the reliability of the anchor and the estimated MID. METHODS: We performed a simulation study in which the reliability of the anchor used for MID estimation was varied systematically. Features of real-life data (e.g., skewed distribution, discreteness of PRO scale) and anchors were used to generate simulated PRO scales and anchors. MIDs were then estimated on the basis of the simulated data. RESULTS: Compared to the MID value obtained with an anchor with perfect reliability (r = 1), a marked attenuation of the MID was observed when reducing the reliability of the anchor. Thus, an anchor with reliability 0.7 gave rise to a 24% to 35% decrease of the MID estimate and an anchor with reliability 0.5 led to a 45% to 55% reduction. Based on the findings and on theoretical considerations, we suggest a method for bias correction. CONCLUSIONS: When determining the MID of a PRO scale by an anchor-based method, the reliability of the anchor plays a crucial role. Anchors with poor to moderate reliability may lead to considerable underestimation of the MID. Bias correction is possible provided the reliability of the anchor is known.

PODIUM SESSION III: PRICING AND MARKET ACCESS

PR1

THE APPLICATION OF PHARMACOECONOMIC MODELING TO ESTIMATE A VALUE-BASED PRICE FOR NEW CANCER DRUGS IN A PUBLICLY FUNDED HEALTH-CARE SYSTEM

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OBJECTIVES: Value-based pricing has recently been discussed by international organizations as a means to estimate a drug price that is linked to the benefits it offers patients and society. However, one of the challenges with value-based pricing is determining the optimal threshold for health policy decision-making. The World Health Organization (WHO) has recommended using multiples of a country’s per capita GDP as the value threshold. In this study, pharmacoeconomic modeling was used to estimate a value-based monthly price for a hypothetical new cancer drug that provides a 3-month survival to patients with metastatic colorectal cancer (mCRC).

METHODS: A decision model was developed to simulate progression-free and overall survival in mCRC patients receiving standard chemotherapy ± the new drug. Outcomes for cancer control and side effects were abstracted from randomized trials in mCRC. Costs for chemotherapy were obtained from Canadian cancer centers. Utility estimates measured as quality-adjusted life-years (QALYs) were determined by interviewing 24 oncology nurses and pharmacists using the Time Trade-Off technique. The monthly price of the new drug was then modeled using a threshold of $117,000 per QALY gained, which is three times the Canadian per capita GDP, as recommended by the WHO.

RESULTS: The analysis suggested that a monthly price of $2180 would be considered cost-effective from the Canadian public health perspective. If the drug were able to improve patient quality of life or survival from 3 to 6 months, the monthly price could increase to $4100 and $3410 and offer the same value. CONCLUSIONS: The use of the WHO criteria for estimating a value-based price is feasible. However, one of the challenges would be to identify an appropriate threshold that would provide a balance between what governments can afford to pay and the commercial viability of the product in the reference country.

PR2

DECIDING ON VALUE FOR MONEY: A COMPARISON OF THE DUTCH, BELGIAN, SWEDISH, AND FRENCH DRUG REIMBURSEMENT SYSTEMS

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OBJECTIVES: Many countries are adapting their pharmaceutical reimbursement system, increasingly emphasizing the role of pharmacoeconomics in decision-making. The aim of our study is to analyze European regulatory systems to obtain insight into the decision level. None of the systems has a fully independent evaluation process and the decision-making process is often embedded in other stakeholders (e.g., the output of a national health technology assessment). The aim of our study was to analyze the French, Belgian, Swedish and Dutch drug reimbursement systems in order to identify similarities and differences.

RESULTS: We performed a comparative analysis of the Belgian, Dutch, Swedish, and French drug reimbursement systems in the The Netherlands, Belgium, Sweden, and France. We investigated policy documents, explored literature, and conducted interviews with policymakers and representatives of the pharmaceutical industry. RESULTS: All systems have a centralized decision body, even though the financial responsibility may be regional (Sweden). Only in Sweden, the minister has no role at the individual reimbursement decision level. None of the systems has a fully independent evaluation process and the impact of the systems is mainly assessed on drug expenditure. All countries make efforts to increase transparency. However, in Sweden manufacturers may withdraw their application before the final reimbursement decision, guaranteeing confidentiality at the cost of less transparency. Policies to deal with uncertainties vary per country: financial risk-sharing agreements by price/volume contracts—France—versus outcomes-based agreements for expensive inpatient drugs—the The Netherlands. The actual value of a drug and disease severity is reflected in the level of reimbursement in France and Belgium, whereas in the The Netherlands and Sweden, enlisted drugs are fully reimbursed. All countries attempt to improve the importance of pharmacoeconomics in decision-making. However, no country expresses the relative importance of cost-effectiveness compared to other criteria nor applies a strictly defined threshold.

CONCLUSIONS: This study reveals that while there is a convergence in scientific evaluation processes, important differences remain between the Dutch, Belgian, Swedish, and French regulatory frameworks. All countries recognize that pharmacoeconomics has a place in decision-making on value for money, but for the time being, pharmacoeconomics seems to play a rather undefined role.

PR3

THE IMPACT OF FINNISH PHARMACEUTICAL PRICING SCHEME IN COST-EFFECTIVENESS ANALYSES

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OBJECTIVES: Finnish retail prices for drugs are determined with a pricing scheme (PS). The PS is of the form “multiplier × wholesale price × fixed sum.” The multiplier ranges from 1.125 to 1.5 (being used for higher wholesale prices), whereas the fixed sum ranges from 0.5 to 47.68 euros (being larger for higher wholesale prices). Although PS is regressive, it nevertheless provides higher absolute pharmacy margins for drugs with higher wholesale prices. At the lower end of wholesale prices, PS results in retail prices that do not cover dispensing costs. Despite this, the retail prices (exclud-

VAT 8%) are used to represent all drug and drug delivery costs in economic evaluations. This study assesses the impact of this Finnish system-derived “distortion” in cost-effectiveness analyses. METHODS: The cost utilitarian of new hypothetical treatments were assessed in a setting where the new and old treatments produce different amounts of quality-adjusted life-years (QALYs) and the only cost difference comes from the pharmaceutical prices. The treatments are assumed not to differ regarding the real costs of drug delivery and patient survival. The PS-induced computational cost difference was deducted from the all-price differences of new and old treatments to estimate the impact of PS on the incremental cost-effectiveness ratios (ICER).

RESULTS: The computational cost differences due to PS ranged from 7.3 to 1951 euros and the QALYs gained ranged from 0.004 to 0.070 in estimated scenarios. The respective ICERs increased by 104 to 457840 euros/QALY due to the PS. CONCLUSIONS: The PS significantly worsens the ICERs obtained for more expensive and often innovative pharmaceuticals. The Finnish PS is problematic when the aim is to provide optimal, cost-effective treatments to Finnish patients. In the current form, the PS discourages innovation and may prevent reimbursement of otherwise cost-effective treatments.

PR4

GLOBAL MARKET ACCESS STRATEGY: AN INTEGRATED APPROACH

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OBJECTIVES: To develop a framework for integrating pricing and reimbursement with health economics and outcomes research and health policy to achieve commercially desirable prices and levels of access in 2010 and beyond. METHODS: A review of recent pricing policy and regulatory changes of countries, especially those in the financially troubled Eurozone, was conducted. This was supplemented by a review of P&R decisions for a selection of drug launches between 2005 and 2009 and categorized according to the level of therapeutic innovation and disease type (conventional, rare diseases, oncology). A search was performed on the OHE and NHS EED databases and HTA reports to establish the level of published value evidence in support of these launches, and finally, the components of most importance to a market access strategy were identified and validated through interviews across different stakeholders.

RESULTS: The review identified since January 2010, there have been 11 pricing policy and regulatory changes. From the review of recent P&R decisions and stakeholder interviews, the main components identified were: competitive and environmental analysis (market assessment, reimbursement, revenue forecasts, policy trends); analysis of payer’s decision drivers (payer, physician, and other stakeholder qualitative analysis); reimbursement (market access tactics (HTA, risk sharing, contracting negotiations with payers). The review of the P&R decisions also demonstrated an increasing trend toward deployment of risk-sharing schemes since 2008. CONCLUSIONS: Development of a successful market access strategy requires an understanding of pricing, health economics and outcomes research, health technology assessment (HTA), and health policy, and continually keeping vigilant and adapting to rapid changes in the policy environment. This research gives direction to health economics, P&R, and government affairs professionals for the development of an integrated framework for the design and implementation of a global market access strategy.

PODIUM SESSION III: HTA IN VACCINE AND EPIDEMICS

VA1

ARE THE BENEFITS OF FLU VACCINATION IN THE ELDERLY CORRECTLY SIMULATED IN ECONOMIC ASSESSMENT MODELS?

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OBJECTIVES: In literature, economic models of fl u vaccination in elderly (+65) most often consider the target population as one homogeneous age group evaluated during a 1-year time period (>1 year 65+ group cohort model). Because the mortality
rates in elderly steeply increase with age and the transition probabilities for specific health states are age specific, this population should be evaluated as non-homogeneous and over a lifetime with annual vaccinations. This study compares the cost results of flu vaccination between these two different modeling approaches. METHODS: Two models were developed to estimate the direct costs of annual flu vaccination compared with no vaccination: 1) a 1-year 65+ group cohort model; and 2) a lifetime multi-age cohort model with target population and clinical pathways stratified in five age cohorts (65-69 years; 70-74 years; 75-79 years; 80-84 years; 85+ years) eligible for annual vaccination. Both models were populated with US specific data. Vaccination coverage and disease management were identical in both models. The decision tree included the following states: natural deaths, infected, and symptomatic states followed by GP visits, hospitalizations (pneumonia, influenza, stroke, myocardial infarction, and congestive heart failure), death-specific death rates, and recovery in nursing homes. Undiscounted costs per individual per year are compared for vaccinated and unvaccinated groups, using both approaches. RESULTS: The cost per individual per year is higher in the 1-year 65+ group cohort model versus the lifetime multi-age cohort model (no vaccination: $203 vs $139; vaccination: $185 vs $113) as expected considering additional age cohorts with decreasing life expectancies in the multi-age cohort lowers the average cost per individual per year. Meanwhile, the selection of model type impacts the estimated incremental cost of vaccinated versus unvaccinated groups (~$20 vs $8—$26). CONCLUSIONS: In economic assessments, a 1-year 65+ group cohort approach underestimates the impact of heterogeneity in elderly on the benefit of flu vaccination, and therefore, a lifetime multi-age cohort is preferred.

GATHERING INFORMATION BY COMPARISON OF DIFFERENT DYNAMIC MODELING APPROACHES FOR EPIDEMIC MODELS

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OBJECTIVES: Several dynamic approaches can simulate epidemics and vaccination strategies. Generally, the models can be divided into top-down approaches like Markov models and differential equations and bottom-up approaches like cellular automata and agent-based models. Top-down approaches are characterized by cumulative values that are representing groups of people. Bottom-up approaches, in contrast, consider individuals. Both approaches have advantages and disadvantages. Top-down approaches can be analyzed very well with mathematical methods, while bottom-up approaches require comparison of the outcome of simulation runs with different parameter sets. To improve validity of model structures, a method that compares different approaches for epidemic models is introduced. METHODS: Statistical calculations and Markov models are static, while other approaches like differential equations or individual-based models are dynamic. In this context, dynamic does not only stand for simulation over time but also for models where the calculation of the next step or period depends on the current state of the model. Since the transition matrices in Markov models are calculated before execution time, it is not considered to be dynamic. The advantage of dynamic models is that they can produce highly nonlinear behavior that cannot be reached with static calculations. To validate the structure of such nonlinear models, different model types are implemented and compared. Results are compared; sensitivity analysis is done separately. RESULTS: Outcomes of vaccination against streptococcus pneumoniae was tested. A differential equations model and an agent-based model could reproduce results of published Markov models. As soon as we consider population dynamics, herd immunity, and serotype replacement, the Markov model was not able to fulfill the structural requirements anymore. Unlike dynamic approaches static models. CONCLUSIONS: Dynamic models offer more information and opportunities for epidemic simulation. Usage of different approaches provides at least comparable reliability.

INFLUENZA RISK AND VACCINATION RATES IN EUROPE: A NATIONWIDE SURVEY OF ADULTS

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OBJECTIVES: The aim of the current study was to determine influenza vaccination rates in UK, France, Germany, Italy, and Spain. METHODS: Data from the 2008 EU National Health and Wellness Survey (NHWS) were used. Demographics, comorbidities, and vaccination behavior in the past year were assessed for all respondents. Health-related quality of life (SF-12v2) and resource use (number of emergency room visits, hospitalizations, and physician visits) in the past 6 months were also measured. RESULTS: Only 23.7% of respondents received an influenza vaccine in the past year (UK: 25.3%, Germany: 25.2%, France: 20.2%, Italy: 24.8%, Spain: 24%; 1), a total of 28,158 respondents (52.6%) were at high risk for influenza complications (i.e., over age 50, had chronic conditions such as asthma, diabetes, COPD, cardiovascular conditions, or HIV/AIDS). Those at high risk reported significantly lower levels of both physical quality of life (mean = 43.88 vs. mean = 32.10) and health utilities (mean = 0.72 vs. mean = 0.73), and were more likely to report costs of annual flu vaccinations (or $22 vs. mean $12), and provider visits (mean was 5.96 vs. mean was 4.14) in the past 6 months relative to those not at high risk, all P < 0.0001. Despite the significantly worse health profile, only 35.9% of high-risk respondents received the vaccine. High-risk status was the strongest driver of vaccination in the UK (high risk: 42.2% vaccinated vs. non-high risk: 5.4% vaccinated, Φ = 0.42) and the weakest in Germany (high risk: 31.8% vaccinated vs. non-high risk: 16.2% vaccinated, Φ = 0.18). The most common reason for nonvaccination was a belief that the vaccine was unimportant (35.9%). CONCLUSIONS: Despite influenza vaccine recommendations guidelines, only a modest percentage of respondents in Europe were vaccinated. Even those at high risk for influenza complications, who reported significantly worse health outcomes than non-high-risk respondents, were vaccinated at less than a 40% rate.

COST-EFFECTIVENESS OF UNIVERSAL HEPATITIS B IMMUNIZATION IN VIETNAM: APPLICATION OF COST-EFFECTIVENESS AFFORDABILITY CURVES IN HEALTH DECISION-MAKING

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OBJECTIVES: To perform a cost-effectiveness analysis of newborn universal vaccination against hepatitis B virus (HVB) and to identify the cost-effectiveness levels of the vaccination program in Vietnam. METHODS: We simulated a birth cohort using 1,693,000 newborns in 2002. Incremental cost-effect ratios (ICERs) per quality-adjusted-life-year (QALY) gained with universal newborn vaccination against HBV was calculated using a Markov model. Two types of analyses (including and excluding expenditure on the treatment of chronic hepatitis B and its complications) were performed. We used 5000 Monte Carlo simulations to examine the cost-effectiveness acceptability and affordability of the vaccination program from the payer's perspective and to derive a cost-effectiveness affordability curve to assess the program's cost and health effects. All costs were expressed in 2002 US dollars. RESULTS: In the base-case scenario, newborn universal vaccination against HBV reduced the carrier rate by 58% at a cost of US$42 per carrier averted. From the payer's perspective, marginal cost per life-year and per QALY gained were US$47, much lower than GDP per capita of US$440 in 2002. The vaccination could be economically affordable starting at a relatively low budget of US$1.7 million. Universal vaccination would save US$ 1 billion from the treatment cost of complications due to chronic HBV infections. The probability of vaccination being both cost-effective and affordable is 27% at an annual budget of US$4.1 million at the cost-effectiveness threshold of US$3.9 per QALY. CONCLUSIONS: Universal newborn vaccination against HBV is highly cost-effective in Vietnam. In low-income, high-endemic countries, where funds are limited and economic results of vaccination are uncertain, our findings on the cost-effectiveness affordability options would assist vaccine purchasers in making proper health investments in vaccination strategies against HBV.

TOLERABILITY OF FIRST-LINE TREATMENTS OF LOCALLY ADVANCED OR METASTATIC NON-SMALL-CELL LUNG CANCER (NSCLC): A SYSTEMATIC REVIEW AND ADJUSTED INDIRECT COMPARISON

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OBJECTIVES: Platinum-based chemotherapy is a common first-line treatment of NSCLC; tolerability impacts choices on regimen. This research compared the tolerability of gefitinib and doublet chemotherapy in this setting in patients with activating epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutations (Mr). METHODS: Systematic searching of CENTRAL, EMBASE, and MEDLINE for randomized controlled trials (RCTs) comparing doubled chemotherapies (carboplatin or cisplatin) in combination with either docetaxel, gemcitabine, paclitaxel, pemetrexed, or vinorelbine (OR) for the first-line treatment of advanced NSCLC was completed in May 2009. Data were extracted on the following grades 3/4 adverse events (AEs) most commonly reported with doublet chemotherapy or EGFR-TK inhibitors: anemia, diarrhea, fatigue, febrile neutropenia, nausea/vomiting, neutropenia, and rash. We performed a meta-analysis of the available gefitinib versus paclitaxel/cisplatin RCTs in EGFR-TK Mr+ patients. We then carried out a mixed treatment comparison (MTC) of doublet chemotherapies in unselected advanced NSCLC patients using paclitaxel/cisplatin as a baseline. Treatment effect for the risk of AE occurrence was estimated as an odds ratio (OR > 1 favors paclitaxel/cisplatin). RESULTS: Three RCTs were identified for gefitinib, of which two were comparisons with paclitaxel/cisplatin. Meta-analysis of these two trials gave the following statistically significant results: anemia—OR 0.12, 95% confidence interval: 0.03–0.47; diarrhea—OR 5.78, 95% CI: 1.01–33.11; neutropenia—OR 0.01, 95% CI: 0.00–0.03. Twenty-nine trials were appropriate for inclusion in the MTC. The alternative double chemotherapy regimens did not demonstrate a statistically significant reduction in risk of any of the AEs assessed versus paclitaxel/cisplatin, with the exception of gemcitabine/cisplatin, which had a lower risk of febrile neutropenia estimate the direct comparison (OR 0.21, 95% credible interval: 0.12–0.96). CONCLUSIONS: In the absence of RCTs comparing all doublet chemotherapies with gefitinib in EGFR-TK Mr+ patients with advanced NSCLC, this adjusted indirect comparison suggests that gefitinib may have important tolerability advantages over other first-line treatments in this targeted population.