in lifetime costs and utilities of $17,208 and 10.4124 QALYs compared with $16,780 and 10.4057 QALYs for prasugrel therapy. The ICER for clopidogrel was $63,840/QALYs. The acceptability curve showed that prasugrel was not likely cost-effective with >80% certainty at any WTP threshold. One-way sensitivity analyses (WTP decision threshold: $100,000/QALY) showed that prasugrel is the most cost-effective strategy when probability of MI is increased by >12%, probability of bleeding is decreased by >24%, and disutility associated with MI is >0.1634. When only patients with variant CYP2C19 were considered, the ICER was found to be $2,313,333/QALY for clopidogrel. **CONCLUSIONS:** Inconclusive results indicate that there is no benefit in prescribing one therapy over the other for the entire patient population. CYP2C19 polymorphism should be given consideration during the decision making process. For the base-case scenario, prasugrel therapy was the preferred strategy in patients with variant CYP2C19.

PCV43

COST-EFFECTIVENESS ANALYSIS OF RIVAROXABAN VERSUS DABIGATRAN AND ENOXAPARIN FOR THE PREVENTION OF VENOUS THROMBOEMBOLISM AFTER TOTAL HIP REPLACEMENT

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OBJECTIVES: To evaluate the cost-effectiveness of rivaroxaban compared with dabigatran and enoxaparin for the prophylaxis of venous thromboembolism in patients undergoing elective total hip replacement (THR) in the context of Russian health care system. **METHODS:** A decision-tree model on the choice of regimens for thromboprophylaxis after THR was adopted from the model, developed by McCullagh et. al. (2009). Primary outcomes was mortality, occurrence of distal and proximal DVT, rates of symptomatic PE. Incidence of gastrointestinal bleeding, stroke and death was also included into the model. Delphi method was used to determine typical practice and cost of management of DVT and PE. It was assumed that patients with DVT were treated for 90 days, patients with PE – for 180 days. All patients in the model received thromboprophylaxis with one of the following regimens: rivaroxaban dose of 10 mg/day orally for 31-39 days (RECORD 2); dabigatran dose of 220 mg/day orally for 28-35 days (RE-NOVETE); enoxaparin dose of 40 mg/day subcutaneously for 10-14 days (RECORD 2). Incremental cost-effectiveness ratios (ICERs) were calculated. **RESULTS:** The cost of prophylaxis with enoxaparin was 6991 USD, with dabigatran - 7076 USD, with rivaroxaban - 7147 USD. Although rivaroxaban has more effectiveness in preventing DVT (0.016 vs. 0.082 vs. 0.045) and PE (0.0012 vs. 0.005 vs. 0.004) than enoxaparin and dabigatran correspondingly. ICER to prevent 1 case of deep vein thrombosis after THR in rivaroxaban versus enoxaparin was 23.6 USD, and in dabigatran versus enoxaparin was 22.9 USD. ICER to prevent 1 case of pulmonary thromboembolism after THR in rivaroxaban versus enoxaparin was 556.7 USD, and in dabigatran versus enoxaparin was 850.3 USD. **CONCLUSIONS:** Despite of higher cost of prophylaxis of DVT and PE with rivaroxaban, comparing to enoxaparin and dabigatran, prophylaxis with rivaroxaban was more effective with acceptable ICERs.

PCV44

CHANGING COST-EFFECTIVENESS EARLY IN THE PRODUCT LIFE CYCLE: THE EXAMPLE OF CLOPIDOGREL BISULFATE

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OBJECTIVES: New medicines are launched based on a limited number of clinical trials. Payers, providers, and patients base their utilization decisions on this information. Furthermore, projected cost-effectiveness and real world cost-effectiveness are moving targets that may differ greatly, especially early in the product life cycle. We examine this divergence using clopidogrel, an antiplatelet medication for preventing strokes and heart attacks, as a case study. **METHODS:** Using the National Ambulatory Medical Care Survey (NAMCS) data from 1998 to 2008, we estimate changes in the volume and distribution of patient prescriptions by age, gender, and race. We combine these time trends with estimates from the pharmacoeconomics literature on cost-effectiveness measured as cost per quality-adjusted life year (QALYs). **RESULTS:** From 1998 (following approval in November 1997) to 2001, the average age of clopidogrel patients dropped from 77 to 70. Over the same period, the percentage of patients who were under 54 years of age increased from 0% to 13%. Comparing the real-world patient population to a pivotal phase 3 trial also reveals a large difference in gender mix: 72% male in the trial vs. 45% in NAMCS in 1998. Similar trends were found for race: by 2008, patients were much less likely to be white than in the trial—only 82% versus 95%. In 1999, 1.7 million office visits included a prescription for clopidogrel, 7.5 times as many as in 1998. By 2008, almost 16 million prescriptions were written—1.5 for every 100 office visits. Adjusting for demographic mix, the estimated real-world CE improved between 2000 and 2001 by 16% ($25,000 per QALY vs. $21,000, respectively). From 1998 to 2008, the CE ratio fell by 23%. **CONCLUSIONS:** These results demonstrate that cost-effectiveness projected at launch may provide only limited indication of the ultimate real-world impact, which improved substantially over time, in this example.

PCV45

COST-EFFECTIVENESS OF CYP2C9 AND VKORC1 GENOTYPE-GUIDED WARFARIN ANTICOAGULATION CARE: THE IMPLEMENTATION OF DISCRETE EVENT SIMULATION MODEL ON THE NATURAL HISTORY OF VENOUS THROMBOEMBOLISM

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OBJECTIVES: To evaluate and compared the long-term costs and outcomes of four warfarin treatment strategies of CYP2C9, VKORC1, both CYP2C9 and VKORC1 genotype-guided dosing, and standard warfarin dosing among nonvalvular VTE patients in the societal perspective. **METHODS:** A discrete event simulation model was used to depict patients' health states as the disease evolves with time, and captured its associated costs (2007 U.S. dollars) and quality of life. Data was extrapolated with the criteria of including VTE patients of age >=18 years on warfarin with INR target of 2-3. Probabilities, costs and humanistic properties were obtained from the literature, HCUP (NIS & SEDD), and the Medicare Reimbursement Schedule databases. Sensitivity analysis was performed for uncertainty parameters in the model. All costs and benefits were discounted at 3%. **RESULTS:** There was a significant difference in the prevalence of bleeding complication between standard anticoagulation (6.1%) and the genotype –guided of CYP2C9 and VKORC1 groups (<5.8%). The mean cost and QALYs per patients were $14,340 and 8.1251. The genotype-guided warfarin anticoagulation strategies projected higher cost and higher QALYs. However, considering the threshold of $100,000/QALY, VKORC1 genotype-guided was indicated to be cost-effective among all strategies. Sensitivity analysis demonstrated 25% of the replications of both CYP2C9 and VKORC1 genotype-guided strategy to be <$100,000/QALY. **CONCLUSIONS:** This study showed that testing for multiple genotypes of CYP2C9 and VKORC1 to guide warfarin anticoagulation therapy is not cost –effective in all population and that patient with higher risk of complications are more likely to benefit from this new innovation. For the genotype-guided test to be cost-effective in the population with VTE, the cost of the test would have to be <$400 or be restricted to patient at high risk for bleeding complications (RR>5.8).

PCV46

LONG-TERM COSTS AND HEALTH OUTCOMES OF TREATING ACUTE CORONARY SYNDROME PATIENTS WITH TICAGRELOR BASED ON THE EU LABEL - COST-EFFECTIVENESS ANALYSIS BASED ON THE PLATO STUDY

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OBJECTIVES: The PLATO trial showed that in patients with acute coronary syndromes (ACS) treatment with ticagrelor compared with clopidogrel significantly reduced the rate of myocardial infarction (MI), stroke, or death from vascular causes without a significant increase in the rate of overall major bleeding. Based on clinical and health-economic data from PLATO the present study evaluates the long-term cost-effectiveness of treating patients with ticagrelor based on the EU label. **METHODS:** A two-part decision-analytic model, comprising a one-year decision tree and a long-term Markov model, was constructed to estimate lifetime costs and QALYs of treating ACS patients for one year with ticagrelor plus acetylsalicylic acid (ASA) compared with clopidogrel plus ASA. Using individual-patient data from PLATO, event rates, health-care costs (Swedish in base-case analysis), and QALYs were estimated for the first year. For the second year onwards, necessary assumptions and external data sources were utilized to extrapolate quality-adjusted survival conditional on whether a non-fatal MI, a non-fatal stroke or no event occurred during the first year. A probabilistic analysis was performed and incremental cost-effectiveness ratios are presented from a health-care perspective in 2010 prices. A generic clopidogrel price of €0.17 ($0.23) per day, and a ticagrelor price range of €2.25 ($3.00) to €3.50 ($4.65) per day were applied. **RESULTS:** Treatment with ticagrelor was associated with a QALY gain of 0.13 compared with clopidogrel. The cost per QALY gained with ticagrelor was in the range of €2,350 ($3,110) to €5,700 ($7,550) compared with clopidogrel. Ticagrelor is likely to be cost-saving if proprietary clopidogrel prices are applied. The results were consistent in major sub groups across the broad ACS population. **CONCLUSIONS:** Based on clinical and health-economic evidence from the PLATO study, treating a broad spectrum of ACS patients with ticagrelor for one year based on the European label is cost-effective compared with clopidogrel.

PCV47

COST-EFFECTIVENESS OF FONDAPARINUX AND ENOXAPARIN IN PATIENTS WITH NON ST-SEGMENT ELEVATION ACUTE CORONARY SYNDROME IN BRAZIL

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OBJECTIVES: Associated use of antithrombotics, antiplatelets and invasive strategies in patients with non ST-segment elevation acute coronary syndromes (NSTE-ACS) reduces cardiovascular events, however, with an increase in the risk of bleeding. Clinical studies showed that fondaparinux is as effective as enoxaparin in treating patients with NSTE-ACS, but with reduced risk of bleeding events. The objective was to determine the cost-effectiveness of fondaparinux versus enoxaparin in patients with NSTE-ACS in Brazil from the perspective of the Brazilian Ministry of Health (MoH). **METHODS:** An analytic decision tree model was conducted to estimate the resultant costs and consequences of the targeted therapies in patients with NSTE-ACS. Model input data derived from the OASIS-5 study (N=20,078 NSTE-ACS patients randomized to fondaparinux or enoxaparin). The analyzed outcome was a composite of cardiovascular events (i.e., death, acute myocardial infarction, stroke, and major bleedings). Model time horizon was 9, 30, and 180 days post-NSTE-ACS. Direct costs of NSTE-ACS events and treatments were computed (i.e., drugs, coronary angiography, myocardial revascularization, percutaneous intervention - PCI, hospitalizations, etc.). Costs were expressed in 2010 Brazilian currency (1BRL=0.59USD). Univariate and multivariate (Monte Carlo) analyses tested model robustness. **RESULTS:** At day 9, the average cost per patient

treated was 2,575 for fondaparinux and 2,688 for enoxaparin. Over 65% of total costs were attributed to the invasive treatment (PCI and revascularization). Drug costs (in-hospital therapies) accounted for 10% (fondaparinux) and 12% (enoxaparin) of total costs. The estimated rates of cardiovascular events were 7.3% and 9.0% for fondaparinux and enoxaparin, respectively. Results kept unchanged on days 30 and 180 post-NSTE-ACS. Sensitivity analysis confirmed base-case results. **CONCLUSIONS:** Fondaparinux was dominant over enoxaparin (lower costs, better long-term benefits). The budget impact after 5 years of anticoagulant substitution (at 20% constant adoption rate per year) could reach 90 million BRL in savings for the Brazilian MoH and healthcare system.

PCV48

COST-EFFECTIVENESS ANALYSIS OF ANTIARRHYTHMIC THERAPIES FOR THE TREATMENT OF SUPRAVENTRICULAR TACHYCARDIA AND SURGICALLY INDUCED TACHYCARDIAS AND HYPERTENSION

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OBJECTIVES: The objective of this analysis was to estimate the cost effectiveness of commonly used antiarrhythmic agents for the treatment of supraventricular tachycardia (SVT) and intraoperative/ postoperative tachycardia and hypertension. **METHODS:** A decision tree model was built to examine the cost effectiveness of esmolol, metoprolol, diltiazem and amiodarone for the treatment of SVT and intraoperative and postoperative tachycardia and hypertension from a hospital perspective. The default pharmacy costs in the model were based on publicly available wholesale acquisition costs (WAC). Literature based values were used for the rates and medical costs of adverse cardiac events including myocardial infarction, stroke, hypotension, bradycardia, and ischemia. The primary efficacy parameter, rate of successful heart rate control, was based on literature values. The outcome was the cost per successful heart rate control with incremental cost effectiveness ratios (ICERs) calculated. No discounting was applied due to the short time frame of the analysis. For the probabilistic sensitivity analysis, a Monte Carlo simulation consisting of 1,000 simulations was conducted to test the joint uncertainty of all modeling parameters simultaneously. **RESULTS:** The total cost of therapy was $1,250.82, $2,630.19, $2,280.21, and $1,555.14 for esmolol, metoprolol, diltiazem and amiodarone, respectively. The rate of successful heart rate control was 90% (esmolol), 64% (metoprolol), 90% (diltiazem) and 74% (amiodarone). The cost per successful heart rate control was $1,389.80 (esmolol), $4,109.67 (metoprolol), $2,533.57 (diltiazem), and $2,101.54 (amiodarone). The ICER of esmolol dominated metoprolol, diltiazem and amiodarone. In the probabilistic sensitivity analysis, esmolol was the most cost-effective antiarrhythmic in 99.6% of simulations. One-way sensitivity analyses showed the model was most sensitive to the cost of hypotension and bradycardia. **CONCLUSIONS:** In this model, esmolol was the least costly and most effective antiarrhythmic. Esmolol is cost-effective in comparison with metoprolol, diltiazem and amiodarone for the treatment of SVT and intraoperative/ postoperative tachycardia and hypertension.

PCV49

COST-EFFECTIVENESS ANALYSIS OF RIVAROXABAN VERSUS DABIGATRAN AND ENOXAPARIN FOR THE PREVENTION OF VENOUS THROMBOEMBOLISM AFTER TOTAL KNEE REPLACEMENT

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OBJECTIVES: Patients after major orthopedic surgery on the joints of the lower extremities require an effective thromboprophylaxis to prevent deep vein thrombosis (DVT) and pulmonary embolism (PE). Objective of this study was to evaluate the cost-effectiveness of rivaroxaban compared with dabigatran and enoxaparin for the prophylaxis of venous thromboembolism in patients undergoing elective total knee replacement (TKR) in the context of Russian health care system. **METHODS:** A decision-tree model on the choice of regimens for thromboprophylaxis after TKR was adopted from the model, developed by McCullagh et. al. (2009). Primary outcomes was mortality, occurrence of distal and proximal DVT, rates of symptomatic PE. Incidence of gastrointestinal bleeding, stroke and death was also included into the model. Delphi method was used to determine typical practice and cost of management of DVT and PE. It was assumed that patients with DVT were treated for 90 days, patients with PE – for 180 days. All patients in the model receive thromboprophylaxis with one of the following regimens: rivaroxaban dose of 10 mg/day orally for 10-14 days (RECORD 3); dabigatran dose of 220 mg/day orally for 12-15 days (RE-MODEL); enoxaparin dose of 40 mg/day subcutaneously for 10-14 days (RE-MODEL). Incremental cost-effectiveness ratios (ICERs) were calculated. Analyses was made from state health care point of view. **RESULTS:** The cost of prophylaxis with rivaroxaban was 5621 USD (dominant technology), with enoxaparin - 5657 USD, with dabigatran - 5763 USD. Rivaroxaban has more effectiveness in preventing DVT (0.096 vs. 0.36 vs. 0.36) and PE (0.00 vs. 0.001 vs. 0.00) than enoxaparin and dabigatran correspondingly. **CONCLUSIONS:** Results of modeling have shown that rivaroxaban is dominant technology for prevention of venous thromboembolism after total knee replacement comparing to enoxaparin and dabigatran in the scope of Russian health care system.

PCV50

COST-EFFECTIVENESS ANALYSIS COMPARING DABIGATRAN AND ADJUSTED-DOSE WARFARIN FOR STROKE PREVENTION IN ATRIAL FIBRILLATION

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OBJECTIVES: Atrial fibrillation has been estimated to affect as many as 2.3 million Americans, making it the second most common cardiovascular condition in the United States. Atrial fibrillation has been found to increase patient's risk of stroke by 5-fold. We sought to calculate the projected total treatment costs, quality-adjusted survival and cost-effectiveness of dabigatran and adjusted-dose warfarin for stroke prevention in patients with atrial fibrillation. **METHODS:** This three-state Markov transition model (healthy with atrial fibrillation, disability, and death) simulated the treatment costs, quality-adjusted survival and cost-effectiveness of dabigatran 150 mg twice daily and adjusted-dose warfarin (international normalized ratio of 2-3) for stroke prevention in atrial fibrillation. Our base-case consisted of a hypothetical cohort of ≥65 year old patients with atrial fibrillation, a moderate risk of stroke ($CHADS_2 \geq 1$) and no contraindications to anticoagulation therapy. The parameters used in the model were adopted from the literature research, Cost-effectiveness was calculated over a patient's lifetime and using a societal perspective (excluding indirect costs). One-way and threshold sensitivity analyses were performed on all relevant variables. **RESULTS:** The mean quality-adjusted life expectancy of simulated patients was 12.9 and 12.2 years for those receiving dabigatran and warfarin. Total lifetime treatment costs were $146,649 and $118,904. The incremental cost-effectiveness ratio was $40,580. Upon one-way sensitivity analysis, our conclusions were found to be sensitive to changes in dabigatran cost and the differential efficacy of the two strategies. Threshold sensitivity analysis further revealed that daily dabigatran costs greater than $13 per day and differential efficacy between the two strategies of less than 0.15% per year resulted in incremental cost-effectiveness ratios greater than $50,000 per quality-adjusted life year gained. **CONCLUSIONS:** Our analysis suggested that dabigatran is cost-effective for stroke prevention in atrial fibrillation; however, this conclusion was sensitive to changes in dabigatran costs and the antithrombotic efficacy of the two treatment strategies.

PCV51

THE VALUE OF ATORVASTATIN OVER THE PRODUCT LIFE CYCLE

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OBJECTIVES: The cost-effectiveness of a drug is often evaluated at a single point in time, yet costs, effects, or relevant comparators may change over the product life cycle. This study models the cost-effectiveness of atorvastatin from product launch in 1997 through 2011 and into the future. **METHODS:** We model the yearly cost-effectiveness of atorvastatin compared to its major competitor simvastatin from 1997 to 2030 from a US payer point of view. Key events include the entry of generic simvastatin in June 2006 and the expected entry of generic atorvastatin in November 2011. Estimates for incremental costs (in USD) and effects (in QALYs) for primary and secondary prevention of cardiovascular events are taken from previous literature and adjusted for drug price changes over time. Total statin use estimates are derived from NHANES. Sensitivity analysis examines variation in study parameters including drug prices, indication use, and discount rates. **RESULTS:** Assuming increasing statin use over time (with a mean of 1m new users per year) and a 3% discount rate, the cumulative incremental cost-effectiveness ratio (ICER) for atorvastatin vs. simvastatin ranges from cost saving at release to a maximum of $45,066 per QALY after six years of generic simvastatin in 2012. Over the full modeled life cycle (1997-2030), the cumulative ICER of atorvastatin is $20,331 per QALY. Results were similar in sensitivity analysis. **CONCLUSIONS:** The ICER of atorvastatin varies across the product life cycle, rising during the period between generic simvastatin entry and generic atorvastatin entry, and declining afterwards. Over its life cycle, atorvastatin is associated with a cumulative ICER of $20,331 per QALY, with a maximum of $45,066 per QALY.

PCV52

COST-EFFECTIVNESS STUDY OF CITICOLINE IN PATIENTS WITH ACUTE ISCHEMIC STROKE IN RUSSIA

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OBJECTIVES: Cerebrovascular diseases are on the second place among all causes of death in Russia. Neuroprotective therapy is one of the main approaches of therapy in patients with acute ischemic stroke in Russia despite the absence of this group of medicines in the recommendations of national standard of care in stroke (GOST R 200). The objective of this research was to evaluate cost-effectiveness ratio for the use of citicolin (a neuroprotective agent widely used in some EU countries, South Korea, Russia and some other countries) in patients treated according to the national standard of care in stroke (GOST R 200). **METHODS:** The data on the efficacy of citicolin in patients with acute ischemic stroke were extracted from pooling analysis of clinical trials "Oral citicolin in acute stroke" (Davalos A. et al., 2002) The clinical effect was measured as global recovery index (proportion of patients with full recovery during 3 months). Cost of treatment with citicolin and cost-effectiveness ratio (CER) were calculated from the point of view of the Russian state health care system. **RESULTS:** According to the results of the above mentioned pooling analysis, the use of citicoline in stroke patients was associated with significantly greater rate of recovery than placebo (OR,1.33; 95% CI, 1.10 to 1.62). Costs of treatment of acute ischemic stroke according to recommendations of the national standard plus citicolin was 1 715.5 USD per 3 months. Costs of the treatment without citicolin was 1 289 USD per 3 months. CER (i.e. direct costs per one fully recovery patient) treated with citicolin and placebo were 6 354 USD and 6 384 USD respectively. Incremental CER was 6 264 USD. **CONCLUSIONS:** According to the applied model a treatment, citicolin appeared to demonstrate its clinically efficacy and cost-effectiveness in treatment of the patients with acute ischemic stroke, compared to placebo.