There were a majority of “stopper” even among those who previously received celecoxib (53.4%). The proportion of patients with long term COX-2 treatment (3 months or over) was higher in the “continuers” group (23.9% vs. 13.7%; p < 0.001). Conversely, patients with history of stroke (4.2% vs. 2.6%; p = 0.026) or coronary heart disease (14.7% vs. 11.5%; p = 0.015) and with a higher risk of gastrointestinal events (50.7% vs. 43.2%; p < 0.0001) were in greater proportion in the “stopper” group. Finally, the percentage of NSAID treated patients receiving a proton pump inhibitor raised substantially from 37.1% to 72.0% (p < 0.001) between the two periods. CONCLUSIONS: French GPs reacted in a non selective way, making little difference between rofecoxib and celecoxib, and between cardiovascular and gastrointestinal risks. This unexpected behaviour may be interpreted as a concern toward a reexamination of the need for the withdrawal decision.

**A HEALTH-ECONOMIC EVALUATION OF RHBP-2 IN SPINE FUSION SURGERY IN GERMANY AND UK**

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OBJECTIVES: Chronic low back pain related to osteoarthritic changes of the lumbar spine has a significant economic impact on health care budgets worldwide. Anterior-Lumbar-Interbody-Fusion (ALIF) surgery can be an effective treatment option after non-operative therapy fails. Frequently, the affected vertebral bodies are fused together using bone (autograft) from patient’s hip, which requires additional surgery and leads to increased comorbidity, blood loss, infection rate, and pelvic instability. We assessed the cost-effectiveness of rhBMP-2 compared with autograft in spine fusion surgery over two years from a health care payer's perspective in Germany and UK. METHODS: An economic model was developed to evaluate differences in the two-year results between spine-fusion surgery with rhBMP-2 and fusion with bone autograft. The cost and health-related quality-of-life associated with both arms were estimated for two years after surgery. Data were obtained from a previously published analysis of pooled data, in which patients in the rhBMP-2 arm showed significant clinical improvements after surgery compared to standard therapy. Cost data were obtained from German-DRGs and UK NHS and are reported in 2005 values. RESULTS: In Germany, significant reduction in secondary interventions, and better fusion rates associated with rhBMP-2 treatment resulted in faster return to work and generated savings of €3453 per patient for health care insurance, leading to net savings of €303 per patient. These savings offset the upfront cost of €2930 for rhBMP-2 therapy. In the UK, the benefits of use of rhBMP-2 lead to an incremental cost-effectiveness ratio of GBP 5483/QALY (£8039/QALY) for the NHS. CONCLUSIONS: The standard use of rhBMP-2 in ALIF surgery lowers costs for surgically treated patients with degenerative changes of the lumbar spine in Germany and is a cost-effective treatment option in the UK.

**RESPIRATORY DISORDERS**

**CAN PHARMACEUTICAL INDUSTRY USE REPS TO PROVIDE MEDICAL PRACTICE GUIDELINES? (MIGRAINE AND ASTHMA)**

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OBJECTIVES: Clinical practice guidelines have been shown to improve medical practice. However the place of the reps to improve compliance with guidelines initiated by state agencies (HAS, AFSSAPS) has not been evaluated. The study has been initiated by several pharmaceutical industries involved in research. METHODS: Two intervention studies were used to provide evidence of the effectiveness of the reps visits on the physician practice. During their visit, the reps gave a written document. The written document was a validated and synthesized version of a guideline initiated by state agencies. The subjects of the guidelines were asthma or migraine. The first intervention study evaluated the physicians’ perception of the reps’ interaction. The second study evaluated the physicians’ knowledge. For the first study, the study material was a questionnaire (12 questions) and the study was conducted by phone. For the second study, the study material was an internet based questionnaire (40 questions) which follows the content of the written document given by the reps to the physicians. A score was constructed to evaluate the level of knowledge of the physicians. RESULTS: For the first study: 800 physicians have been included. 81% (82%) find the intervention of the reps useful and 76 % (81%) legitimate the guidelines for asthma (migraine). For the second study: 294 physicians have been included. The level of knowledge was significantly higher for asthma after the reps’ visit (16.37/14.44) and for the physician who conserved the written document. No significant results were found for migraine. CONCLUSION: The reps can be another way to diffuse the clinical practice guidelines.

**TREATMENT WITH INHALED CORTICOSTEROIDS IN ASTHMA TOO OFTEN DISCONTINUED**

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OBJECTIVES: Inhaled corticosteroids (ICS) are the cornerstone of asthma-treatment. Yet, adherence with ICS-treatment is very low. Therefore, the aim of the study was to investigate adherence, in terms of persistent use, with ICS and its determinants in asthma-patients. METHODS: The PHARMO database includes, among others, drug-dispensing and hospital discharge records for >2 million subjects in The Netherlands. All asthma-patients (age <35 yrs) with a first prescription for ICS in 1999-2002 and ≥2 prescriptions in the first year were included in the study. Persistence during the first year was defined as the number of days from start to time of first failure to continue renewal of the initial ICS, and ascertained based on the method of Catalan. Potential determinants of persistence were assessed at ICS-start and one-year before. RESULTS: The study-cohort included 5363 new users of single ICS and 297 of fixed combined ICS. Less than 10% of patients using single ICS, and 15% of patients using fixed combined ICS were persistent at one year. Increased persistence with single ICS was observed with type of ICS (budesonide), prescriber (specialist), prior use of long-acting beta-agonists, previous hospitalization for asthma, metered-dose inhaler, low starting dose, and once-daily dosing regimen at start. Decreased persistence with fixed combined ICS-treatment was found in patients having high starting dose of ICS and prior use of antibiotics. CONCLUSIONS: Persistence with ICS-treatment for asthma in clinical practice is low for both single and fixed combined ICS-treatment. Persistence was mainly related to patient-factors, such as severity of disease, and to treatment-related factors, such as once-daily dosing frequency and low dose.
THE COST-EFFECTIVENESS OF TIOTROPIUM VERSUS IRPATROPIUM IN A US VETERANS POPULATION DIAGNOSED WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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OBJECTIVE: This study models the cost-effectiveness of tiotropium versus ipratropium in a veterans population while incorporating information on medication compliance, disease severity, and history of health care utilization. METHODS: Electronic medical records from the Veterans Affairs (VA) Maryland Health Care System for 2004 were analyzed. Inclusion criteria: 1) filled prescription for ipratropium in 2004; 2) pulmonary function test (PFT) results; 3) PFT-based evidence of chronic obstructive pulmonary disease (COPD). Hospitalizations and emergency room (ER) visits for COPD exacerbations, COPD severity, and medication adherence were identified via chart review. The relative effectiveness of tiotropium was based on published clinical trial results. The incremental cost-effectiveness ratio (ICER) was calculated for 702 actual ipratropium patients and 720 modeled tiotropium patients for two effects: avoided exacerbations (ICERex) and avoided hospitalizations (ICERhos). Sensitivity analysis was also conducted. RESULTS: The ipratropium sample characteristics were: mean age of 69 years; 98 percent male; 21 percent Black; and 40 percent smokers. The distribution by severity was: mild (7%), moderate (42%), severe (40%) and very severe (11%). The total (exacerbation-related) ER visits and hospitalizations were 879 (171) and 462 (75), reflecting the exclusion of 40 ER and 9 hospital encounters following missed medications. The overall ICERex and ICERhos were $1318.38 and $4284.75. Tiotropium was dominant in very severe patients: ICERex of $-2099.00 and ICERhos of $-6297.00. Tiotropium was dominant (−$4215.46) for patients with one hospitalization and ranged from $433.29 to $117.27 for patients with one to three ER visits. The results were most sensitive to variation in tiotropium compliance, the cost of ipratropium, and the relative efficacy of tiotropium. CONCLUSIONS: Assuming VA efficacy similar to published estimates, tiotropium is more cost-effective in patients with more severe disease or a history of ER visits and is dominant when considering patients with very severe COPD or with a previous hospitalization.

CLINICALLY IMPORTANT FACTORS CONTRIBUTING TO COSTS OF CARE DEFINED VIA ANALYSIS OF COMPREHENSIVE PATIENT RECORDS

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OBJECTIVES: To evaluate the use and costs of all health care provider services among 1000 patients with chronic asthma during a five year period. METHODS: Patients who had visited the Pulmonary Clinics of Helsinki University Hospital during the yrs 2000–2004 were invited to the study. The participants’ consent was obtained and a comprehensive medical history collected from all health care providers who had treated the participant during the last 5 years. Data included all physician recorded symptoms, signs, adverse drug effects, complications, diagnostic test results, given treatments, and procedures as unstructured text. Using advanced linguistic analysis methods, we identified for each event both cost related attributes (location, personnel, type of contact, urgency) and clinical attributes (age, gender, BMI, smoking, lung functions, co-morbidities, and prescribed medication) potentially explaining the differences across their clinical outcomes. We developed a medication independent score for the stability of asthma based on physician recorded observations. Membership [0.1] of an asthma related contact was defined as a probability-like function P. RESULTS: Our regression model is based on 65,698 health care contacts explaining a significant proportion (43%) of all direct non-pharmacological costs of the patients. Fifty-six percent of the contacts were asthma related. An asthma related event occurred on average 6 times per year with an average cost of $256 (based on average costs in Finland). Unexpectedly the use of prescription antihistamines resulted less frequent patient interaction with the health care system and potentially in better asthma control. Smoking, adverse drug events, co-morbidities, existing allergy symptoms increased asthma related expenditures significantly. Use of antihistamines, normal FVC in spirometry, and male gender decreased the costs. CONCLUSIONS: This empirical model of health care utilization can be used to explain differences in health care utilization among patients with different co-morbidities and different treatment protocols.

PODIIUM SESSION IV: CANCER

TREATMENTS FOR METASTATIC MELANOMA: SYNTHESIS OF EVIDENCE FROM RANDOMIZED TRIALS

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OBJECTIVES: Advanced melanoma is usually fatal, with few effective treatments. Dacarbazine (DTIC) is considered standard therapy, but newer drugs have recently been marketed. The study objective was to quantify success rates (Complete + Partial response) of DTIC alone versus all other comparators in treating Stage-III (non-resectable) and Stage-IV melanoma of cutaneous origin. METHODS: We reviewed all head-to-head randomized controlled trials involving dacarbazine (DTIC) and other active drugs or multiple-drug combinations. Two reviewers searched the literature, and compared results, with differences resolved through consensus. Success rates were combined using random effects meta-analysis. Heterogeneity was tested using chi-square and publication bias using funnel plots and the Begg-Mazumdar test. Quality was assessed using Jadad’s method. RESULTS: We found 23 studies (3356 patients, 1966 DTIC, 1390 other treatments, average age 52.8 ± 4.3) with DTIC as standard treatment. Studies were generally of poor quality; 2 scored “high” quality and 21 scored “low” quality. Heterogeneity was non-significant (chi-square = 24.63, P = 0.032), suggesting combinability. Funnel plots were not abnormal and the Begg-Mazumdar test was non-significant (tau = −0.13, P = 0.38), indicating no publication bias. DTIC success rate was 14.9%. All other treatments combined were somewhat superior to DTIC alone (OR = 1.31, CI95%: 1.06–1.61). Average survival time was 7.5 ± 2.0 months for DTIC and 8.7 ± 3.6 months for all others. Adjunct therapy [DTIC+additional drug(s)] was supe-