITIVITY ANALYSIS

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OBJECTIVES: To compare the computation speed when running a microsimulation model and probabilistic sensitivity analysis (PSA) on four widely-available programming platforms: Excel, Visual Basic for Applications (VBA), R, and Java. **METHODS:** A simple microsimulation model predicting the number of handouts collected by 2500 ISPOR attendees during a congress was created to test efficiency measured by model running speed. Speed was based on the system time and included only the portion of code used to run the model, excluding any code for parameter input or output. Calculations were performed on a computer running Windows 7, dual core 2.6 GHz processor, with 4 GB RAM. All platforms except Excel were cross-validated by using a list of pseudo-random numbers as model inputs to ensure consistency of model outputs. PSA was conducted by sampling random probabilities from beta distributions and replicating the model 1000 times. Ten simulations of each base-case and PSA model type were run to assess variability in platform efficiency. **RESULTS:** The speed of Excel could not be timed in the base-case microsimulation since results were calculated instantly. VBA was slower than R with means of 0.09 seconds and 0.02 seconds, respectively. Java generated a system time of zero, indicating the program required <0.001s. The Excel PSA simulations required the most time with 33.4s, followed by VBA (29.4s). R required 19.0s and Java required the least amount of time (4.0s). CPU usage for PSA simulations was highest with Excel (~80%) and similar for all other platforms (~25%). **CONCLUSIONS:** With the obvious caveats that program speed is a function of computing power and coding efficiency, the results of this analysis demonstrate Java was consistently faster than Excel, VBA and R, which are commonly used for pharmacoeconomic models. With increasing model complexity and running times, exploration of alternate implementations for their execution is recommended.

PRM69

NETWORK META-ANALYSIS OF INTERVENTIONS FOR OVERACTIVE BLADDER AND DETRUSOR INSTABILITY – A HIERARCHICAL MODELLING APPROACH

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The current recommendations for the conservative management of overactive bladder symptoms and detrusor overactivity, given by NICE 2012, are pelvic floor muscle training, bladder training, sacral nerve stimulation, mid-urethral tape and antimuscarinic drugs- oxybutynin, darifenacin, solifenacin, tolterodine, and tropsium. More recently, emerging evidence suggests that Botulinum toxin type A is also an effective intervention for overactive bladder and idiopathic detrusor overactivity. Although a number of meta-analyses have been published reporting pairwise comparisons of the various interventions, to date no network meta-analysis has been undertaken comparing all interventions simultaneously. **OBJECTIVES:** To evaluate the clinical effectiveness of drug therapy, neuromodulation, botulinum toxin, and behaviour therapy, in the prevention of overactive bladder symptoms and detrusor overactivity. **METHODS:** Mixed treatment network meta-analyses for the individual, and classes (i.e. behaviour, drugs etc.), of interventions using WinBUGS. The correlations between the interventions within a class were addressed by conducting a mixed treatment network meta-analysis using a hierarchical model structure. **RESULTS:** Evaluation of the class of interventions, i.e. 'lumping' individual interventions with classes, demonstrates an increased precision in the outcome; however, categorising the interventions decreases the interpretability of the results. At the individual intervention level, the sparseness of the data decreases the precision of the estimates, but enables comparisons to be made between individual interventions. The hierarchical model, allows both increased precision, due to the utilisation of all of the available data, whilst still allowing comparisons to be made between individual interventions both within and between classes. **CONCLUSIONS:** Use of a hierarchical model increases the interpretability of the mixed treatment network meta-analysis whilst maximising the precision in terms of outcome. However, defining the hierarchical structure can prove difficult in some instances, with potential comparators residing at different levels in the hierarchy.

PRM70

WHAT IF ALL OTHER THINGS ARE NOT EQUAL? – ACCOUNTING FOR FUTURE CHANGES IN THE DECISION CONTEXT WHEN EXTRAPOLATING COST-EFFECTIVENESS RESULTS OVER TIME

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OBJECTIVES: Cost-effectiveness studies of health technologies where data are extrapolated from short term clinical trials to estimate results over appropriate decision making time horizons typically assume that the decision context remains