presented model provides an opportunity to simulate burden in specific age bands, population burden, change in burden due to vaccination, and the seasonal/long-term cost effectiveness of vaccination with/out accounting for indirect protection effects. This study was sponsored by MedImmune.

VA7

COMPARISON OF DIFFERENT STATIC AND DYNAMIC SIMULATION TECHNIQUES FOR THE INFLUENCE OF CHILDREN PNEUMOCOCCAL VACCINATION

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OBJECTIVES: Estimating the possibility of preventing pneumococcal illnesses by vaccination of infants with the 7-valent serum is realized with decision tree based models as "State of the Art". A new network of models introducing the possibility of 1) Comparing and validating the different approaches in a qualitative and quantitative way with each other, and 2) improving the capacity of simulation with dynamical behavior, structural insights and extended sensitivity analysis. **METHODS:** Based on a Markovian-Model from literature [1] the system was re- implemented and validated with the given data set. Starting with this model, results for Austrian data were computed. After this an ODE was implemented as a "transponder" model, validated with the Markovian-Model and extended by dynamical behavior. In parallel an Agent Based model was implemented, validated with the transponder model and extended by individual agent behavior to simulate herd immunity and serotype replacement. **RESULTS:** Models can be adapted comfortably to additional data or new structural information; the approach is complex due to the fact that dynamic behavior can be represented and still flexible for adapting to different scenarios; the model has modular structure, as population dynamics, illness and economical effects are modelled in different modules, which can be exchanged if necessary; and outcomes are comparable to each other in a qualitative and quantitative way. **CONCLUSIONS:** Results in the final version of the agent based simulation vary from the starting model significant. The reasons for the changes are described and can be followed step by step as all models are White-Box-Models and therefore can be re-simulated with given data. The Agent Based Model is identified as more realistic simulation of real behavior. Reference: [1] McIntosh, et al: The cost-burden of paediatric pneumococcal disease in the UK and the potential cost-effectiveness of prevention using 7-valent pneumococcal conjugate vaccine.

VA8

HOW SHOULD HEALTH GAINS OF VACCINATION STRATEGIES BE DISCOUNTED?

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OBJECTIVES: Recently the Dutch government started immunizing Dutch girls with the human papillomavirus (HPV)-vaccine. Implementation of HPV-vaccination was controversial because different health-economic studies have estimated that the incremental cost-effectiveness ratios (ICER) of HPV-vaccination were just below or above the informal Dutch cost-effectiveness threshold. In the Netherlands, there are no differences in pharmacoeconomic guidelines and acceptable ICERs for vaccines and pharmacotherapies. It has recently been proposed that vaccines might warrant a different approach in estimating, interpreting and valuing the ICER. One of the aspects considered relates to the discount rate. In this study, we estimated the impact of different discount rates and approaches for discounting the health benefits of HPV-vaccination. **METHODS:** A previously developed HPV Markov model was used to estimate the impact of discounting on the ICER of HPV-vaccination, with the discount rate for health benefits ranging from -4% to +4%. Besides the discount rate, the impact of two different discounting methods was estimated. The first method has been specifically developed for infectious diseases, and proposes that health gains should be discounted from the moment of risk reduction (averted HPV infection). The second method uses proportional discounting, which implies that the discount rate decreases over time. **RESULTS:** When we estimated the ICER of HPV-vaccination according to the Dutch guidelines, we found an ICER of €18,400/QALY. Ranging the discount rate from –4% to +4% resulted in an estimated ICER of €680 and €84,200 per QALY, respectively. Applying both alternative models resulted in ICERs of €12,800 and €8,960 per QALY, respectively. **CONCLUSIONS:** As expected, the exact discount rate and the underlying model for discounting have a considerable impact on the ICER of HPV-vaccination. The use of different discounting methodologies for vaccination, in comparison with therapeutic interventions, might provide a more realistic estimation of future health benefits for vaccination strategies and result in more favorable ICER values.

PODIUM SESSION IV: COST STUDIES

CO1

ESTIMATE AVERAGE MEDICAL COSTS IN THE PRESENCE OF RIGHT-CENSORING

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OBJECTIVE: To address the common issue of incomplete follow-up data in cost-effective analysis, we compared the actual average cumulative medical costs with the estimated costs using a set of statistical methodologies applicable to censored cost data. **METHODS:** A study cohort with monthly recorded concomitant medication costs was selected from the population of a randomised clinical trial. Among a total of 70 subjects, a pattern of 25% non-informative censoring was applied prior to the endpoint of interest (the first event between death and 1-year follow-up visit). Statistical methods applied to deal with censored data included naïve estimators from complete case analysis (CCA) and available-case analysis (ACA), as well as Lin's, inverse-weighted and regression-based multiple-time-interval estimators. The covariate considered in regression models was continuous variable age. Bootstrapping with 10,000 replications was used to obtain the standard deviation (SD). **RESULTS:** The actual average total cost per subject was £268.7 (SD: £52.0). Estimations from the 5 methods given by mean (SD) were: CCA: £467.7 (£110.8), ACA: £246.0 (£49.8), Lin's estimator: £301.6 (£60.6), inverse-weighted estimator: £294.5 (£15.6), regression-based method: £245.5 (£49.2). **CONCLUSIONS:** By ignoring subjects with incomplete cost data, CCA overestimated the average cumulative cost as subjects with shorter survival tend to cumulate higher costs. Lin's and inverse-weighted non-parametric estimators that make no assumption for the distribution of cost data slightly overestimated the average total cost. Regression-based method gave better results for both mean and SD than one-sample estimators (Lin's and inverse-weighted) as it considered one cost-related factor (age) as covariate. The multiple-time-interval strategies (Lin's, inverse-weighted and regression-based) effectively assess cost information from censored subjects by treating them as uncensored in some of the time intervals. However, in this situation, small-size dataset and light censoring make ACA the best estimator.

CO2

ACCOUNTING FOR THE DRUG LIFE CYCLE AND FUTURE DRUG PRICES IN COST EFFECTIVENESS ANALYSIS

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OBJECTIVES: Economic evaluations of health technologies typically assume constant real drug prices and model only the cohort of patients currently eligible for treatment. It has recently been suggested that in the UK, we should assume that real drug prices decrease at 4% p.a., and in New Zealand, that real drug prices decrease at 2% p.a. and at patent expiry, the drug price falls. It has also recently been suggested that we should model cohorts of patients starting treatment in the future. In this paper, the cost-effectiveness of drugs is modelled based on these ideas. **METHODS:** Algebraic expressions are developed to capture all costs and benefits over the entire life cycle of a new drug. The lifetime of a new drug in the UK, a key model parameter, is estimated as 33 years, based on the historical lifetime of drugs in England over the last 27 years. Cost-effectiveness is calculated for seven new drugs recently appraised in the UK. **RESULTS:** Under the proposed methodology, all seven drugs appear far more cost-effective in the UK than published. For example, the incremental cost-effectiveness ratio decreases by 45%, from £31,100 to £17,000 / QALY, for imatinib versus interferon-a for chronic myeloid leukemia. **CONCLUSIONS:** The "life cycle correction factor" is introduced, which is used to convert estimates of cost-effectiveness as traditionally calculated into estimates under the proposed methodology. Under the methodology, all drugs in the UK and New Zealand appear more cost-effective, many far more cost-effective. Therefore, I suggest that the willingness to pay threshold should be reduced in the UK and New Zealand. The ranking of cost-effectiveness will change with drugs assessed as relatively more cost-effective and medical devices and surgical procedures relatively less cost-effective than previously thought. The methodology is very simple to implement and should be parameterized for other countries.

CO3

INDIRECT SOCIAL COST OF MULTIPLE SCLEROSIS: RESULTS FROM A REAL-WORLD OBSERVATIONAL STUDY

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OBJECTIVES: To assess work productivity loss among multiple sclerosis (MS) patients and the resulting indirect social cost due to MS from a real-world observational study. **METHODS:** ROBUST is a 12-month, US prospective, observational, open-label, single-arm, multi-center outcomes study of Interferon β-1b given every other day for relapsing forms of MS. For this analysis, baseline data from the Work Productivity and Activity Impairment questionnaire specific for MS (WPAI) were used. Productivity outcomes including absenteeism (work time missed), presenteeism (reduced on-the-job effectiveness) and overall work productivity loss were calculated from WPAI. Indirect social cost was estimated by modeling US national average wage

data by education level from the Bureau of Labor Statistics to the WPAI scores. Work productivity and indirect social cost were compared across patient sociodemographic characteristics and disease severity. **RESULTS:** A total of 191 MS patients were evaluated at baseline with 114 working either full-time (78.1%) or part-time (21.9%). In this working sample, 75.4% were females, 72.8% were married, 71.1% were below 50 years old and a majority were White (88.5%). The overall productivity loss due to MS among full-time employed patients and part-time employed patients was 42.5% (SD: 26.9) and 42.1% (SD: 30.6), respectively. This translates into a substantial productivity loss of 17 hours of loss time in a 40-hour work-week for full-time workers and 8.4 hours of loss time in a 20-hour work week for part-time workers. At average wages, this productivity loss equates to an indirect annual social loss of $18,106 per patient (SD: $13,265) among full-time workers and $8,871 per patient (SD: $7,080) among part-time workers. Indirect social costs were significantly correlated with increasing MS severity ($r = 0.21$; $p = 0.0.029$). **CONCLUSIONS:** Multiple sclerosis results in a substantial loss of work productivity among patients, which collectively results in significant indirect social cost. The MS-related indirect social costs increase with increasing MS severity.

CO4

MICRO-COSTING VS GROSS-COSTING IN THE ESTIMATION OF COSTS FOR THE PHARMACOECONOMIC EVALUATION OF GLAUCOMA IN KOREA

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OBJECTIVES: This study compares the result of cost estimation for glaucoma outpatients using micro-costing and gross-costing methods. It also examines the factors contributing to the difference in results and investigates the impact of the result by costing method on Budget Impact Analysis(BIA). **METHODS:** Per year costs of glaucoma outpatients were estimated for micro-costing, which consists of medical fee, eye examinations and laser therapy. A decision tree designed with 6 pathways was used. A patient's visit frequency and transition probability for each pathway were obtained from literature and clinical expert opinions. In gross-costing, yearly per-capita outpatient average costs were calculated by using health insurance statistics data on glaucoma (ICD 10 code: H40). For BIA, each costing result was applied to the patients nationwide. **RESULTS:** The calculated costs of annual outpatient were $148.7 and $71.1 for micro-costing and gross-costing, respectively. The cost calculated by pathway in micro-costing ranged from the minimum of $142.9 to the maximum of $589.8. BIA result were $11,302,788 for micro-costing and $5,407,527 for gross-costing. **CONCLUSIONS:** One factor contributing to the difference between the two methods is the gap between the standard model and the actual use of medical services. Another factor particular to gross-costing is that in the case a patient changes medical institutions, data from previous institutions do not accumulate, which underestimates the total cost of medical care. As a result, different costing methods may result in different decision-making of new drugs.

PODIUM SESSION IV: DIABETES STUDIES

DB1

USING POPULATION-BASED ESTIMATES FOR DISEASE MODELING: POTENTIAL BIAS COMPARED TO USING DISEASE-SPECIFIC DEATH AND COMPLICATION RISK ESTIMATES

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Most previous work estimating survival rates for diabetes has been based on logistic regression or standardized ratios to derive odds ratios rather than being based on survival analysis with risk estimates over time. Few studies have estimated the excess risk between those with and without diabetes. **OBJECTIVES:** The purpose of this study was to estimate the excess risk and cumulative relative risks of death and complications between those with newly diagnosed diabetes and those without. **METHODS:** Newly diagnosed type 1 and 2 diabetes cases aged 35 and over were identified from the Ontario Diabetes Database and matched 1:2 using propensity scores with controls (non-diabetes cases). Using linked provincial administrative databases, data on death and the following complications were recorded: myocardial infarction, stroke, angina, heart failure, blindness, amputation, nephropathy and cataract. Kaplan Meier curves were calculated to estimate the probability of being event-free for those with and without diabetes for up to 10 years of follow-up. **RESULTS:** A total of 610,852 patients aged 35 and over with diabetes were matched with 1,221,704 patients without diabetes. For those with diabetes vs. those without, there was a statistically significant increased relative risk at 10 years for death (1.417, [95%] CI 1.415–1.418), myocardial infarction (2.094, [95%] CI 2.092–2.095), stroke (1.877, [95%] CI 1.874–1.879), angina (1.526, [95%] CI 1.525–1.527), heart failure (2.520, [95%] CI 2.529–2.522), amputation (6.824, [95%] CI 6.823–6.824), nephropathy (2.902, [95%] CI 2.901–2.904), blindness (1.212, [95%] CI 1.205–1.218) and cataract (1.326, [95%] CI 1.324–1.327). **CONCLUSIONS:** Diabetes is a significant health problem with excess risk of death and complications typically associated with diabetes. Using estimates of risk of death or complications for a general (non-diseased) population can result in significant underestimates of disease burden or cost-effectiveness in decision analytic models of disease management or prevention.

DB2

PERSISTENCE WITH BASAL SUPPORTED ORAL THERAPY—COMPARISON OF INSULIN GLARGINE VERSUS NPH INSULIN

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OBJECTIVES: To assess the persistence of type-2 diabetic patients treated with basal supported oral therapy (BOT) with insulin glargine (GLA) compared to NPH insulin (NPH). **METHODS:** We performed a retrospective cohort study using claims data for ambulatory prescriptions within the German statutory health-insurance scheme, based on a representative sample of more than 80 % of German community pharmacies. Insulin-naive patients treated with oral antidiabetic drugs (OAD) who were additionally initiating therapy with GLA or NPH between January 2003 and December 2006 were included and followed up until December 2007. Persistence was defined as the duration of time from initiation of GLA or NPH until switching to intensified conventional insulin therapy (ICT). A switch to ICT was assumed whenever a short-acting insulin was prescribed for the first time followed by at least one prescription of a long-acting insulin within six months. Univariate and multivariate Cox proportional hazards models were used to compare both cohorts. **RESULTS:** In total, 97,998 patients (61,070 Glargine and 36,928 NPH) were included. Within the observation period, 23.5 % of GLA patients and 28.0 % of NPH patients switched to ICT. On average, these patients stayed 388 days on GLA and 313 days on NPH, respectively ($p < 0.001$, log-rank test). The risk of switching to ICT was significantly higher for NPH patients compared to GLA patients (unadjusted hazard ratio [HR] 1.34 (99 % CI: 1.29–1.38)). After adjustment for predefined covariables i.e., type of physician (general practitioner vs. specialist), region, insurance status (member, family member, retired), health insurance company, comedication, number of OAD, dose of basal insulin, the risk for NPH patients remained significantly higher (adjusted HR: 1.22 (99 % CI: 1.18–1.27). **CONCLUSIONS:** Type 2 diabetic patients under basal supported oral therapy treated with insulin glargine stay significantly longer on initial therapy until they switch to ICT when compared to NPH.

DB3

USING ELECTRONIC MEDICAL RECORDS TO IDENTIFY UNDIAGNOSED DIABETES MELLITUS IN PRIMARY CARE PRACTICES

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OBJECTIVES: To assess the prevalence of potentially undiagnosed diabetes mellitus (UDM) in a nationally representative patient sample. **METHODS:** The data source was GE's Medical Quality Improvement Consortium (MQIC) database (February 2009) containing electronic medical record (EMR) data on >11 million patients in the U.S. Two previously published (Holt, et al, 2008) search strategies were applied to identify patients without diagnosis or medication evidence of DM, but with a fasting (FBG) or random blood glucose (RBG) result available (denominator for prevalence estimates). Strategy A patients were non-DM patients whose last glucose on record (LGOR) = RBG ≥11.1 or FBG ≥7.0 mmol/l. Strategy B patients were non-DM patients with LGOR (FBG or RBG) ≥7.0 mmol/l. Strategy A and B patients were each grouped by age/sex categories, and prevalence of UDM calculated. The time since LGOR to datacut date was also assessed. **RESULTS:** From 11,196,881 total patients, 923,007 had diagnosed DM on record (n = 570,723) or were presumed to have DM on the basis of prescribed oral hypoglycemics or insulin (n = 352,284). After excluding additional patients with gestational diabetes and impaired glucose tolerance/pre-diabetes,10,147,355 remained. Of these, 3,799,599 had a glucose result available, with 38,068 identified as possible UDM using Strategy A (prevalence 0.38%), and 221,624 using Strategy B (prevalence 2.18%). In both instances, UDM prevalence increased with increasing age, in both sexes. Over 2 years had elapsed since the LGOR for over 50% of Strategy A patients, and 40% of Strategy B patients. **CONCLUSIONS:** The application of simple search algorithms to a large EMR database suggests there may be substantial underdiagnosis of DM in the US general population.

DB4

RISK OF STROKE OR MYOCARDIAL INFARCTION OF T2DM PATIENTS TREATED WITH PIOGLITAZONE OR NON-THIAZOLIDINEDIONE IN A MANAGED CARE SETTING IN THE UNITED STATES

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OBJECTIVES: To evaluate the risk of stroke or myocardial infarction (MI) in patients with type-2 diabetes mellitus (T2DM) receiving pioglitazone (PIO) or non-thiazolidinedione (Non-TZD) therapies. **METHODS:** A analysis of I3 Innovus database from January 1, 2000 to June 30, 2007 was conducted. T2DM patients (ICD-9 diagnosis codes 250.x0 or 250.x2) were grouped into PIO or Non-TZD cohorts based on the study drugs initiated. The index date is the first dispensing of pioglitazone or Non-TZD medications. Follow-up started at the index date and ended upon disenrollment from the health plan, first occurrence of stroke or MI, or the end of the period,