patent applications, and regulatory quality have been controlled. Negative impacts of the recent reforms on R&D expenditures for Germany and Norway and, in some instances, for Italy and Japan are detected. A positive impact of the 2003 reform on R&D related indicators has been found for the US. The reforms reduced R&D expenditures by 0.7% for Italian firms, decreased R&D intensity of Norwegian firms by 2.42%, lowered cash flows of French firms by 0.72%, but increased the R&D of American firms by 0.27%. These results can be explained by the degree of the reform rigidity for price and reimbursement controls, drug development lags, the importance of pharma off-shore, and firm valuation, and growing exports to the US and the Singapore markets. The results can also be explained by a theoretical R&D reproduction cycle model.

**CONCLUSIONS:** Stronger shifts to more rigid cost-containment reimbursements impeded R&D expenditures. However, despite the adverse regulatory shocks, most firms’ R&D related indicators tend to be persistent in the short run.

**DE4**

**PRESCRIPTION DRUG FORMULARIES AND COVERAGE: DOES A DRUG BY ITS NAME SMELL AS SWEET?**

Hau J, Price M, Fung V
Kaiser Permanente. Oakland, CA, USA

**OBJECTIVES:** We investigated the impact of eliminating brand name drug coverage on statin drug spending, adherence, and physiologic outcomes in a cohort of Medicare beneficiaries, compared with a concurrent control group of beneficiaries with coverage of both brand and generic drugs. **METHODS:** All subjects were age 65+ years. In 2002-03, beneficiaries with restricted coverage had an annual drug benefit cap of $1,200; in 2004-05, these beneficiaries lost brand name drug coverage, but had no coverage for generics. **RESULTS:** Controls had no restrictions or changes in brand-generic drug coverage 2002-05. We used fixed-effects regression models to examine the association between coverage and quarterly outcomes. We adjusted for time-varying covariates including time, comorbidity (DiCG scores), plus time²-covariance interactions. **CONCLUSIONS:** The study had a mean age of 73.6 years, and 59% were female. In 2002, 53% of subjects had restricted benefits, and the remaining had no drug benefits. Restricted compared to those with unrestricted benefits and after multivariate adjustment, subjects with restricted benefits had less spending on and worse adherence to statin drugs, and worse LDL levels, particularly after the elimination of brand drug coverage: for example, statin drug spending differences were $13,500/quarter (95% CI: $12–37); the odds ratio of non-adherence was 1.27 (95% CI:1.19–1.36); and LDL differences were 2.00 mg/dl (95% CI: 1.65–2.34 mg/dl) for subjects with restricted vs. unrestricted coverage, in Q4 2004 vs. Q1 2002. The LDL differences were related primarily to reductions in the prescribed daily dose among those with restricted coverage; in 2003, 10% of subjects had prescriptions above the maximum recommended dose of lovastatin, the only available generic during the study period. **CONCLUSIONS:** Prescription drug changes within a therapeutic class are not clinically equivalent, even within narrow classes with few differences such as statins. Careful attention is needed to the clinical needs of individual patients when imposing drug coverage restrictions.

**PODIUM SESSION I: MENTAL HEALTH – MODELING STUDIES**

**MH1**

**A DISCRETE EVENT SIMULATION MODEL IN MAJOR DEPRESSIVE DISORDER—COST-EFFECTIVENESS ANALYSIS OF AGOMELATINE**

Faria J, Almeida J, Vazandar P
Exigo Consultores, Lisboa, Portugal, 2Hospital dos Lusíadas, Lisbon, Portugal

**OBJECTIVES:** The recent evidence supports the use of agomelatine as a new drug for the treatment of major depression. Agomelatine is a cost-effective drug for the treatment of major depressive disorder in Portugal, when compared to current clinical practice.

**METHODS:** The cost-effectiveness of agomelatine was studied using a decision-analytic approach with Markov models. However, evidence shows that probabilities of relapse and remission of depressive episodes are time and past events dependent, suggesting the appropriateness of discrete event simulation models (DESM). Our aim was to assess the cost-effectiveness of agomelatine in major depression from the Portuguese societal perspective using a DESM. **METHODS:** Sequential time to remission and time to relapse/recurrence were sampled from weibull distributions. Remission rates were obtained from a meta-analysis of randomized, venlafaxine-controlled clinical trials with either agomelatine, escitalopram, fluoxetine, paroxetine or sertraline. Probability of relapse/recurrence was assumed dependent on the number of previous depressive episodes and time since last remission. We compared agomelatine 25 mg/day with possible dose titration to a mixed comparator composed by escitalopram(12 mg/day), fluoxetine(38 mg/day), paroxetine(25 mg/day), sertraline(116 mg/day) and venlafaxine(150 mg/day), weighted according to the defined daily doses consumed between January and June 2008. Only direct costs were considered (drugs, medical visits, side effects treatments and monitoring). Effectiveness was measured in quality-adjusted life years (QALY) and life years in remission (LYR). Time horizon varied from 6 to 37 months according to each individual simulation characteristics. When appropriate discount rates of 5%/year were applied to costs and effectiveness. **RESULTS:** A gain of 4.9 QALY (95% CI[6.2,12.4]) or 10 LYG (95% CI[5.2,21.5]) was estimated for each 100 patients treated with agomelatine. The estimated incremental cost of agomelatine treated patients was €323 (95%CEI[167, 672]). Corresponding incremental cost-effectiveness ratios were €3460/QALY or €3197/LYR. Probabilistic sensitivity analysis revealed 11% probability of agomelatine dominance and 97.5% of being cost-effective at a threshold of €10,000, regardless of the effectiveness measure considered. **CONCLUSIONS:** DESM is a valuable tool to model the cost-effectiveness of major depression. Agomelatine is a cost-effective drug for the treatment of major depressive disorder in Portugal, when compared to current clinical practice.