various elective knee surgeries with rFVIIa coverage in hemophiliacs with inhibitors from a US payer perspective. **METHODS:** A literature-based Markov model was used to compare the direct medical costs and quality-adjusted life-years (QALYs) of 2 hypothetical cohorts of hemophiliacs with inhibitors and frequent bleeding episodes: one undergoing elective orthopedic surgery and the other not undergoing surgery. Based on the published literature, surgery was assumed to reduce bleeding frequency by 82%, from 9.13 to 1.64 episodes per year, and improve pain and quality of life. Surgery costs included perioperative rFVIIa costs, inpatient and rehabilitation care, and repeat procedures. **RESULTS:** Estimated knee surgery costs ranged from $677,000 (in knee arthrodesis [KA]) to $840,000 (in total knee replacement [TKR]). Surgery reduced the incidence of bleeding episodes and resultant costs. Specifically, the cumulative discounted savings in bleeding-related costs were $537,000 and $991,000 at 5 and 10 years, respectively. Overall, the cost of surgery was offset within 7 to 9 years of the index procedure, depending on the surgery. Surgery also resulted in discounted net gains of 1.88 and 3.47 QALYs after 5 and 10 years, respectively. The cost per QALY gained with KA and TKR fell under $50,000 during the 6th and 7th years, respectively. Changes in assumptions regarding prophylaxis regimen, survival, baseline bleeding frequency, patient weight, and rate of repeat surgery affected the results to various degrees. **CONCLUSION:** Despite high upfront costs, knee surgery with rFVIIa in hemophiliacs with inhibitors leads to cost savings and QALY gains within a few years, primarily due to reductions in bleeding episodes.

PHM12

COST-EFFECTIVENESS OF DASATINIB VS IMATINIB 800 MG/DAY IN PATIENTS WITH IMATINIB-RESISTANT CHRONIC MYELOID LEUKEMIA IN SPAIN

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OBJECTIVES: The cost-effectiveness of dasatinib was evaluated, comparing dasatinib (2 × 70 mg) to 800 mg imatinib per day in imatinib-resistant chronic CML, from the perspective of the Spanish health care system. **METHODS:** A Markov model was developed (cycle length one month) which incorporates clinical, epidemiological and cost data to assess the cost-effectiveness of dasatinib compared to imatinib in imatinib-resistant chronic CML patients (95% of CML patients in Spain). The model allows the simulation of the distribution of patients over the chronic, accelerated and blast phase of CML. At model entry, patients are classified according to initial best response rates, from randomised Phase II clinical trial data comparing dasatinib with imatinib (800 mg) in imatinib resistant patients. Distinction is made between no response, complete hematological response, partial cytogenetic response and complete cytogenetic response. Disease progression depends on initial response to treatment. Treatment costs were obtained from eSalud, a health care cost database in Spain. Health effects and costs were counted until all patients reached the "death" state. Both costs and effects were discounted annually at 3.5%. The robustness of the results was tested in deterministic sensitivity analyses. **RESULTS:** In the base case analysis, treatment with dasatinib is associated with a gain of 0.64 quality adjusted life-years (QALY) and cost savings of €16,600, resulting in an estimate of dominance for dasatinib. Sensitivity analysis of key variables confirmed that results remain located in the south-east quadrant of the CE-plane (i.e. dominance). **CONCLUSION:** Compared to imatinib, dasatinib is associated with increased life expectancy and lower overall costs, indicating that dasatinib is a dominant treatment strategy for the treatment of patients with CML who are resistant to imatinib.

HEMATOLIGICAL DISORDERS—Health Care Use & Policy Studies

PHM13

THE EFFECT OF RESTRICTING FERTILITY SERVICES IN GERMANY

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OBJECTIVES: In 2004 the German government limited the adoption of assisted reproductive technology (ART) treatment costs by statutory health insurance from 100 to 50 percent. Furthermore age limits were adapted and the number of funded ART cycles was restricted from four to three cycles. The aim of this study was to estimate the effect of restricting fertility services from a health fund's perspective. **METHODS:** Over the period of 2002 to 2005 our study investigated the changes in the number of ART cycles, treatment costs and birth rates after assisted reproduction. The analysis is based on health insurance frequency statistics including fee schedule items reimbursed by health insurance funds. ART cycles included intrauterine insemination (in natural or stimulated cycles), in vitro fertilisation and intracytoplasmic sperm injection. **RESULTS:** The number of funded ART cycles ranged from 73,405 in 2002, 104,542 in 2003, 35,352 in 2004 to 32,099 in 2005. The number of ART cycles increased expectedly between 2002 and 2003. The gain add up to 42%. In 2004 the number of ART cycles decreased by 66%. This downward trend continued in 2005 with a decline by another 9%. In 2004 treatment costs funded by the health insurance decreased by 84% according to the limitation of reimbursement. Corresponding to the falling number of ART cycles the birth rate depending on ART decreased too. However, the decrease had no statistically significant impact on the common birth rate in Germany. **CONCLUSION:** With restricting fertility services the number of ART cycles declined statistically. The absolute number of births decreased too. One of the reasons may be high co-payments which will mean many patients can not longer afford this special kind of medical treatment.

PHM14

PATIENTS WITH MYELODYSPLASTIC SYNDROMES (MDS) CHALLENGE TRANSFUSION RESOURCES NOW AND IN THE FUTURE

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OBJECTIVES: To find evidence on the economic impact of anemia and transfusion in MDS and estimate the prevalence of transfusion-dependent MDS patients in Germany and make a first appraisal of the economic impact of these patients. **METHODS:** Literature search via PUBMED was systematically conducted (covering January 1996 to December 2006) using defined search terms, e.g. Myelodysplastic Syndrome AND Transfusion AND Cost and cost analysis OR cost of illness. From the German transfusion medicine's perspective desk-top researches were conducted to evaluate the economic burden of transfusion-dependency of MDS patients in Germany. **RESULTS:** Three cost-analyses regarding transfusion costs of MDS patients were identified with major distinctions in study design, methods,

and comparative treatments. Based on data from the literature review, approximately 50% of MDS patients are transfusion dependent across all risk groups. In Germany, between 3800 and 5400 MDS patients needed transfusions in 2005. With an estimated growth rate of approximately 6% per year, MDS will occur in between 9,800 and 13,900 patients in 2010. Taking into account 24 erythrocyte concentrates (EC) per MDS patient per year, 2% to 3% of the whole erythrocyte production in Germany is allocated to MDS. This calculates to total medical transfusion costs between 8 and 23.5 million Euro depending on the number of transfusion-dependent patients and unit costs of EC. **CONCLUSION:** A comprehensive cost-of-illness study covering all settings of care is necessary to learn about MDS resource consumption and economic consequences. Rational allocation of blood will be of special public health interest in the future due to the demographic development in Germany. The increasing scarcity of blood creates a strong need for therapies which terminate or reduce transfusion dependency. Due to the fact that innovative therapeutics for MDS will be available soon, it is important to evaluate their economic consequences with a special focus on their blood saving potentials.

HEMATOLIGICAL DISORDERS—Methods and Concepts

PHM15

POSITIVE INVESTMENT INTERVAL (PII) AND PAYBACK PERIOD (PP) OFFER DIFFERENT INTERPRETATIONS IN HEALTH TECHNOLOGY INVESTMENT DECISIONS: PII IS A MATTER OF BEING AND PP IS A MATTER OF TURNING BENEFICIAL—A CASE OF HEMOPHILIA A

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OBJECTIVES: Investment views have been more or less neglected in economic evaluations. Fortunately, investments can be efficiently and easily assessed by evaluating the most uncertain feature of investment—Time—from two perspectives. The innovation, Positive Investment Interval (PII), its estimation and interpretation are presented here in relation to Payback Period (PP) with a safety example of Hemophilia A (HA), where the best safety is achieved using plasma/albumin-free methods (PFM). **METHODS:** PII estimates the interval when sc. safety costs are compensated by the treatment costs of adverse event/events (AE). PP, on the other hand, estimates the time when the safety costs become compensated by the AE treatment costs. **RESULTS:** Both PII and PP are acceptable if the effectiveness of treatment options is equal. PII estimates the interval when investment to e.g. safety offers positive margin. In simple terms, PII is interval when no security threats should occur, if more risky treatment is used. Mathematically, PII compares the incremental costs of new minus old therapy (e.g. safety costs) to the incremental AE costs of old minus new therapy in a given interval (e.g. annual budgeting period). PP is the reversed version of PII. Stochastic PIIs can be presented in an AE costs-safety costs plane. In HA case, when base-case PIIs for annual PFM Advate vs. non-PFM Kogenate investment were 1–7 years depending on patient's weight, age, and treatment modality, were PPs 2–11 months. Longer PII, the better and shorter PP, the better. Thus, PII > PP is usually a potentially good and beneficial investment depending on the expected time horizons of possible AEs or other patient security risks. **CONCLUSION:** PII is related to e.g. safety need as time and, thus, it has hands-on interpretation for political debate. PII can be compared to the time intervals of emerging security problems—not just to the probability of problem.

PHM16

PHARMACOKINETIC-PHARMACODYNAMIC-PHARMACOECONOMIC (P^3) MODELING TO INFORM PHARMACOGENOMIC TRIAL DESIGN AND RISK MANAGEMENT

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OBJECTIVES: Our objective is to develop a quantitative, model-based protocol simulation approach for evaluating the clinical and economic effects of adverse drug outcomes related to genetic variation at early stages of drug or test development, using warfarin pharmacogenomics as a case-study. **METHODS:** We implemented a previously published (Hamberg et al. (2007)) population pharmacokinetic/pharmacodynamic (PK/PD) model of warfarin distribution and effect that incorporates the effects of genetic variation in the *CYP2C9* and *VKORC1* genes and other relevant demographic variables. We simulated outcomes (INR distribution) of a non-pharmacogenomic-based warfarin dosing protocol, and plan to simulate various pharmacogenomic-based dosing protocols and then integrate these results with pharmacoeconomic simulation models. **RESULTS:** INRs were modeled for 500 simulated patients using the same patient demographics (median and range) as those reported in the Hamberg analysis. The 5 mg/daily INR nomogram of Kovacs et al. (2003) was simulated. Baseline INRs were uniformly distributed over a range of 0.9 to 1.3. The INR at day 6 after initiation of therapy ranged from 0.97 to 10.31 with a median of 3.61. Median INR grouped by *CYP2C9* expression ranged from 3.17 for *1*1 patients to 5.29 for *3*3 patients. INR variations are linked to the risks of bleeding and stroke, and ultimately to the pharmacoeconomic outcomes of costs and quality-adjusted life years. **CONCLUSION:** 'P-cubed' (P^3) modeling will be feasible only when sufficient population PK/PD data are available and valid long-term linkages can be made. It may serve as a tool to explore the robustness of such linkages and probe alternative therapeutic scenarios. Although our findings are preliminary to date, P^3-modeling may provide a useful quantitative framework to help inform pharmacogenomic trial design, regulatory decisions, and potentially clinical guidelines and reimbursement policies.

PHM17

RECOMBINANT ACTIVATED FACTOR VII (RFVIIA) VS. ACTIVATED PROTHROMBIN COMPLEX CONCENTRATE (APCC) FOR ON-DEMAND TREATMENT OF JOINT BLEEDS IN HEMOPHILIACS WITH INHIBITORS: A SYSTEMATIC REVIEW AND BAYESIAN META-REGRESSION SURVIVAL MODEL WITH TIME-DEPENDENT COVARIATES

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OBJECTIVES: The recent FENOC 2006 comparative trial reported comparable efficacy for rFVIIa and APCC in the treatment of joint bleeds in hemophiliacs with inhibitors. A literature-based Bayesian meta-regression analysis was carried out to place these results within the context of earlier, non-comparative studies and to identify key variables influencing treatment efficacy. **METHODS:** A systematic search of the literature identified 15 studies reporting usable and relevant data, which were pooled in a Bayesian random-effects survival model. A repeating Gompertz hazard function was selected to model an initial increase in the hazard of bleed resolution after each injection, followed by a decrease until the next injection was administered. Model covariates included medication type and the combination of the time-