increased risk of secondhand smoking on morbidity and mortality. The impact of secondhand smoking was included in a previously published Markov model called the BENESCO model to estimate the economic burden in Korea. Transition probabilities and costs were acquired from Korean public data. The time horizon was lifetime and assumed 5% discount rate for costs. The estimated cost was compared with published estimates to establish external validity of the model. **RESULTS:** 13.7% of women (≥ 19 years old) and 30.7% of children (13-18 years old) from general population were exposed to secondhand smoke in household. Relative risks of secondhand smoking related diseases were lung cancer 1.9(95% CI 1.0-3.5), coronary heart disease 1.27(95% CI: 1.19-1.36), stroke 1.25(95% CI: 1.12-1.38) in women married for smoking husbands. The odd of Asthma onset was 1.32 times higher in children whose father smokes. The estimated costs were increased by 10 to 50%, compared with the model without the impact of secondhand smoking. **CONCLUSIONS:** Cigarette smoking and exposure to secondhand smoke is associated with significant economic burden. Policymakers should be advised that tobacco control should be aimed not just smokers, but those who are vulnerable to secondhand smoking, especially women and children lived with smokers.

PRM98

INVESTIGATING THE IMPACT OF CONTEMPORARY RISK FACTORS FOR DIABETES COMPLICATIONS AND THEIR EVOLUTION ON RISK PREDICTION USING THE UKPDS 82 EQUATIONS

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**OBJECTIVES:** UKPDS 82 provided updated and new event equations for use in type 2 diabetes mellitus (T2DM) that include new risk factor (RF) predictors. These new RFs do not routinely get reported in clinical studies; consequently, the objective of this study research was to report plausible baseline RF values and their time-dependent trajectories and quantify their impact upon predicted complication rates. **METHODS:** Availability of baseline and time-dependent RF data was assessed using a pragmatic literature review. Univariate sensitivity analysis of the UKPDS 82 equations (over a 40-year horizon ) was undertaken to assess the impact of low-density lipoprotein [LDL]; microalbuminuria (MA); heart rate (HR); white blood cell count (WBC): haemoglobin (Hb) and estimated glomerular filtration rate (eGFR) on predicted diabetes complications per 1,000 patients, using UKPDS baseline values (varied within the 95% central range). **RESULTS:** The review identified 32 studies reporting baseline RF values typically consistent with UKPDS (review versus UKPDS): LDL (2.6-3.8 versus 3.49mmol/l); MA (11-45% versus 6.5%); HR (67-72 versus 72bpm); WBC (5.7-7.9 versus 6.6x106/ml); Hb (12.4-14 versus 14.5g/dl); the exception was eGFR where baseline values (33-101 versus 77.5ml/min/1.73m2) and decline (0.3-5.2ml/min/1.73m2/year) varied widely. Utilising UKPDS 82 baseline values resulted in 877 macrovascular and 133 microvascular events predicted with 691 to 1,181 and 116 to 182, respectively, predicted in sensitivity analyses; drivers of risk were LDL and eGFR. Varying eGFR decline between 0.3 to 5.2ml/min/1.73m2/year resulted in annual event rates for end stage renal disease (ESRD) between 0.021 to 1.251%; holding eGFR constant over time resulted in ESRD annual event rate of 0.020%, significantly lower than observed in UKPDS (0.13%). **CONCLUSIONS:** Appropriate specification of RF is important in diabetes modelling. This study suggests that the UKPDS profile is generally consistent with other identified T2DM populations. Modelling a decline in eGFR improved the predictive accuracy of ESRD incidence.

PRM99

BETTER REIMBURSEMENT DECISION-MAKING BASED ON EXPECTED COST-EFFECTIVENESS: USING VALUE OF INFORMATION DECISION ANALYSIS TO IMPROVE THE DESIGN AND EFFICACY OF A PHASE III PROGRAM FOR ERLOTINIB

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**OBJECTIVES:** Erlotinib, a tyrosine-kinase inhibitor, has been recommended for use in non-small cell lung cancer patients harbouring an EGFR mutation. The present study is retrospective in nature; using published clinical trial data for erlotinib, it demonstrates how an analysis of Phase II data could be used to identify what data Phase III studies should focus on collecting. **METHODS:** Phase II data were identified through a targeted literature search and used to determine the cost-effectiveness of erlotinib, utilising a simple Markov model framework. Data from the literature were mapped to model inputs using statistical data analysis methods. Value of Information (VOI) analysis tools, such as Expected Value of Perfect Information (EVPI) and Expected Value of Partial Perfect Information (EVPPI) were used to identify those uncertain parameters having research value in a prospective Phase III program. These findings helped to optimise the design of a hypothetical Phase III trial for erlotinib that could collect data that is most relevant for reimbursement decision-making. **RESULTS:** At a cost-effectiveness threshold of £30,000 per quality-adjusted life year (QALY) gained, the population EVPI was £3,269,358, indicating that further research is valuable. The EVPPI identified the log hazards of erlotinib (intervention) and gefitinib (comparator) for progression-free survival and overall survival as the parameters for which uncertainty was the most valuable. The value of the uncertainty associated with other parameters, such as utilities and costs, was much lower. Hence, subsequent studies should focus on providing further information on efficacy parameters rather than on utilities and costs. **CONCLUSIONS:** Undertaking VOI analysis on data collected at Phase II can help ensure that Phase III trials are designed efficiently, in turn ensuring that uncertainty in future decision-making is minimised. This model demonstrated the VOI from a public policy perspective. This could be extended to other perspectives to ensure greater relevance in different settings.

PRM100

MODELING THE NATURAL HISTORY OF SECONDARY-PROGRESSIVE MULTIPLE SCLEROSIS: A NEW MODELING APPROACH USING DISCRETE EVENT SIMULATION

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**OBJECTIVES:** The ongoing ASCEND trial of natalizumab utilizes a novel composite endpoint, comprised of the Expanded Disability Status Scale (EDSS), Timed 25-Foot Walk (T25FW) and 9-Hole Peg Test (9HPT) to assess disability progression in patients with secondary-progressive multiple sclerosis (SPMS), due to the limited ability of EDSS alone to assess disability progression in this patient population. Given that the ASCEND data are not available, data from the IMPACT study was used to assess the cost-effectiveness of SPMS treatments in an economic model capturing the interrelated changes of these measures for individual patients. This study presents the model concept and assesses its external predictability. **METHODS:** A discrete event simulation was developed to predict times to disability progressions on EDSS, T25FW, and 9HPTand the occurrence of relapses over time, using four parametric (Weibull) functions, each adjusted by a Cox model to ensure that each event time was estimated based on patients' baseline and time-varying factors. Each disability scale's value is updated as events occur. Data from the IMPACT study (n=436, followed for 2 years) was extrapolated for longer term. Published data on EDSS from the University of British Columbia (UBC) MS database were used for long-term external validations. **RESULTS:** The model closely replicated all four endpoints as observed in the IMPACT study at two years. The predicted times for 25% of patients to reach EDSS 8 were consistent with those from the UBC data, with 13.4 (model) vs. 14.8 (UBC) years from EDSS 3.5–4.5, and 8.7 vs. 8.6 years from EDSS 6.0. The distributions of T25FW and 9HPT by EDSS level predicted at 10 years were consistent with those observed from the IMPACT study. **CONCLUSIONS:** This SPMS model reliably predicts short- and long-term disability levels, and can serve as the basis for economic evaluations of treatments for SPMS.

PRM101

IMPLEMENTATION OF POPULATION DYNAMICS IN MODELLING HEALTH AND BUDGET IMPACT OF AN INTERVENTION FOR A CHRONIC DISEASE WITH MULTIPLE DISEASE SUBTYPES

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**OBJECTIVES:** In a budget impact analysis (BIA), the population is supposed to include all patients eligible for the new intervention during the time span of decision: new incident cases and patients leaving due to death, cure, migration or other reasons, must be captured. Additionally, temporal changes in the actual number of individuals receiving the intervention must be quantified. While most of the guidelines for BIA emphasize this population dynamics aspect, recommendations on how to technically implement it are lacking. We introduce a method for implementing population dynamics in a chronic disease with multiple disease subtypes using object-oriented programming (OOP), and demonstrate its application in modelling health and budget impact of a treatment strategy for ankylosing spondylitis (AS). **METHODS:** A generic hierarchical patient class structure was developed to systematically organize the prevalent population and incident cohorts of patients with different disease subtypes. Using the concepts of inheritance and polymorphism in OOP, we formulated algorithms to efficiently compute health measures and resource utilization of individual patients in different classes, and to perform probabilistic sensitivity analysis. In the case study, a dynamic population model was developed to predict the burden of AS in the Dutch society over a 20-year period from January 1, 2015 onwards when a sequential treatment strategy including tumour necrosis factor antagonists was applied. Data for model parameterization were obtained from the Outcomes Assessment of AS International Study (OASIS) and literature. **RESULTS:** The case study demonstrated that our dynamic population modelling method offers an efficient approach to quantify annual as well as total health and costs for different decision time spans. Annual direct costs incurred by the AS patients in the Dutch Society would range from 471 to 496 million Euros between 2015-2035. **CONCLUSIONS:** Our method for implementation of population dynamics is efficient and generic, so it can be applied to other chronic diseases.

PRM102

BUDGET IMPACT ANALYSIS OF DELAYED-RELEASE DIMETHYLFUMARATE IN THE TREATMENT OF RELAPSING-REMITTING MULTIPLE SCLEROSIS IN ITALY

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**OBJECTIVES:** To evaluate the economic impact of a recently approved therapy, delayed-release dimethylfumarate (DMF; also known as gastro-resistant DMF), on the overall management costs of relapsing-remitting multiple sclerosis (RRMS) in Italy. **METHODS:** A budget impact model, adopting the perspective of the Italian National Healthcare Service (NHS), was used to compare healthcare costs of two different treatment scenarios: a) base-case, in which DMF is not reimbursed/funded by the NHS, vs. b) reimbursement-case, in which DMF is reimbursed and funded by the NHS. Healthcare costs sustained by the Italian NHS to manage the RRMS population (drug treatment, administration, therapy and disease monitoring, relapse management, treatment-related adverse events) have been calculated over 3 years and compared for the two scenarios. Impact of relapses for the disease modifying therapies (DMTs) included in the analysis was estimated using results from published literature. RRMS population treated with DMTs was estimated using Italian prevalence and incidence data. According to these estimates, the number of treated patients amounted to 35,100 at Year 1, 36,800 at Year 2, and 38,700 at Year 3. **RESULTS:** According to current price and reimbursement conditions established by the Italian NHS, it was estimated that the introduction of DMF (reimbursement-case) would determine a decrease of the budget impact, if compared with the base-case (non-reimbursement case). Over three years, the budget impact would be €1,388,640,000 in the base-case and €1,359,800,000 in the reimbursement-case (-€28,840,000; -2.1% relative budget variation). The main drivers for cost-saving were pharmacological treatment costs and reduced burden of relapses (corresponding to about 1,500 avoided relapses). **CONCLUSIONS:** At the current reimbursement

and cost conditions applied in Italy, the use of DMF is economically sustainable for the NHS. Plausibly, the introduction and usage of this new therapy in RRMS patients will ensure clinical benefits for patients without resulting in additional costs for the NHS.

**PRM103**

**QUANTITATIVE ASSESSMENT OF THERAPEUTIC VALUE OF INNOVATIVE MEDICAL TECHNOLOGIES: METHODOLOGY AND PRELIMINARY RESULTS**

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**OBJECTIVES:** Ministry of Health of Russian Federation announced the support of innovative development of pharmaceutical industry. In accordance with these plans, we aimed to develop a methodology for quantitative assessment of therapeutic value of innovative medical technologies in a multi-criteria decision analysis manner. **METHODS:** The questionnaire was developed during pilot survey (10 experts). Then 248 respondents assessed criteria significance (weights) of 14 features of an innovative drug and 7 features of a relevant disease. Also they estimated scale's values. The respondents were medical practitioners and decision makers in healthcare. Results of the survey were analyzed using statistical methods. **RESULTS:** The most valuable features are clinical efficacy and clinical safety with the weights of 9.77% and 9.08%, respectively. Absence of effective treatment of the disease, mortality and influence on quality of life also are among the valuable features with the weights of 8.08%, 7.72% and 7.47%, respectively. Minimal weights have new manufacturing technique of the drug (0.69%) and new drug formulation (0.03%). **CONCLUSIONS:** Significant and non-significant features of an innovative medical technology and disease for which it is intended in terms of therapeutic value were identified. We plan to optimize set of criteria and scales and then to assess reliability and validity of the developed instrument. This methodology being incorporated in the system of evaluation of medical technologies and combined with other methods of analyses will help decision-making regarding innovative drugs in Russia become more harmonious and transparent.

**PRM104**

**EIGHT WAYS TO IMPROVE THE INTERPRETATION AND REPORTING OF COST-EFFECTIVENESS ANALYSES OF SCREENING INTERVENTIONS**

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**OBJECTIVES:** The cost-effectiveness of screening interventions is typically examined using simulation models. These permit comparisons of multiple screening strategies. Cost-effectiveness estimates from such models depend, in part, on what alternatives analysts choose to compare and how the simulation results are interpreted. Sometimes the comparisons and interpretations made are inappropriate, which can obscure evidence and lead to the wrong policy conclusions. The objective of this study is to explain eight simple steps that analysts can take to avoid these problems. **METHODS:** We use examples from the literature to show how these problems can arise and to explain how they can be avoided. The examples chosen are from a recent systematic review of the cost-effectiveness of cervical screening. **RESULTS:** The eight recommendations are: (i) report costs and effects, rather than just incremental cost-effectiveness ratios (ICERs); (ii) present a cost-effectiveness plane; (iii) report cost and effects for all strategies, not just those on the efficient frontier; (iv) do not report ICERs for dominated strategies; (v) report costs and effects to sufficient significant figures; (vi) include all simulated strategies in the basecase analysis; (vii) do not report ICERs for strategies for which it is anticipated the inclusion of additional strategies would lead to significant changes in the estimated ratio; (viii) when there are multiple factors to vary in a screening programme, only vary these factors one at a time when creating alternative strategies. **CONCLUSIONS:** The cost-effectiveness estimates from simulation models are particularly dependent on the choices taken by analysts regarding both the modelling of alternatives and the interpretation of the cost and effects estimates. Although the analytical flaws informing our recommendations might seem obvious, they occur with surprising frequency in the literature. The simple eight-item list presented here will support better use of screening models in identifying optimal policy choices.

**PRM105**

**IMPACT OF GREXIT ON PHARMACEUTICAL PRICING: AN INTERNATIONAL REFERENCE PRICING ANALYSIS**

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**OBJECTIVES:** The possibility of Greece leaving the European Union (Grexit) is well-publicized, but its impact on the pharmaceutical industry has not been fully determined. Majority of established markets use pricing rules that reference products both across (international reference pricing; IRP) and within (therapeutic reference pricing; TRP) country-lines. IRP and TRP are used as effective measures to control price of pharmaceutical products. There is a growing need to understand how Grexit will impact these mechanisms through direct or indirect means. **METHODS:** Navigant's Price and Revenue Impact Simulation Model (PRISM), which simulates the impact of IRP and TRP, as well as parallel trade and generic entry, was used to quantitatively assess the impact on drug prices across 50 markets in the EU, North America, Latam, MENA-CIS and Asia. Respiratory products were analysed as a class to prevent a biased analysis towards particular pharmaceutical companies. Two potential scenarios were analysed with respect to Grexit: Markets referencing Greece switch referencing to Slovakia, a replacement low-priced Euro currency Mandatory price cut in Greece resulting from a currency shift to the Greek Drachma **RESULTS:** Outputs of the analysis include impact on price, revenue and net present value as well as parallel trade of the respiratory product class. Using a dynamic price development graph, the model provides explanations for price changes at re-referencing time-points. The model clearly demonstrates that Greece leaving the EU will have a significant impact on price and revenue across markets, demonstrating the spill-over caused by international referencing. **CONCLUSIONS:** The impact of Grexit goes well beyond Greece, directly affecting pharmaceutical price and revenue throughout Europe. PRISM can be used to assist manufacturers in developing a comprehensive pricing strategy and facilitate dialog with governments operating within fiscally constrained environments. The model can also be used to test future scenarios as emerging markets are increasingly adopting reference pricing.

**PRM106**

**DEVELOPMENT OF A CONCEPTUAL MODEL OF MULTIPLE MYELOMA FOR USE IN ECONOMIC MODELLING: A SYSTEMATIC LITERATURE REVIEW TO IDENTIFY THE EVIDENCE BASE**

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**OBJECTIVES:** This study sought to identify disease- and patient-specific characteristics impacting on disease progression and outcomes, and to determine key attributes to be used in developing a conceptual model of multiple myeloma (MM). **METHODS:** English language studies reporting MM attributes and their association with disease progression and outcomes were identified from Embase and Medline (2004–2014) and congress abstracts (2012–2014) in a systematic literature review (SLR). A second SLR of treatment guidelines, economic models, health technology reports and studies on the burden of MM was also used. An attribute was defined as a metric or characteristic of MM that plays a potential role in the disease process. These attributes can be explanatory (e.g. patient characteristics) or dependant (e.g. survival). **RESULTS:** From both SLRs, 95 MM attributes were identified. These were grouped into disease characteristics (e.g. light chains, International Staging System [ISS] stage, bone marrow plasma cells, extramedullary disease, karyotypic abnormalities), genetic factors [e.g. t(4;14), del(13p), del(17p), hypodiploidy, hyperdiploidy], patient characteristics (e.g. age, serum lactate dehydrogenase, gender, Eastern Cooperative Oncology Group performance status, comorbidities), outcomes (e.g. overall survival), quality of life and symptoms (e.g. pain, fatigue, weakness, bone fractures, infection). Attributes were then categorised as explanatory or dependent variables. Age, serum lactate dehydrogenase, light chains and M protein were among the most common explanatory variables in the literature. The most commonly reported dependent variable was overall survival, followed by quality of life. None of the studies presented a comprehensive set of determinants of disease progression and outcomes. **CONCLUSIONS:** MM is a heterogeneous condition and it is not yet clear which attributes play a key role in determining disease progression and survival. The next step in developing the conceptual model for MM is to ask physicians to validate the potential attributes identified and to clarify the relationships between validated attributes.

**PRM107**

**SIMULATING INDIVIDUAL PATIENT LEVEL DATA USING AN ILLNESS-DEATH MODELLING FRAMEWORK IN ORDER TO ADJUST FOR TREATMENT SWITCHING WHEN ONLY SUMMARY DATA ARE AVAILABLE**

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**OBJECTIVES:** Treatment switching commonly occurs in the pivotal HTA evidence for advanced or metastatic cancer treatments submitted to reimbursement agencies. Simple approaches, such as Intention-to-treat (ITT) analysis, have typically been applied to data with treatment switching, despite simulation studies showing these to drastically underestimate the underlying treatment effect. Therefore, before these studies are included in secondary analyses, the data must be re-analysed appropriately. When only summary data are available, individual patient level data can be reconstructed using a simulation approach. Given patients switch on disease progression, their progression time is assumed equivalent to their switch time. Simulating this effectively requires an illness-death modelling framework; the process of which is the aim of this research. **METHODS:** An example was used, where Kaplan-Meier curves for all three transition rates were available. The coordinates were extracted digitally from these scanned survival curves, and used to model the times for each transition. Many datasets were created, where the times for the transitions were simulated from the respective models. ITT summary statistics were calculated for each dataset; then averaged over. Examples with increasingly less information on which to estimate the transition rates were also systematically investigated. **RESULTS:** When information on transition rates is available, the process is easy to implement; giving data that are, on average, broadly representative of the original dataset with median survival times and overall survival hazard ratio differing by less than 10% and 0.05 respectively. As the information becomes more limited, the process requires additional assumptions, and ultimately may not be feasible. **CONCLUSIONS:** Using an illness-death modelling framework to simulate individual patient level data is affected by the information available to the analyst. However, this approach is important, when addressing treatment switching where only summary data are available, as the relationship between time to progression and overall survival is modelled correctly.

**PRM108**

**MARKOV MODELING OF HIV INFECTION IN RUSSIAN POPULATION**

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**OBJECTIVES:** Over the past five years, the prevalence and incidence of HIV in Russian Federation have increased dramatically. The application of global Markov models,