and €47,000/QALY for the remaining two models. Differences in the outcomes could mainly be explained by differences in input values for disease progression, exacerbation-related mortality and all-cause mortality with high input values resulting in low ICERs and vice versa. Lifetime results were mainly influenced by the input values for mortality. The probability of intervention four to be cost-effective at a willingness-to-pay of €50,000/QALY was 90-100% for five models and about 70% and 50% for the other two models. **CONCLUSIONS:** Mortality was the most important factor determining the differences in cost-effectiveness outcomes between models.

PRM85

A DE-NOVO MODEL TO PREDICT OUTCOMES OF A NEW HYPOTHETICAL INTERVENTION TO REDUCE CV RISK IN POST MI PATIENTS

Jain M[1], Sonathi V[1], Rathi H[1], Bakuli A[1], Thomas SK[2], Mollon P[3]

[1]*Novartis Healthcare Pvt. Ltd., Hyderabad, India,* [2]*Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA,* [3]*Novaris Pharma AG, Basel, Switzerland*

OBJECTIVES: The risk of cardiovascular (CV) events in post myocardial infarction (MI) patients poses a significant burden on the UK health care system despite the current standard of care (SoC). The objective of this analysis was to develop a model to quantify the relationship between efficacy and outcomes of a new hypothetical drug given in addition to current SoC to reduce the risk of CV events in post-MI patients when compared to SoC. **METHODS:** A 6-state lifetime Markov model with a 1-year cycle length was developed from a UK health care perspective. Recurrent MI, stroke and CV death were modeled. The hypothetical drug was assigned efficacy values for its ability to reduce the incidence of CV events. The outcomes were measured in terms of QALYs and LYs. A linear regression model was fitted to estimate the expected outcome/patient based on relative risk reduction (RRR) in the incidence of CV events. All outcomes were discounted at 3.5% annually. **RESULTS:** The model structure addressed some of the limitations of previous economic models, namely increased risk due to stroke in MI patients and increased risk of subsequent events in the first year. For identical cohorts, the outcomes from the model compared well with other published studies. For a cohort of patients aged 40-years, the model predicted on an average, LYs of 17.6 and QALYs of 13.64. A hypothetical drug achieving a 5% RRR in CV events resulted in an incremental LYs of 0.28 and QALYs of 0.23. The increase in incremental QALYs and LYs per percentage point reduction in relative risk as compared to SoC was estimated to be 0.043 and 0.054 respectively. **CONCLUSIONS:** A de-novo economic model quantifies the relationship between the efficacy and outcomes of a hypothetical drug when compared to the SoC to reduce the risk of CV events in post-MI patients.

PRM86

ESTIMATING THE LIFETIME HEALTH OUTCOMES OF TYPE 2 DIABETES MELLITUS (T2DM) PATIENTS INADEQUATELY CONTROLLED ON METFORMIN PLUS SULPHONYLUREA RECEIVING EITHER CANAGLIFLOZIN OR SITAGLIPTIN USING THE UKPDS OUTCOMES MODEL V1.3

Nuhoho S[1], Worbes-Cerezo M[2]

[1]*Janssen-Cilag A/S, Birkerød, Denmark,* [2]*Janssen-Cilag UK, High Wycombe, UK*

OBJECTIVES: The goals of type 2 diabetes management are to control glycaemia and other micro- and macrovascular risk factors such as weight, blood pressure and lipids in order to prevent death and other complications due to the disease. The natural history of the disease makes it challenging to estimate the effects of treatments on these long term complications and mortality from standard clinical trials. Modelling is therefore a key bridging tool for predicting long term health outcomes from intermediate endpoints. The objective of this analysis was to estimate the relative effects of canagliflozin 300mg and sitagliptin 100mg on mortality, micro- and macrovascular complications in T2DM patients in triple line as add on to metformin plus sulphonylurea using the UKPDS Outcomes Model v1.3. **METHODS:** A probabilistic patient generator was developed which generated 10,000 patients with applied treatment effects based on data from head to head randomised clinical trials. Upon loss of glycaemic control (HbA_{1c} ≥7%), patients were assumed to switch to insulin. 1% point reduction in HbA_{1c} was applied on rescue. For model stability, patients were looped 1,000 times (creating 10 million patients in each arm) with 100 bootstrap simulations. Outcomes were discounted 3.5% annually. **RESULTS:** At the end of the 40 years simulation, patients initiating canagliflozin 300mg had 49 more survivors and 16,918 fewer diabetes-related deaths. Micro- and macrovascular complications were estimated in fewer patients on canagliflozin 300mg than on sitagliptin 100mg (between 5,948 fewer renal failures and 41,157 fewer myocardial infarctions). There were discernible relative risk reductions in all complications and diabetes-related death ranging from 1.40% (heart failure) to 2.96% (amputation). **CONCLUSIONS:** Results of the analysis using the UKPDS Outcomes Model v1.3 suggest that canagliflozin 300mg compared with sitagliptin 100mg as add on to metformin plus sulphonylurea reduces long-term diabetes-related mortality and complications.

PRM87

ALL-CAUSE MORTALITY VALIDATION OF THE CORE DIABETES MODEL AGAINST PREDICTIONS OF THE CHARLSON COMORBIDITY INDEX

Foos V[1], McEwan P[2], Lamotte M[3], Grant D[4]

[1]*IMS Health, Basel, Switzerland,* [2]*Health Economics and Outcomes Research Ltd, Cardiff, UK,* [3]*IMS Health Consulting, Brussels, Belgium,* [4]*IMS Health, London, UK*

OBJECTIVES: All cause mortality (ACM) validations with the IMS CORE Diabetes Model (CDM) have demonstrated below average fit when compared to overall validation scores from 96 validation end points (EP) with a R^2-statistic of 0.651 (vs. 0.93 All-EP). Lack of fit was associated with a model overestimation of ACM when compared to contemporary outcome studies (ACCORD, ADVANCE, VADT). The objective of this investigation was to put these findings into perspective by comparing the model to mortality risk predictions from the Charlson-Comorbidity-Index (CCI). **METHODS:** The CCI was applied to predict the 10 year mortality risk for diabetes patients with age of 50,60,70 and 80 years and four different co-morbidity levels: no complications (NC), myocardial infarction (MI), MI and stroke (MI+S), MI+S and heart failure (MI+S+HF) and MI+S+HF and renal failure (MI+S+HF+RF). CCI mortality scores were compared to corresponding 10 year ACM predictions from the CDM. Base case (BC) analyses applied UKPDS-68 risk equations (UK68-RE) for CV risk and mortality. Two sets of sensitivity analyses were conducted using UK68-RE for CV risk but mortality tracked individually per complication event (non combined mortality approach) (SA1) and UKPDS-82 risk equations (UK82-RE) applied for CV risk and mortality (SA2). **RESULTS:** Across all age and co-morbidity states, CDM simulations demonstrated the closest match to CCI-scores in SA1 with an R^2-statistic of 0.877. This compared to R^2-statistics of 0.757, and 0.851 for BC and SA2, respectively. BC and SA2 analyses noteworthy underestimated ACM risk in analyses with increased co-morbitity level by 68% (BC) and 49% (SA2) vs. 17% (SA1) in (MI+S+HF) and 44% (BC) and 36% (SA2) vs. 3% (SA1) in (MI+S+HF+RF). **CONCLUSIONS:** The CDM demonstrated a closer match to CCI mortality scores (vs. outcome studies) with a trend to underestimate ACM. This trend increased with baseline age and (only BC and SA2) co-morbidity level.

PRM88

DETERMINISTIC VERSUS STOCHASTIC PREDICTION OF RISK FOR CARDIOVASCULAR EVENTS

Villa G[1], Lothgren M[1], Gandra SR[2], Lindgren P[3], van Hout B[4]

[1]*Amgen (Europe) GmbH, Zug, Switzerland,* [2]*Amgen, Inc., Thousand Oaks, CA, USA,* [3]*IVBAR, Karolinska Institutet, Stockholm, Sweden,* [4]*University of Sheffield, Sheffield, UK*

OBJECTIVES: Multivariate functions can be used to predict individual risk for cardiovascular (CVD) events and also to estimate baseline risk in economic models. We present a comparison of deterministic versus stochastic risk predictions using Framingham's [D'Agostino 2008] and REACH's [Wilson 2012] functions. Stochastic risk prediction accounts for patient-level heterogeneity, but involves a number of issues including increased complexity, data requirements, need for assumptions and computational burden. To our knowledge, this topic has not been studied in the CVD setting. **METHODS:** D'Agostino 2008 and Wilson 2012 modeled primary (PE) and recurrent event (RE) risks, respectively. Both studies considered fatal and non-fatal aggregate CVD events and estimated a Cox Proportional Hazards (CPH) multivariate risk function. In the deterministic prediction, the means of the risk factors were used to predict the population's risk directly from the functions. In the stochastic prediction, individual patient profiles (n=10,000) were generated using Monte Carlo simulation. Individual risks were then estimated from the functions and averaged to compute the population's risk. Multinomomial distributions were assumed for discrete variables (e.g. diabetes, number of vascular beds) and normal or log-normal distributions were assumed for continuous variables depending on skewness (e.g. age, total cholesterol). Probability distributions were parameterized based on the risk factors descriptives reported in the original references. Simulations were performed with and without considering dependence of risk factors. **RESULTS:** Due to the non-linearity of the CPH function, the stochastic prediction yielded 23% (PE) and 17% (RE) higher risks than the deterministic approach (14% and 10%, respectively, if age was kept constant). Differences between prediction approaches are even higher if the estimated correlation structure of risk factors is accounted for. **CONCLUSIONS:** When compared to the stochastic prediction, the deterministic approach leads to lower estimates of CVD risks. Therefore, economic models using this approach might underestimate treatment effect.

PRM89

ARE CYCLES NEEDED IN MARKOV MODELS? – THE CONTINUOUS MODEL AS A SIMPLER APPROACH

Tichy E

Evidera, Budapest, Hungary

OBJECTIVES: To present an alternative implementation for the conventional Markov models with area under the curve (AUC) approach: the continuous model (CM). To present how the CM avoids the need of determining cycles in theory and to compare the traditional and the CM approach in terms of results and complexity in an oncology model example. **METHODS:** The AUC model assumes that the survival function is known at any timepoint not only at the beginning and end of model cycle. The CM calculates the model outcomes for the whole timehorizon by using the values of the survival function in every timepoint, instead of the discrete timepoints defined by cycle length. The CM approach overcomes the issue of the artificial characterization of time using cycles, that is often criticized in Markov models. Using CM can also lead to more precise estimates. A simple oncology AUC model with three health states (progression free survival, progression and death) and four-weekly cycles was built and converted to a CM model in Excel®, using user defined Visual Basic functions. Results, generalizability and user friendliness were compared. **RESULTS:** The results of the two models were similar: for health outcomes differences were around 1%, for costs and incremental cost-effectiveness ratios around 0.5%. Calculations were done in a single cell/outcome instead of a column of 100-200 cells depending on cycle length and time horizon, giving less scope for bugs and facilitating easier debugging. As a result the implementation of the CM model was faster and technical validation easier. **CONCLUSIONS:** The CM approach requires more technical background from the developer; custom functions have to be built even for point estimates. However, results of a CM, requires smaller spreadsheet space, and provides more transparency and easier debugging, while providing similar or potentially more precise estimates compared to the AUC model results.

PRM90

A COMPARISON OF MODELLING TECHNIQUES: PATIENT SIMULATION VERSUS MARKOV MODELLING IN OPHTHALMOLOGY

Claxton L[1], Malcolm WA[2], Hodgson R[1]

[1]*York Health Economics Consortium, York, UK,* [2]*Novartis UK, Frimley, UK*

OBJECTIVES: Markov models are a currently popular means of estimating the cost-effectiveness of interventions; however they are associated with certain limitations which may make them ill-suited to inform some health care decisions. Patient simulation models offer an alternative methodology which may overcome some of these