deaths attributable to AAA in Italy represented 28.0% of the 5EU total, despite Italy accounting for only 19.3% of the 5EU population in 2013. **CONCLUSIONS:** Our study reveals that the burden of AAA among the 5EU markets is most severe in Italy, which accounted for the highest number of both prevalent cases and deaths attributable to AAA in the 5EU. Throughout the 5EU, females accounted for a disproportionately high percentage of deaths despite constituting a low percentage of prevalent cases. Consequently, current screening guidelines should target both sexes, rather than males only.

PRM71

COST-EFFECTIVENESS OF ESCALATING TO NATALIZUMAB OR SWITCHING AMONG IMMUNOMODULATORS IN RELAPSING-REMITTING MULTIPLE SCLEROSIS IN ITALY

Furneri G[1], Santoni L[2], Ricella C[2], Prosperini L[3]
[1]*EBMA Consulting, Melegnano, Italy,* [2]*Biogen, Milan, Italy,* [3]*3Department of Neurology and Psychiatry - Sapienza University, Rome, Italy, Roma, Italy*

OBJECTIVES: Published literature suggests that treatment escalation to natalizumab, in relapsing-remitting multiple sclerosis (RRMS) patients with inadequate response to first-line injectable treatments, is clinically more effective than switching among immunomodulators. This analysis evaluates the cost-effectiveness of escalation vs. switching, adopting the Italian social perspective. **METHODS:** A lifetime horizon Markov model compared early escalation to natalizumab vs. switching among immunomodulators (interferons or glatiramer acetate) followed by escalation to natalizumab, in a cohort of patients who failed a first-line therapy. Specifically the two compared treatment algorithms were: a) escalation until progression of Expanded Disability Status Scale (EDSS) score of 7.0; b) switching until EDSS=4.0, followed by escalation until EDSS=7.0. For the two options, the model analyzed social costs and quality adjusted survival (QALYs). The model captured the effects of therapies in prolonging time without disability progression and burden of relapses. Clinical data was derived from a published study comparing the two treatment strategies. Unit tariffs and costs were adapted to the Italian setting. **RESULTS:** Early escalation to natalizumab was dominant over switching among immunomodulators. The two options led to similar costs (€1.008 mln/patient in the escalation group, vs. €1.034 mln/patient in the switching group), but early escalation was associated to prolonged quality adjusted survival (11.54 vs. 9.94 QALYs; +16.05%). A slight overall survival increase was also observed (21.14 vs. 20.80 life years). The increased acquisition costs related to prolonged treatment with natalizumab were offset by savings due to decreased burden of relapses and a reduction of disability-related costs. **CONCLUSIONS:** Early escalation to natalizumab is a cost-effective option in RRMS patients who don't adequately respond to conventional immunomodulators compared to switching among immunomodulators and escalation later. This shows that patients benefit from early escalation to natalizumab and prolonging immunomodulation, using therapies with similar mechanisms of action, could determine inappropriate usage of economic resources and poor benefit for patients.

PRM72

CONTRASTING PREDICTIONS OF CARDIOVASCULAR INCIDENCE DERIVED FROM ALTERNATIVE RISK PREDICTION MODELS IN TYPE 1 DIABETES

McEwan P[1], Foos V[2], Lamotte M[3]
[1]*Health Economics and Outcomes Research Ltd, Monmouth, UK,* [2]*IMS Health, Basel, Switzerland,* [3]*IMS Health, Vilvoorde, Belgium*

OBJECTIVES: Cardiovascular disease (CVD) risk prediction models are available for the general population (Framingham) and for type-2-diabetes (T2D) (UKPDS 68 and 82) but may not be appropriate in type-1-diabetes (T1D). The IMS CORE Diabetes Model (CDM) uses Framingham and UKPDS risk equations (REs) to predict CVD incidence in T2D and has recently been updated to include two CVD risk prediction approaches specific to T1D populations based on data from the Epidemiology-of-Diabetes-Interventions-and-Complications-study (EDIC) and a novel RE from the Pittsburgh-Epidemiology-of-Diabetes-Complications-Study (PEDC). The objective of this study was to compare CVD incidence across T1D model projections utilizing UKPDS, EDIC and PEDC REs and compare these to published EDIC findings. **METHODS:** The CDM was applied to project the incidence of myocardial-infarction (MI), stroke, heart-failure (HF) and ischemic-heart-disease (IHD) utilizing three alternative CVD REs, the UKPDS 68 RE (UK68-RE), EDIC-RE and PEDC-RE. The risk profile of a newly diagnosed T1D population (age 21 years, HbA1c 7%, systolic-blood-pressure 114 mmHg, body-mass-index 32 Kg/m2, high-density-lipoprotein 45 mg/dl and total-cholesterol 170 mg/dl) was projected over 30 years. The incidence of total CVD was estimated as the sum of the individual composites (%CVD=%MI+%stroke+IHD+HF) to enable comparison to published EDIC findings. **RESULTS:** When UK68-REs were applied, the 30-year cumulative incidence of CVD for a newly diagnosed T1D individual was projected at 2.66%, 0.27%, 3.88% and 0.72% for MI, stroke, IHD and HF, respectively. This compared to 4.10%, 0.66%, 3.36 and 0.58% utilizing EDIC-RE and 5.27%, 1.01%, 3.44 and 1.18% utilizing PEDC-RE. Total predicted CVD incidence added up to 7.53%, 8.70% and 10.90% for UK68-RE, EDIC-RE and PEDC-RE respectively, which compares to 8.70% incidence of CVD as observed during the EDIC study. **CONCLUSIONS:** As expected, the CDM reproduced the published EDIC CVD incidence when using the EDIC approach but demonstrated a slight underestimation utilizing UK68-RE and overestimation with PEDC-RE.

PRM73

VALIDATION OF A MARKOV MODEL FOR ECONOMIC EVALUATION OF SCREENING AND PREVENTIVE INTERVENTIONS IN ALZHEIMER'S DISEASE IN DENMARK

Sopina E[1], Martikainen JA[2], Spackman E[3], Sørensen J[1]
[1]*University of Southern Denmark, Odense, Denmark,* [2]*University of Eastern Finland, Kuopio, Finland,* [3]*University of York, Heslington, York, UK*

OBJECTIVES: Alzheimer's disease (AD) afflicts up to 9% of people aged 65 and over worldwide, with prevalence projected to increase. AD is associated with reduced quality of life and high treatment and management costs. A number of recently developed screening and preventative interventions offer reduction in resource use and improvement in quality of life for AD patients. The majority of existing models for economic evaluation of AD interventions focus on pharmaceuticals and due to their limited scope and time-horizon are unsuitable for evaluation of screening and preventative strategies. It is proposed to develop a decision model to ascertain the most cost-effective 'mix' of preventative and screening methods for Denmark. The objective of this study is to develop and validate such a model for economic evaluation of non-pharmaceutical interventions for AD **METHODS:** A Markov model was developed, representing transitions of a hypothetical cohort of 65 year olds from 'no AD' to different stages of AD (Very Mild through to Severe). AD could either be 'identified' or 'not identified' to reflect the difference in costs associated with treatment and management. Due to absence of Danish data, the model utilised transition probabilities based on US data; AD-associated costs and utilities were obtained from Danish and Swedish data, respectively. The model was externally validated against an epidemiological study of AD in Denmark to predict prevalence and stage of AD by age. **RESULTS:** The model accurately predicted Danish age-specific prevalence of AD, although the prevalence for the 75-79 age group was overestimated by 3%. The model also produced accurate predictions of the distribution of AD severity. **CONCLUSIONS:** The model provides a simple and robust framework for economic evaluation of screening and other non-pharmaceutical interventions for AD. The lack of up to date epidemiological data on AD is a challenge for model validation and introduces uncertainty.

PRM74

CONTRASTING MODEL PREDICTED LIFE EXPECTANCY IN PATIENTS WITH TYPE 2 DIABETES ACROSS DIFFERENT MORTALITY RISK PREDICTION MODELS VERSUS DATA FROM THE CANADIAN CHRONIC DISEASE SURVEILLANCE SYSTEM

McEwan P[1], Foos V[2], Lamotte M[3]
[1]*Health Economics and Outcomes Research Ltd, Monmouth, UK,* [2]*IMS Health, Basel, Switzerland,* [3]*IMS Health, Vilvoorde, Belgium*

OBJECTIVES: Diabetes is known to be associated with a considerable decline in life expectancy (LE). The aim of this study was to use a modelling approach to assess LE in low, intermediate and high-risk type-2-diabetes (T2D) populations and to compare these to observations from the Canadian-Chronic-Disease-Surveillance-System (CCDSS). **METHODS:** This study used the IMS-Core-Diabetes-Model (CDM), a validated diabetes simulation model, to project the LE of T2D individuals with a low-risk (age=55, diabetes duration=5, no CVD history), intermediate-risk (age=65, diabetes duration=15, moderate CVD history) and high-risk profile (age=80, diabetes duration=30, advanced CVD history). LE was predicted utilising three alternative mortality risk prediction models (RPMs) from the UKPDS 68 study (UK68), the UKPDS 82 study (UK82) and a risk equation based on Western Australia (WA) administrative data. Life-years-lost (LYL) in diabetes vs. no-diabetes populations was estimated based on the difference in age matching LE obtained from UK-national-life-tables subtracted by CDM projected-LE. Results were finally contrasted to LE and LYL estimations from the CCDSS study. **RESULTS:** When UK68 mortality RPMs were applied, LE projected was 23.29, 15.94 and 7.78 years for the low, intermediate and high risk cohort. This compared to 22.16, 14.88 and 7.29 years utilising UK82 RPMs and 25.94, 18.11 and 9.05years when utilising the WA RPMs. Based on UK life table data, LYL in diabetes vs. no-diabetes populations were 4.76, 3.61 and 1.11 (UK68), 5.89, 4.67 and 1.60 (UK82) and 2.11, 1.44 and -0.15 (WA) years. The CCDSS study reported outcomes for the low risk (age 55) and high risk (age 80) profile at 24.5 and 8.3 years (LE) and 5.5 and 2.25 years (LYL), respectively. **CONCLUSIONS:** UKPDS based models predicted LE and LYL very closely to CCDSS study findings. The Western Australian RPM seems not to be applicable to a UK and Canadian population.

PRM75

THE EFFICIENCY PATH: AN ESTIMATION OF COST-EFFECTIVENESS THRESHOLDS FOR 185 COUNTRIES BASED ON PER CAPITA HEALTH EXPENDITURES AND LIFE EXPECTANCY

Pichon-Riviere A, Augustovski F, Garcia Marti S, Caporale J
IECS-Institute for Clinical Effectiveness and Health Policy, Buenos Aires, Argentina

OBJECTIVES: Cost-effectiveness (CE) is increasingly used for resource allocation worldwide. One key hurdle for its widespread use is the lack of a widely accepted methodology to derive thresholds at the healthcare system (HS) or country level. The objective is to propose a methodology and derive local CE thresholds based on per capita health expenditures (pcHE) and life expectancy (LE). **METHODS:** Our approach is based on the relationship between pcHE and LE; assuming that the increase in expenditures reflects the CE of the interventions added to reach current LE. For HS willing to maintain or increase their secular trend of raising pcHE in order to improve health, the threshold (measured in units of pcHE) will be: Threshold=(LE+1)*i-LE; where LE is measured in life-years (LY) or QALYs; and "i" is the ratio of increase in pcHE that the HS is willing to accept to increase LE by one unit (eg i=1.09 for a 9% increase). For HS with cost-containment mandates: Threshold=LE-((LE-1)/i), where "i" represents the past increase in pcHE to gain the last unit of LE. We used OLS to predict "i" for 185 countries, following both a cross-sectional (2013) and a longitudinal approach (2003-2013) using World Bank data. **RESULTS:** Depending on income strata and LE, countries can expect to increase pcHE by 7-10% for an additional LY and between 10-13% for an additional QALY. This represent cost per QALY thresholds ranging from 9-11 pcHE in High-Income to 5-8 in Low-Income countries, which translates to thresholds of 32-40 thousands US dollars in UK; 83-101 in USA; 6-7 in Mexico and 0.5 in Uganda (around 0.9, 1.8, 0.6 and 0.7 GDP per capita respectively). **CONCLUSIONS:** This approach, based on widely available data, can be useful to inform decisions in all countries using economic evaluations. Our results show thresholds usually lower than those promoted by WHO.

PRM76

HOW TO HANDLE LEVELS OF EVIDENCE IN HEALTH ECONOMIC MODELLING

Nuijten MJ[1], Krol M[2], Redekop WK[3]
[1]*Ars Accessus Medica, Jisp, The Netherlands,* [2]*Merck Serono, Schiphol-rijk, The Netherlands,* [3]*Erasmus University Rotterdam, Rotterdam, The Netherlands*

OBJECTIVES: To address the practical and methodological issues associated with using low-quality evidence outcomes in health economic modelling. **METHODS:** A cost-effectiveness model for disease-modifying drugs (DMDs) in multiple sclerosis (MS) in The Netherlands was used to assess how to deal with low-quality evidence in health economic modelling. The model adopted a 10-year time horizon and a societal perspective. A Markov model was constructed based on EDSS staging in MS, including relapse. The central focus was on disease progression — instead of relapse — which appeared to be the driver of the cost-effectiveness outcomes. The main data source was a recent Cochrane review estimating relative efficacy and acceptability of DMDs in relapse-remitting MS. Other data sources included additional published literature, clinical trials, and official price/tariff lists. **RESULTS:** The analysis based on the Cochrane review data showed that interferon beta-1a-R (Rebif) is cost-effective over interferon beta-1a-A (Avonex) (dominant) and interferon beta-1b (€27,654/QALY), but that interferon beta-1a-R is not cost-effective over glatiramer acetate. However, for disease progression, the level of evidence is considered very low (level 1) for all drugs, except interferon beta-1a-R (moderate - level 3), implying unreliable effectiveness outcomes which, consequently, can result in unreliable cost-effectiveness outcomes. Two reasonable alternative approaches may be to exclude very low evidence from the cost-effectiveness analysis or assume placebo efficacy. Alternative analyses, including placebo efficacy for disease progression for drugs of which the evidence is labelled very low by Cochrane (all except interferon beta-1a-R), strongly impacted outcomes: interferon beta-1a-R was cost-effective over interferon beta-1a-A (dominant), interferon beta-1b (€6,265), and glatiramer acetate (dominant). **CONCLUSIONS:** Inclusion of very low-quality evidence in health economic modelling may lead to unreliable cost-effectiveness conclusions. However, a gold standard is lacking for handling levels of clinical evidence in health economic models. One alternative, presented here, would be to assume placebo efficacy in such cases.

PRM77

BEST PRACTICES FOR NETWORK META-ANALYSIS METHODOLOGY: COMPARATIVE EFFECTIVENESS OF INTERFERON-BETA THERAPIES IN RELAPSING-REMITTING MULTIPLE SCLEROSIS

Beckerman R[1], Locklear JC[2], Jiang Y[3], Solon C[4], Smith NJ[3], Phillips AL[2]
[1]*Maple Health Group, LLC, New York, NY, USA,* [2]*EMD Serono, Inc., Rockland, MA, USA,* [3]*CBPartners, New York, NY, USA,* [4]*CBPartners, San Francisco, CA, USA*

OBJECTIVES: To evaluate different statistical methodologies in a network meta-analysis (NMA) comparing the effectiveness of interferon-beta (IFNβ) therapies across several endpoints in relapsing-remitting multiple sclerosis (RRMS) to determine potential best practices. **METHODS:** A systematic literature review (1996-2014) was conducted to identify randomised, controlled trials of FDA- and EMA-approved IFNβ DMDs in RRMS, including subcutaneous (SC) IFNβ-1a (44µg or 22µg 3x/wk), SC pegIFNβ-1a (125µg every 2wks), intramuscular (IM) IFNβ-1a (30µg 1x/wk), and SC IFNβ-1b (250µg EOD). Data were extracted for patients relapse-free, patients without disability progression, and patients without new MRI activity at study end. A random-effects Bayesian model was utilised for the base case analysis, and sensitivity analyses investigated results using different analysis frameworks or effects distributions. **RESULTS:** 644 articles were retrieved; 14 met inclusion criteria and reported evaluable data. The evidence networks had few connections between nodes, with a maximum of 10 connections for the proportion of "patients relapse-free" endpoint. In addition, there were few connections with multiple studies linking nodes, with a maximum of 50% (5/10) of connections having more than one study on the relapse endpoint, and there were at most two studies linking any two nodes. Because of the small number of studies linking nodes, a random-effects Bayesian model with uninformative priors resulted in wide credible intervals, complicating interpretation of results; uncertainty decreased using a random-effects Bayesian model with an informative prior as well as with a fixed-effects Bayesian model. Estimates for the treatment effects were similar across all Bayesian approaches. Utilising a Frequentist approach resulted in similar estimates for treatment effects compared to the Bayesian analyses framework, although with slightly less uncertainty. **CONCLUSIONS:** While similar estimates for treatment effects were found across statistical methodologies, the combination of a Bayesian approach and a random-effects distribution with informative prior allowed for methodological robustness while yielding interpretable findings.

PRM78

REVIEW OF ECONOMIC MODELS FOR THE EVALUATION OF BIOLOGIC DMARDS IN RHEUMATOID ARTHRITIS

Van Laer J[1], Gubbels L[2], Rodriguez IL[3], Maervoet J[4], Nijhuis T[2], Nielsen AT[5], Peterson S[6], Hemels M[5], Ganguly R[7]
[1]*Janssen Pharmaceutica N.V., Beerse, Belgium,* [2]*Quintiles Advisory Services, Hoofddorp, The Netherlands,* [3]*Quintiles Consulting, Reading, UK,* [4]*Quintiles Consulting, Vilvoorde, Belgium,* [5]*Janssen-Cilag A/S, Birkerød, Denmark,* [6]*Janssen, Horsham, PA, USA,* [7]*GlaxoSmithKline, King of Prussia, PA, USA*

OBJECTIVES: Over the last decade, several biologic disease-modifying anti-rheumatic drugs (bDMARDs) have become available providing additional treatment options for rheumatoid arthritis (RA) patients. This study was conducted to identify and compare existing economic models used by health technology assessment (HTA) bodies to evaluate bDMARDs. **METHODS:** The HTA Accelerator database and websites of HTA agencies (NICE, SMC, NCPE, ZIN, TLV, PBAC, CADTH, INESSS, MOHLTC, DECIT-CGATS and AHRQ) were screened to identify assessments of bDMARDs published since 2005 that included a cost-utility analysis (CUA). In addition, a targeted literature review was performed to gain further insights on model constructs, key data elements/assumptions, and recent modeling advances. **RESULTS:** Thirty-three HTAs comprising 60 CUAs were considered relevant and investigated further. Albeit individual sampling models and discrete event simulations have some advantages over Markov models, these three techniques may provide similar cost-effectiveness estimates and were all deemed appropriate for HTA submissions. At least ten different structural components were identified for which data sources and/or assumptions have evolved over time, several of which have a major bearing on model outcomes. The characteristics of patients entering the model (e.g. disease severity and prior treatments), assumptions about long-term disease progression whilst on treatment and the rebound effect upon treatment discontinuation, and mapping of Health Assessment Questionnaire and/or pain scores to Quality of Life utility values were repeatedly mentioned as key elements affecting the results. **CONCLUSIONS:** A wide variety of economic models for the evaluation of bDMARDS in RA have been developed and are continuously being refined. Despite recent initiatives to reach consensus on how RA models should be designed, substantial differences in the data sources and assumptions that are used still remain. This limits the comparability across and also generalizability of the various results obtained by using these models and poses problems to all stakeholders involved in HTAs.

PRM79

INVESTIGATING THE IMPACT OF STRUCTURAL CHANGES IN A NICE SINGLE TECHNOLOGY APPRAISAL COST-EFFECTIVENESS MODEL

Alam MF[1], Barton P[2], Monahan M[2]
[1]*Swansea University, Swansea, UK,* [2]*University of Birmingham, Birmingham, UK*

OBJECTIVES: One of the major critiques with submitted manufacturer's cost-effectiveness models is surrounding the structural uncertainty. However, methods dealing with structural uncertainties are not well-developed, even though these might have a significant impact on model results. This study investigates the impact of structural changes in a National Institute for Health and Care Excellence (NICE) single technology appraisal cost-effectiveness model of Erlotinib versus Best Supportive Care as a maintenance therapy for patients with non-small cell lung cancer. The manufacturer's model submission was criticised for having a "Markov" model not governed by transition probabilities. It considered an independent projective survival functions for progression-free survival and overall survival, which allowed a negative post-progression survival (PPS) estimate to appear in later cycle. **METHODS:** Using published summary survival data, this study adopted three approaches, covering both fixed- and time-varying, to estimate health state transition probabilities that are used in a restructured Markov model. **RESULTS:** Unlike for placebo, the parametric approach estimates post-progression probabilities and probabilities of death for Erlotinib differently than fixed-transition approaches. The best fitting curves are achieved for both PPS and probability of death across the time for which data were available, but the curves start diverging towards the end of this period. The alternative (Markov) model which extrapolates the curves forward in time suggests that this difference between a time-varying and fixed-transition becomes even greater. The alternative models produce an Incremental Cost-Effectiveness Ratio (ICER) of £54k -£66k per quality adjusted life year (QALY) gain, which is comparable to an ICER presented in the MS (£55k/QALY gain). **CONCLUSIONS:** The results from restructured alternative models do not suggest different cost-effectiveness results to those reported in the manufacturer submission; however, in terms of magnitude they vary. This variation in cost-effectiveness results produced by restructured models might be crucial for interventions falling near a threshold value.

PRM80

INVESTIGATING THE VALUE OF PATIENT LEVEL DATA TO INFORM ESTIMATES OF ADPKD PROGRESSION GENERATED WITHIN THE ADPKD OUTCOMES MODEL

McEwan P[1], Bennett H[2], O'Reilly K[3], Robinson P[3]
[1]*Health Economics and Outcomes Research Ltd, Monmouth, UK,* [2]*Health Economics and Outcomes Research Ltd, Cardiff, UK,* [3]*Otsuka Pharmaceutical Europe Ltd, Wexham, UK*

OBJECTIVES: Autosomal dominant polycystic kidney disease (ADPKD) is a genetic disorder characterised by enlarged kidneys and declining renal function. ADPKD progression rates are heterogeneous, influenced by age, gender, renal size and genotype. Disease models often utilise progression rates derived from published studies. This study aimed to compare ADPKD progression, in terms of changes in total kidney volume (TKV) and renal function, modelled from summary versus patient-level data (PLD), and assess the consistency of predictions with trial observations. **METHODS:** Regression equations were derived from the TEMPO 3:4 trial placebo arm (natural history) to predict annual changes in TKV and estimated glomerular filtration rate (eGFR). Candidate covariates included age, gender, ethnicity, region/country, TKV and eGFR. Predictions were compared using the PLD regression equations or linear interpolation of summary rates of change in four patient categories. Finally, the model was initiated with published baseline patient profiles representing early and late disease from the HALT-PKD trials, and predicted progression compared to trial observations. **RESULTS:** For patients initiated with the average TEMPO 3:4 placebo profile, predicted eGFR trajectories based on PLD or summary data were similar (average decline: -5.3 and -5.1ml/min/1.73m2/year, respectively); however, TKV predictions deviated as TKV exceeded 2,500ml, with increasingly rapid growth predicted based on summary data. The model closely replicated ADPKD progression among patients with early disease; all predicted values within the 95% confidence interval of HALT-PKD observations. In patients with late disease, modelled baseline TKV of 1,000-1,500ml led to closest replication of eGFR observations (average decline: -3.2 to -4.4, versus -3.9ml/min/1.73m2/year during trial). **CONCLUSIONS:** Though predictions based on summary and PLD were consistent, the PLD regression equations produced more realistic results at extreme values. The availability of relevant PLD to describe the natural history of ADPKD progression provides a more robust foundation for disease and economic modelling than summary data alone.