vant chemotherapy (ACT). The collection and assessment of data inputs for a U.S. economic analysis using this program has been reported. METHODS: Models from Litz and Tufts' CEA Registry were selected for model parameters using the following terms and MeSH headings: NSCLC, adjuvant chemotherapy, recurrence, utilization, economics, cost, quality of life, utility, cost-effectiveness-utility-benefit. Inclusion criteria were randomized controlled trials (RCTs), meta-analyses, health technology assessments, North American and European studies, quality of life analyses, and early lung cancer. Results were limited to full text and English articles. We also excluded relevant references listed in these articles. RESULTS: The search yielded one meta-analysis and 7 RCTs assessing ACT in resected NSCLC. These studies reported survival (HR 0.75–0.95 favoring ACT), ACT toxicity (30–85% experiencing grade 3–4 toxicity), and stage distribution (Stage IA 7–6%, IB 29–9%, II–35%, III–27%). They also included disease-free survival (HR 0.6–0.91 favoring ACT), but not stratified by NSCLC stage. Monthly cost of NSCLC was found in two studies (initial $15,255–11,496, continuing $2,602–3,733, terminal $9959–16,470). Two studies reported the U.S. cost of ACT treatment ($84,294), and measured relative grade 3–4 event rates and proportions of specific to early NSCLC including one with values related to ACT and toxicity with values varying from 0.60 to 0.75. Data reporting current U.S. ACT utilization was not identified. CONCLUSIONS: Early NSCLC literature contains the majority of inputs. Model limitations exist, specifically regarding recency by stage, current ACT utilization and cost of health care resources. These limitations can be overcome using expert opinion, assumptions for guideline adherence and/or conducting observational studies to inform the model.

PMR85 ANALYSIS OF CAUSAL RELATIONS IN STROKE REGISTRY DATA
Bakulji M1, Niewada M2
1Institute of Econometrics, Warsaw School of Economics, Warsaw, Poland; 2Department of Experimental and Clinical Pharmacology, Medical University of Warsaw, Warsaw, Poland
OBJECTIVES: Stroke–one of the leading causes of death and disability—represents substantial clinical and economic burden. Understanding treatment patterns and causal relations may help e.g. to identify outcomes predictors and cost drivers. We analyzed Polish Hospital Stroke Registry data on patient characteristics (demographics, risk factors, pre-stroke disability, stroke severity), hospital management, treatment outcomes and drugs (pre-admission, during hospitalization, and prescribed at discharge). We used inferred causation approach that deduced (non-causal) associations from (causal) independence. We found that demographic and natural sequel of drug management (drugs used prior to, in acute stroke and at discharge), surprisingly suggested no causal relation between some clinical characteristics and drug use (e.g. history of stroke/diabetes and oral anticoagulants) or acute stroke treatment (e.g. aspirin, thrombolysis, stroke unit based treatment) and mortality/post-stroke disability; determined the causal direction between some risk factors (e.g. hypertension and diabetes, gender and AF) and patient history and hospital management, treatment outcomes and drugs (pre-admission, during hospitalization, and prescribed at discharge). We used the Tetrad 4.3.10-6 with PC algorithm. Variables were grouped into five tiers, a priori forbidding some directions of causal influence. Large number of variables led us to a restrictive significance level (p<0.001).
RESULTS: New insight can be gained from existence, lack of, and direction of causal relations. Our results [confirmed (without imposing prior knowledge)] the belief that the current selected anticoagulants are effective in reducing the risk of new strokes, only in the absence of other coexisting factors and natural sequel of drug management (drugs used prior to, in acute stroke and at discharge), surprisingly suggested no causal relation between some clinical characteristics and drug use (e.g. history of stroke/diabetes and oral anticoagulants) or acute stroke treatment (e.g. aspirin, thrombolysis, stroke unit based treatment) and mortality/post-stroke disability; determined the causal direction between some risk factors (e.g. hypertension and diabetes, gender and AF) and patient history and hospital management, treatment outcomes and drugs (pre-admission, during hospitalization, and prescribed at discharge). We used the Tetrad 4.3.10-6 with PC algorithm. Variables were grouped into five tiers, a priori forbidding some directions of causal influence. Large number of variables led us to a restrictive significance level (p<0.001).
CONCLUSIONS: Apart from statistical or econometric criteria, causal-type reasoning is needed to confirm the intuition, and to detect new patterns in data. Further research should include the possibility of hidden variables and try to quantify the causal relations.

PMR86 HOW TO SELECT THE RIGHT COST-EFFECTIVENESS MODEL? A SYSTEMATIC REVIEW AND STEPSWISE APPROACH FOR TRANSFERRING AN EXISTING HEALTH ECONOMIC MODEL FOR RHEUMATOID ARTHRITIS
van Haalen HGM1, Tran-Duy A2, Boonen A3, Severens JL2
1Erasmus University, Rotterdam, The Netherlands; 2Maastricht University Medical Center, Maastricht, The Netherlands
OBJECTIVES: To a) perform a systematic literature review to identify existing models for cost-effectiveness analysis of disease modifying anti rheumatic drugs in Rheumatoid Arthritis, and b) to develop and test a method for the selection of a model that is transferable to the Dutch health care setting by simple adaptation. METHODS: We searched Medline and Embase to identify relevant studies in the English language between 1-1-2002 and 31-8-2012. For studies that met the inclusion criteria, we applied a 3-step approach in model selection. First, models that did not meet all minimal methodological requirements based on the OMERACT criteria were excluded. Second, the models were assessed based on their fit when transferred to the Dutch health care setting. Transferability factors as published by Welte et al., except for those that were deemed transferable by simple adaptation, were used for this ranking procedure. Finally, the remaining models underwent a general quality check using the Philips checklist. Models showing good fit and high quality were selected. The transferred model was finally tested using simple adaptation. RESULTS: The systematic literature search resulted in 498 papers, which included 33 unique health economic models. Only six models passed the OMERACT criteria and were selected for further model transferability fit according to Welte. The remaining four models were, according to Philips, of good quality and were expected to be transferrable by a simple adaptation. CONCLUSIONS: This study introduces a stepwise approach to the identification and selection of a cost-effectiveness economic model for moderate to severe rheumatoid arthritis through simple adaptation. This approach can be applied in various therapeutic areas, provided that the minimal methodological requirements are defined accordingly. Availability of health economic models coupled with structured model selection could improve the efficiency, quality, and comparability of health economic evaluations.

PMR87 INTERNAL VALIDATION OF THE SYRONE DIABETES MODEL
Zubekom A1, Meréz G2, Nagyjánosi L1, Nagy Istikó S1, Nagy B1, Káli Z1, Vécsey Z2
1Eötvös Loránd University, Budapest, Hungary; 2Syrone Research Institute, Budapest, Hungary
OBJECTIVES: The Syrone model was developed to predict the long term effects of sodium-glucose cotransporter type 2 diabetes. After a successful internal validation the model’s outcomes needs to be compared to outcomes of cohorts that were not used for the modeling exercise. The objective of this study was to demonstrate the methods and results of the external validation. METHODS: As a first step, we identified the applicable clinical trials and cohort studies which had not been used to build the model and simulated the patient cohorts for each study according to the published demographic, epidemiologic characteristics and treatment pattern. The incidence rates of the predicted and observed outcomes were calculated for comparison and the results were evaluated using statistical methods and expert opinion. RESULTS: 92 validation analyses were performed. The differences between the actual and the modelled incidence rates of major adverse effects ranged from 44% - and 100%. The slope of the fitted linear regression line was 0.5326 while the R² value was 0.6956. The macular oedema submodel presented the best fit and the estimated values from the foot ulcer submodel had the lowest accuracy compared to observations in other studies. CONCLUSIONS: Overall the model performed well, however it frequently underestimated the incidence of the outcomes observed in the studies. This is most likely due to the limited information about the patient characteristics from the studies under evaluation. In most cases the information published about the population characteristics, treatment patterns and effectiveness were not sufficiently detailed to precisely match the model’s input parameters. Without sufficient information average values were used as input parameters, and this way the model presumably simulated healthier patient cohorts than the ones participated in the studies.

PMR88 DISENTANGLING EFFECTS ON FATAL AND NON-FATAL CARDIOVASCULAR EVENTS OVER TIME
Khan W1, Van Hout B2, S. Vanclay3
1Pharmacia Ltd., York, UK
OBJECTIVES: Within acute coronary syndromes (ACS), the risk of experiencing fatal and non-fatal cardiac events is highest immediately after diagnosis and decreases over time. In this paper we report results from three trials of low intensity (LID) statins to prevent three potential risk periods. The highest risk (unstable disease) period typically lasts up to 10 days from diagnosis. Patients then become more stable but are still at a high risk of events until approximately 30 days from diagnosis. Beyond 30 days patients are considered stable and at a lower risk of events. Different agents may be best suitable for different periods and may affect different events. The objective of this research is to estimate a model which enables the effects on fatal and non-fatal events following acute coronary syndrome to be disentangled between periods of disease without accurately knowing how long these periods are. METHODS: A Markov model is estimated which distinguishes between three time periods and between fatal and non-fatal events. A likelihood function is derived as well as a Bayesian procedure to estimate the model parameters. The approach is tested using simulated data. Subsequently, event free survival data and overall survival data comparing ticagrelor with clopidogrel are taken from the Kaplan-Meier curves presented in the publication of the PLATO trial and model parameters are estimated based on these data. RESULTS: Using simulated data the model mimics the data generating process perfectly and the approach seems quite powerful in distinguishing periods and different causal effects. CONCLUSIONS: Cases presented with stable disease and with unstable disease experience different treatment effects. The results of the PLATO study we conclude from the model that ticagrelor lowers the probability to experience an event in the unstable and stable high risk disease periods.

PMR89 A DE NOVO ECONOMIC MODEL TO ASSESS THE COST AND QUALITY OF LIFE CONSEQUENCES OF AN INTERVENTION FOR LEVODOPA INDUCED DYSKINESIA AMONG PATIENTS WITH PARKINSON’S DISEASE
Bhattacharyya S1, Sacco F2, Shimore RM1, Sonathi V1, Thomas S2
1NovaSures Healthcare Pvt. Ltd., Hyderabad, India; 2NovaSures Pharmaceuticals Company, East Norwich, NY, USA
OBJECTIVES: Emergence of long-term side effects of treating Parkinson’s disease (FD) patients with levodopa, particularly dyskinesia (levodopa induced dyskinesia - LID), limit the ability to optimally treat symptoms and complications of FD. LID-LID severity with performance of activities of daily living, ambulation and balance and increases health care costs. There are no approved treatments and no studies examining cost-effectiveness of an intervention for FD-LID. Objective of the present study is to develop a de-novo economic model to identify the value drivers for a drug to be cost-effective for treatment of FD-LID. METHODS: The model combines a short-term (6 months) decision tree, to determine initial response to the drug, with a long-term Markov approach to model transition of patients across LID severity over lifetime. The model classifies LID severity using modified Abnormal Involuntary Movement scale (mAIMS) with disease states defined as mild (0–12), moderate (13–18) and severe (19–24). Disease state specific costs included costs of doctor visits, medication, hospitalization, radiological examinations, hospitalizations, community/social services and unpaid services. State specific utilities were calculated and assigned based on the Pain, Disability, and Quality of Life (PDQ39) questionnaire. The model estimated probability of improvement and halt worsening dyskinesia health states are the greatest benefit the model can gain from the PLATO study we conclude from the model that ticagrelor lowers the probability to experience an event in the unstable and stable high risk disease periods.
to characterize the underlying disease progression parameters and strengthen these assessments.

PRM90
OVERVIEW OF HEALTH ECONOMIC MODELS IN TYPE 2 DIABETES MELLITUS (T2DM): A SYSTEMATIC REVIEW OF THE LITERATURE

Chandrapau M1, Babater FJ1, Townsend R1, Roudaut M1, Verheggen BG1
1Pharminter International, Rotterdam, The Netherlands, 2Bristol-Myers Squibb, Rueil-Malmaison, France

OBJECTIVES: To identify and compare economic models developed to evaluate the cost-effectiveness of treatments for type 2 diabetes mellitus (T2DM), and their use in health care decision-making. METHODS: This research updates two previously published systematic reviews. The current systematic literature review was performed according to a pre-defined search strategy and review criteria in six commonly used databases from September 2008 to January 2013. In addition, websites of Health Technology Assessment (HTA) organizations across multiple major disease conferences’ proceedings were also reviewed. For each identified model, key information was extracted and assessed. RESULTS: Overall, 226 citations were identified, 122 full text publications, 369 conference proceedings and 106 HTA literature search using a predefined strategy in MEDLINE, EMBASE and the Cochrane Library identified 16 unique placebo-controlled RCTs reporting FEV1 trough, total TIO18 (n=13) and AB400 (n=3). The development of trough FEV1, over time for AB400, TIO18 and placebo (FLA) was modeled with fractional polynomials, and the difference between the parameters of these polynomials within a trial were used to force the model outcomes into different quadratic shapes that the curve can take.

To explore and explain different results: We obtained by applying Robins’ method that repeated combination therapies decreased the risk of liver related complications and the frequency of retreatment of responder patients on features of status, and tumor are higher than the corresponding costs of patients with sustained complete response. The cause-effect analysis of the strategy of treatment, especially the frequency of retreatment of responder patients on features of status, events, and costs of patients diagnosed Hepatitis C. METHODS: Causal inference is particularly useful in drug development, as the causal relationship have been becoming widespread. By these new methods, analyses similar to assessment of randomized clinical trials have become available. In our research, we studied the causal effects of the strategy of treatment, especially the frequency of retreatment of responder patients on features of status, events, and costs of patients diagnosed Hepatitis C. RESULTS: Causal inference in longitudinal (e.g. patients’ data) is a growing field of study. Conclusions: Robins’ method is appropriate for measuring the causal effects of various factors of care on patient pathways, especially if patient turnover data are supplemented with physiological, diagnostic and lab information found in clinical registers.

PRM95
APPRPRIORATE EVIDENCE SOURCES FOR POPULATING DECISION ANALYTIC MODELS WITHIN HEALTH TECHNOLOGY ASSESSMENT (HTA): A SYSTEMATIC REVIEW OF HTA MANUALS AND HEALTH ECONOMIC GUIDELINES

Technimetrics Klaas C1, Schnell-Indest P2, Zauuner G2
1Technimetrics, Vienna, Austria, 2MIT, Israel University for Health Sciences, Medical Informatics and Technology, Hall 1 T, Tsfat, Israel

METHODS: Decision analytic models use various types of evidence for populating model parameters. Detailed methodological advice on the type of evidence that is used for what type of parameter model is required. We aim at reviewing existing HTA manuals and health economic (modelling) guidelines in order to gain insight into the evidence sources for parameter estimation. METHODS: We identified manuals and guidelines via the International Network of Agencies for Health Technology Assessment (INAHTA) and by hand search. We included documents from the USA, Canada, Australia, New Zealand as well as transnational guidelines written in English or German. We systematically sum-