PMS98

DEVELOPMENT AND VALIDATION OF A DISEASE MODEL FOR POST-MENOPAUSAL OSTEOPOROSIS

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OBJECTIVES: Develop and validate an epidemiological model to estimate the burden of post-menopausal osteoporosis (PMO) in terms of prevalence (women with low bone mineral density: BMD and/or a history of fracture), fracture incidence and attributable mortality up to 2020. **METHODS:** For validation purposes, the model was developed for Sweden (where the epidemiology of osteoporosis is well documented) and provided estimates from 1990. For each year of the study period, the "incident cohort", defined as women experiencing a first osteoporotic fracture, was identified and run through a Markov model of 1-year cycles until 2020. Health states were based on the number of fractures (1, 2, 3+) and death. Fracture by site was tracked for each health state (hip, vertebral, non-hip non vertebral). Transition probabilities reflected site-specific risk of death and subsequent fractures. BMD was included as a model output and reflected difference between women with and without a history of fracture. Model inputs included census from 1970 to 2020, incidence of fracture, relative risk of subsequent fractures based on prior fracture, relative risk of death following a fracture by site, mean and standard deviation BMD by age. **RESULTS:** Model predictions averaged across age groups estimated the incidence of hip, vertebral and other osteoporotic fractures within a 5% margin of error compared to published data. Between 2010 and 2020, the number of women aged 50+ years is expected to increase by 9% whereas the number of osteoporotic fractures and women suffering from PMO (T-score < −2.5 or history of fracture) is expected to increase by 11% and 12% respectively. **CONCLUSIONS:** A PMO disease model was developed and validated against Swedish data. This model can be adapted to other countries to assess the burden of illness and used to estimate the budgetary impact of therapies that reduce bone loss.

PMS99

MANAGEMENT OF KNEE OSTEOARTHRITIS: IMPACT ON PAIN ON A DAILY BASIS

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OBJECTIVES: To observe, under actual conditions of use, the effect obtained, in the context of management of knee osteoarthritis, combining a prescription of Avian ACS (1 g/day) between 2 courses of treatment of 3 injections of hyaluronic acid spaced out by a maximum of 12 months. **METHODS:** Pragmatic, longitudinal and prospective follow-up carried out by rheumatologists in the context of their daily professional activities **RESULTS:** The results presented come from a preliminary analysis concerning the first patients assessable at 6 months. Forty-five percent of the patients are treated with hyaluronic acid for left knee osteoarthritis and 52% are treated with hyaluronic acid for right knee osteoarthritis (3% treated for both). Average pain during activities of daily living was measured by means of a visual analogue scale. It is 53.28 ± 20.83 at inclusion. At 18 weeks, this same average pain measured under the same conditions is 37.96 ± 17.17. A third measurement at 24 weeks situates it at 35.62 ± 17.95. Pain during activities of daily living is significantly reduced between inclusion and week 18 (p = 0.0056). The average reduction in pain during activities of daily living measured between inclusion and 6 months is also significant (p = 0.001). Accordingly, the reduction obtained in 6 months is 33%. **CONCLUSIONS:** Our study, which assesses the effect on pain obtained in the context of management of subjects with knee osteoarthritis, combining a prescription of Structum® (1 g/day) between two courses of treatment of three injections of Structovial®, showed a reduction in pain during activities of daily living. This reduction in pain, which is significant at 18 weeks, then perpetuated at 6 months, shows the relevance of the treatment protocol used by the doctors.

SENSORY SYSTEMS DISORDERS – Clinical Outcomes Studies

PSS1

VERTEPORFIN IN NEOVASCULAR AMD: REAL LIFE CONFIRMS CLINICAL TRIALS RESULTS

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OBJECTIVES: Verteporfin is the first product approved for neovascular age-related macular degeneration (AMD). The severity of AMD, the innovative aspect of Verteporfin and its financial implications motivated French Authorities to request a real life drug utilization study. To describe in France patients treated by Verteporfin for neovascular AMD, their visual acuity changes (responders: VA loss <15 letters) and number of needed treatments. **METHODS:** Observational, prospective, multi-center study with two parts: a registry for all patients treated by Verteporfin for AMD or other diseases; a cohort with two years follow-up of neovascular AMD patients treated by Verteporfin. **RESULTS:** In the registry, 96.8% of patients were treated by Verteporfin in its approved indication. Iin the cohort, from May 2004 to December 2006, 438 patients were included (39 ophthalmologists). Population was 78.3 ± 7.6 years, 67.6% women. At baseline, 58.2% of patients had bilateral AMD. Diagnosis was

done 9.0 months ago. In the study eye, lesion type was predominately classic in 270 patients (61.6%) and occult in 168 patients (38.4%); 35.5% of patients were previously treated by Verteporfin. A total of 65.5% of population was retreated by Verteporfin during the follow-up, the first retreatment was at 4.3 months from baseline; average number of treatments was 2.21 (predominately classic: 2.50; occult: 0.80). Comparing to year 1, proportion of patients treated by Verteporfin decreased in the second year: 64.4% vs 11.5%. At two years, responder rates were 67.8% in whole naïve population, 67.2% and 68.2% for predominately classic and occult respectively. In average, visual acuity change was −7 letters (from 43 to 36 letters). No unexpected adverse event was observed. **CONCLUSIONS:** This study confirms the efficacy of Verteporfin in real life setting but treatment rate was lower than in pivotal studies.

PSS2

COMPARISON OF OUTCOMES FOR MULTIFOCAL INTRA-OCULAR LENSES (MIOLS): A META-ANALYSIS

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OBJECTIVES: To compare the clinical outcomes of different MIOLs using a meta-analysis based on the available information reported in the international literature. **METHODS:** All comparative clinical trials including at least one MIOL were extracted from the literature. Patients had to have surgery for either cataract or presbyopia. Clinical outcomes included uncorrected near and distance visual acuity (UNVA, UDVA in LogMAR), spectacle independence and halos. Random effects meta-analyses were conducted to compare outcomes for different types of implants. **RESULTS:** Twenty papers were identified with 11 monofocal IOLs and 35 MIOLs (19 diffractives including 12 ReSTORs, 14 refractives and 2 accommodatives). In comparison to monofocal IOLs, MIOLs had better UDVA (0.165 vs. 0.093, p < 0.001) and better UNVA (0.47 vs. 0.14, p < 0.0001) resulting in a higher spectacle independence incidence rate (IRR = 3.62, P < 0.0001). In comparison to refractive MIOLs, diffractive MIOLs had similar UDVA (0.105 vs. 0.085, p = 0.78), and better UNVA (0.22 vs. 0.082, p < 0.0001) resulting in a higher spectacle independence incidence rate (IRR = 1.75, P < 0.001). In comparison to other MIOLs, ReSTOR had better UDVA (0.067 vs. 0.109, p < 0.0001), and better UNVA (0.064 vs. 0.184, p < 0.006) resulting in a higher spectacle independence incidence rate (IRR = 2.04, P < 0.004). We found no statistically significant differences in halo incidence rates for different types of implants. **CONCLUSIONS:** MIOLs provide better UNVA and UDVA than monofocal IOLs, which lessens the need for spectacles. The design of the MIOL might play a role in post-surgical outcomes of different models. ReSTOR, a diffractive MIOL, showed better UNVA, UDVA and higher rates of spectacle independence than the other MIOLs.

PSS3

TREATMENT PERSISTENCY OF XALATAN-XALACOM, LUMIGAN-GANFORT AND TRAVATAN-DUOTRAV: AN ANALYSIS CONDUCTED ON THE UNITED-KINGDOM GENERAL PRACTITIONER RESEARCH DATABASE

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OBJECTIVES: The objective of this analysis was to compare treatment persistency of three treatment sequences: Xalatan-Xalacom (XX), Lumigan-Ganfort (LG) and Travatan-DuoTrav (TD) according to data collected in the United-Kingdom General Practitioner Research Database (UK-GPRD). **METHODS:** Patients with a diagnosis of ocular hypertension or glaucoma, or treated with a topical treatment, surgery or laser were selected. Patients with sequence prescription of XX, LG and TD were selected. A treatment failure was defined as a prescription change (adding or removing a topical treatment). Time to treatment failure was compared using Wilcoxon test applied to survival curves. Adjustment on confounding variables was performed with the propensity score method using a logistic stepwise regression. **RESULTS:** 1562 patients were treated by XX, 110 by LG and 114 by TD. Mean age was 75 years and the sex-ratio was close to 1 male/ 1 female. No demographic or co-morbidity differences between treatment sequences were observed. At 30 months, 66.5% of the XX patients had not failed (remain with the same treatment sequence), versus 60.5% of the LG and 75.1% of the TD patients (Wilcoxon, P = 0.005). At 60 months these results became, 42.2%, 49.9%, and 52.0%, respectively (Wilcoxon, P = 0.04). Adjustment for confounding variables did not change these estimates. **CONCLUSIONS:** According to the UK-GPRD information, the Travatan-DuoTrav treatment sequence was associated with longer treatment persistence

PSS4

SYSTEMATIC REVIEW OF THE EFFICACY AND SAFETY OF IMIQUIMOD 5% CREAM FOR THE TREATMENT OF ACTINIC KERATOSES

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OBJECTIVES: The aim of the review was to evaluate the efficacy and safety of imiquimod 5% cream compared with vehicle for the treatment of actinic keratoses. **METHODS:** The analysis was performed in accordance with the rules of systematic review, based on the Cochrane Collaboration (Cochrane Reviewer's Handbook) guidelines and the Health Technology Assessment Agency in Poland (AOTM) recommendations. **RESULTS:** Imiquimod 5 percent cream versus vehicle in short time

period: In the period of four as well as eigth – weeks course of treatment with imiquimod 5% cream, therapy resulted in significantly higher chance of achieving complete clearance. Patients treated with imiquimod more frequently achieved clearance level higher than 75% of baseline actinic keratoses compared with the subject in vehicle group. Adverse events were more frequently recorded within the group of subjects who received imiquimod in comparison with vehicle group. The chance of experiencing local skin reaction such as erythema, flaking/scaling/dryness, scabbing/crusting, oedema, vesicles, erosin/ulceration was significantly higher in experimental group. Imiquimod five percent cream versus vehicle in long time period: Imiquimod 5% cream used 3 times a week for 24 weeks was an effective treatment for actinic keratosis measured by the probability of achieving complete clearance and partial clearance rate (more than 75% reduction in baseline lesions). Frequency of adverse events and local skin reactions was higher during the imiquimod treatment in comparison with placebo. Imiquimod five percent cream versus vehicle in patient with solid organ transplants: Treatment with imiquimod 5% cream for 24 weeks in kidney, heart and liver transplant patients resulted in significantly higher probability of achieving complete and partial clearance rates of actinic keratoses. There were no significant differences in incidence of adverse events between groups. **CONCLUSIONS:** Imiquimod five percent cream appears to be effective and safe alternative therapy for the treatment of actinic keratoses.

PSS5

RESTOR® VERSUS ACRILISA® : ND-YAG LASER INCIDENCE RATE COMPARISON 18 MONTHS AFTER SURGERY

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OBJECTIVES: The aim of this study was to compare the 18 months Nd : Yag laser incidence rate of two multifocal intra-ocular lenses, ReSTOR® and Acrilisa®, implanted by a single surgeon following his usual practice. **METHODS:** This retrospective study was based on all patients implanted with a ReSTOR® or Acrilisa® multi-focal lens since Q3–2004 at one site. All patients with either cataract or clear lens were operated by the same surgeon. Medical data were obtained from patient charts. 18-months post surgical data were obtained from the surgeon's medical files and from other ophthalmologists, if involved in post-surgical care. Time to Nd : Yag laser analysis was carried out using Kaplan-Meier survival curves. Imbalance on confounding variables was adjusted with a Cox model. **RESULTS:** Eighty patients (160 eyes) were bilaterally implanted with ReSTOR® and 76 (152 eyes) with Acrilisa®. Patients with ReSTOR® were more often male (52.5% versus 30.7%; P < 0.01) and younger (63.1 versus 65.8; P < 0.01). After one year of follow-up, 3.6% of the ReSTOR® eyes had Nd : Yag laser versus 6.8% of the Acrilisa® eyes. After 18 months, the incidence rates were 4.6% and 26.0%, respectively (P < 0.0001). Age was weakly associated with Nd : Yag laser (p = 0.09). Eyes with Acrilisa® had 5.62 [2.64–14.02; P = 0.0002] more chances to have Nd : Yag laser than ReSTOR®. This persisted after adjusting on age [Hazard Ratio: 6.61; 2.61–16.76; P < 0.0001]. **CONCLUSIONS:** This analysis conducted at 18 months suggested that following usual surgical practice, ReSTOR® eyes had significantly less capsulotomy than those implanted with Acrilisa®. Young population were slightly more exposed at Nd : Yag laser. Analyses at two and three years will be required to confirm these findings.

PSS6

CONJUNCTIVAL HYPERAEMIA ASSOCIATED WITH THE FIXED COMBINATIONS OF LATANOPROST/TIMOLOL AND BIMATOPROST/TIMOLOL IN THE TREATMENT OF OCULAR HYPERTENSION OR GLAUCOMA

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OBJECTIVES: To assess the association of conjunctival hyperaemia with the fixed combinations of latanoprost/timolol (LT/TM) and bimatoprost/timolol (BM/TM) in the treatment of ocular hypertension or glaucoma using a systematic review and meta-analyisis of randomized clinical trials (RCTs). **METHODS:** A systematic search for RCTs published between 2000 and 2009 was conducted in Medline, Embase and Controlled Trials Register databases. The outcome measured was the appearance of conjunctival hyperaemia in studies comparing the use of either LT/TM or BM/TM versus different therapeutic options. Statistical analysis was performed including the calculation of odds ratio (OR) and its respective confidence interval, along with the inter-trial statistical heterogeneity. A sensitivity analysis was also carried out. **RESULTS:** A total of 16 RCTs comparing LT/TM versus distinct therapeutic alternatives and 5 CT comparing BM/TM versus different therapeutic options fulfilled criteria to be included in the meta-analysis. Although heterogeneity of both comparisons was not very high in both the LT/TM group (Q = 24.47; p = 0.057; I^2 = 38.7 %) and the BM/TM group (Q = 5.19; p = 0.268; I^2 = 22.94 %), the estimation of the OR by the random effects model was considered the most appropriate. According to this model the final OR for the LT/TM group was 0.56 (IC95%: 0.37–0.83), p < 0.05 and for the BT/TM group the OR was 0.94 (IC95%: 0.66–1.34), p > 0.05. In the sensitivity analysis performed, none of the RCTs included in this meta-analysis had an important effect in the global estimation of OR. **CONCLUSIONS:** According to available data, the use of LT/TM is associated with a significant reduction in the development of conjunctival hyperaemia versus the comparators used in the RCTs, whereas the use of BM/TM produces a conjunctival hyperaemia rate similar to its comparators.

PSS7

THE APPLICATION OF DISCRETE EVENT SIMULATION TO QUANTITATIVE RISK BENEFIT ANALYSIS

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OBJECTIVES: To date, quantitative risk benefit has mainly involved the translation of Cost-Effectiveness techniques or utility adjusted epidemiological statistics. We aim to describe how Discrete Event Simulation "DES" offers the possibility of modelling the occurrence of several adverse events and beneficial events simultaneously whilst accounting for competing events. **METHODS:** Firstly, a longitudinal patient database is used to identify the target patient population. Secondly, incidence rates for the outcomes are calculated from the entire database, thereby providing the necessary granularity in terms of the predictive factors for the outcomes. The annual probability for each outcome is then assigned to each patient in the cohort and DES generates time to each event. Thereby the expected events for an unexposed patient cohort is created to which relative risks are applied to model drug exposure. An example using glaucoma patients is presented using data from The Health Improvement Network. **RESULTS:** We obtained data on 17,652 glaucoma patients who were known to be receiving glaucoma therapy at January 1, 2007. Patients were characterised according to the principal determinants of the outcomes (heart failure, asthma/COPD exacerbation). The same database provided general population incidence rates for the outcomes which were assigned to each patient according to their characteristics. National statistics provided death rates. The expected events over one year for a cohort of 10,000 glaucoma patients were: HF = 95; asthma/COPD = 143; deaths = 605. **CONCLUSIONS:** These expected numbers represent the occurrence of events in the natural history cohort. They were obtained by summing the outcome probabilities across the patient group. They do, however, represent the first step in creating a comprehensive method for risk-benefit quantification via DES and large patient databases; benefit can be modelled if expressed as the occurrence of an event. The method will need to incorporate uncertainty in all the input parameters and to update the probabilities after an event has occurred.

SENSORY SYSTEMS DISORDERS – Cost Studies

PSS8

COSTS-OF-ILLNESS OF ULCUS CRURIS IN GERMANY: RESULTS OF TWO APPROACHES

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OBJECTIVES: Estimation of cost-of-illness (COI) of leg ulcers in two German cross-sectional studies using different methodical approaches. **METHODS:** A direct and an indirect method for cost estimation were utilized. In a nationwide cross-sectional study in 33 specialized dermatological, surgical and general-medical wound centres, resource consumption and associated costs of venous leg ulcer(s) were collected directly from physicians and patients. In a second cross-sectional regional study, involving 147 institutions (hospitals, residencies, nursing services, dermatological offices, services for homeless and addictives) treating patients with ulcus cruris, resource consumption and associated costs were inferred from history, wound condition and actual/previous treatments based on standardized cost categories. Main economic parameters in both studies were direct, indirect and intangible costs (health related quality of life, HRQoL) from the societal perspective. **RESULTS:** The national study enrolled n = 218 patients with a mean age of 69.8 years (regional study: n = 502, 71 years). Wounds existed for 7 (regional 9) years on average. The mean total COI per year and patient was €9,569 (€10,624). While direct costs summed up to €8658 (€9851), indirect costs were much lower €911 (€772). Of direct costs, €7631 (€9122) were covered by the Statutory Health Insurances (SHI) and €1027 (€730) by the patients. For SHI, major cost factors were inpatient costs, non-drug treatments and physicians/nurses fees. Moreover, clinical predictors such as wound size, number and duration as well as wound etiology and characteristics of care (quality, support) were identified. All patients were severely impaired in their HRQoL, implying a high burden of disease and relevant intangible costs. **CONCLUSIONS:** Chronic leg ulcers generate highly relevant COI. Despite different recruitment and cost estimation methods, both studies resulted in comparable direct, indirect and intangible costs; observed differences can be attributed to sample characteristics. The results point to early and qualified disease management in all related health services areas.

PSS9

COSTS OF PATIENTS WITH OCCUPATIONAL SEVERE CHRONIC HAND ECZEMA REFRACTORY TO TOPICAL CORTICOSTEROIDS FOR EMPLOYER'S MUTUAL INSURANCE COMPANIES IN SPAIN

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OBJECTIVES: To estimate the direct and indirect costs of occupational severe chronic hand eczema (OSCHE) in patients refractory to topical corticosteroids from the perspective of employer's mutual insurance companies (EMIC) in Spain. **METHODS:** An employer's mutual insurance company in Spain usually covers 75% of salaries and 100% of medical treatments of patients on occupational sick leave. A decision analytic