OBJECTIVES: A systematic review of the literature was performed to gather all official recommendations on the prevention in infants of allergic manifestations (AMs), and, more specifically, atop dermatitis (AD), by using hydrolyzed infant formulas (HF) such as partially or extensively hydrolyzed formula (PHF, EHF).

METHODS: OVID MEDLINE® and the grey literature were searched by two reviewers using the keywords AM, AD, prevention and guidelines. A third person acted as adjudicator. The inclusion criteria were recommendations of guidelines or institutions to the prevention of AM issued by national or regional associations of pediatric professionals.

RESULTS: This review yielded 11 sets of guidelines published for Australia, France, Germany, Spain, Switzerland (all in = 1), Europe and the US (both n = 3) between 1999 and 2010. Most guidelines included AD either specifically (n=3) or in the broad context of AMs. Six guidelines (of which 2 recommended PHF over EHF) endorsed the use of HFs for the prevention of AM in “at risk” infants when exclusive breastfeeding was not or no longer possible. Two other publications did not explicitly recommend HFs, but rather formulas with a documented reduced allergenicity. The need for an appropriate level of nutritional support was stressed in one publication. Five guidelines acknowledged that not all HFs have the same protective benefit. Four publications underlined the importance of sound clinical evidence when determining the preventive efficacy of HFs. None of the guidelines based their recommendations on recent evidence from meta-analyses focusing on a specific brand of PHF NAN-HA®. Conclusions: HFs and specifically PHFs are endorsed for the prevention of AMs. The need for a strong validity and universality of the clinical evidence and methodology is acknowledged by national or regional medical associations. Recent evidence regarding the preventive efficacy of a specific brand of HF, NAN-HA®, should provide the basis for new recommendations.

PRS75 MEASUREMENT OF A POSSIBLE PATCH TESTING OUTCOME INDICATOR

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OBJECTIVES: Patch testing is a well-established method to determine whether contact sensitization to certain agents has occurred and it can directly influence the clinical outcome of patients with allergic contact dermatitis (ACD) where detection of causative allergens is crucial for appropriate prevention and treatment. Its positive predictive value, however, is influenced by many variables. In particular, not all patients referred for patch testing actually have ACD and not all positive reactions are clinically relevant. The objective of our study was to develop an outcome indicator of patch testing. METHODS: We identified and measured as a possible indicator the ratio of patients with allergic and/or photo-allergic contact dermatitis in clinical care cured/improved as a result of identification of relevant allergens. Patients with positive reactions considered relevant to their current dermatitis were interviewed by telephone 2 months after patch/photo-patch testing in order to assess their clinical outcome in relation to the recommended elimination of suspected allergens. We parallelly evaluated the prevalence of referral diagnosis different from ACD in patients whose test results were negative/non-relevant. RESULTS: Over a 4-year period positive reactions were seen in 1397 out of 2857 tested patients. Relevance was considered current in 578 subjects, and 506 of them were interviewed. Remission/significant improvement following allergen(s) contact avoidance was reported by 431 patients, the outcome indicator (431/506) thus scoring 85.2%. Among the 75 patients who reported no improvement, 41 had not avoided contact with the offending substance(s), 17 had other persistent comorbid skin conditions, and 17 were untreated despite elimination of the alleged relevant allergens. The likely diagnoses of patients whose test results were negative/non-relevant were: non-/partial-eczematous diseases (39% of total patients), endogenous eczema (22%), irritant contact dermatitis (10%), unknown (5%), possible ACD from unidentified haptens (4%). CONCLUSIONS: The ratio of relevantly patch-test-positive patients resolved/improved after allergen avoidance is a useful patch-testing outcome indicator.

PRS76 APPLICATION OF INNOVATIVE METHODS TO IDENTIFY AND CHARACTERIZE DIFFERENTIAL RESPONDERS IN CLINICAL TRIALS OF COPD: THE USE OF MIXTURE MODELS

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OBJECTIVES: Applying innovative methods to clinical trial data to identify and characterize unobserved subgroups of differential responders. METHODS: Data from three COPD clinical trials was retrospectively analysed using Growth Mixture Models (GMMs): INHANCE (indacaterol 150µg and 300µg vs tiotropium 18µg and placebo); INLIGHT-2 (indacaterol 150µg vs salmeterol 50µg and placebo); and IN-LIGHT (indacaterol 300µg and 600µg and formoterol 12µg and placebo). GMMs were conducted on SGRQ Symptoms domain data at baseline, 12 weeks, and six months to identify unobserved subgroups. Baseline characteristics were compared between emergent subgroups of differential responders in post hoc analyses. RESULTS: Within INHANCE and INLIGHT-2, two subgroups of patients emerged per treatment arm: responders (improvement) and non-responders (little change/deterioration). Within INOLVE, three subgroups of patients emerged per treatment arm: responders, non-responders, and partial-responders. When responders were analysed separately, mean trough symptom scores in treatment responders were generally larger than when all patients were included: INHANCE responder improvements ranged from 8 -12 units compared with 7-14 for all patients; INLIGHT-2 responder improvements were 3 -13 units versus 3 -6 for all patients; INOLVE responder improvements were 5 -17 units vs 3 -11 for all patients. Within each trial, responders made up the largest proportion of the sample (55% - 82%) but non-/partial-responder groups were large enough and different enough to dampen treatment effects when group means were analyzed as a whole. Responders had significantly better baseline SGRQ symptom scores than non-responders. Further significant differences were found between non-responders, partial-responders and responders in terms of smoking history, age, and breathlessness.

PRS78 INHANCE - A SYSTEMATIC REVIEW OF THE GUIDELINES ON THE PREVENTION OF ALLERGIC MANIFESTATIONS IN CHILDREN

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OBJECTIVES: At the current level of knowledge, no guidelines specifically addressed the issue of divergence between actual and evaluated drug pathways and resultant consequences for the appropriateness of technology appraisals and reimbursement coverage decisions. METHODS: A systematic literature review of conceptual models to inform economic modelling in COPD was performed. RESULTS: Thirty-nine studies identified. All studies were reviewed and classified according to whether they contained: a) an underlying conceptual model; b) a statistical model; and c) a cost-effectiveness model. No studies were found that included all three components. Most models included cost-effectiveness and economic evaluations focused on specific interventions (90%), followed by cost-effectiveness and clinical outcomes (30%), and cost-effectiveness only (10%). No models were found that included clinical outcomes and economic evaluations focused on specific interventions. CONCLUSIONS: While some models include evidence from clinical outcomes and economic evaluations focused on specific interventions, none of the guidelines reported a comprehensive set of determinant of disease progression and outcomes. Only 1 described a broader set of determinants of health status in COPD patients (physiological functioning, patient complaints, functional impairment and ability to cope with everyday life). 2 review articles on cost-effectiveness and functional performance and 1 reporting determinants of functional performance and dyspnoea based on patient/expert interviews were identified. 31 studies using regression analyses to estimate associations between relevant parameters in COPD, including smoking status, gender, age, body mass index, medication use, and comorbidities and health care interventio were found. No studies on the use of conceptual models for economic modelling in COPD were identified. None of the studies presented a comprehensive set of determinants of disease progression and outcomes. CONCLUSIONS: It is recommended that models used to support economic evaluations of health care interventions are based on conceptual models capturing all relevant aspects of the disease and outcomes of value. The available evidence does not provide a full spectrum of relationships between disease, disease progression and outcomes and economic analyses for a comprehensive disease based economic model in COPD.
CONCLUSIONS: GMsMs have the potential to increase understanding of treatment effects and identify patients more likely to benefit from treatment. The ability of baseline characteristics to predict responders/non-responders needs to be tested prospectively.

Sensory Systems Disorders – Clinical Outcomes Studies

PSS1

OCULAR DISCOMFORT, COMPLIANCE AND INTRA-OCULAR PRESSURE (IOP) CONTROL IN PATIENTS TREATED FOR GLAUCOMA

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OBJECTIVES: To investigate the associations between ocular discomfort, compliance and efficacy of IOP lowering drugs. METHODS: This was a prospective observational survey. Centres were selected at random from the CEGIDIM list. Consecutive participants were included. Results were obtained after one month of treatment (visit 1) and at the last visit (visit 2). Adjustments were made for confounding variable unbalances. RESULTS: 410 patients (66 years old, 23% females, 101 ocular hypertensions) were included. 32.9% reported good compliance, 44.8% minor compliance and 22.3% poor compliance. The proba-

tral RVO (CRVO) in a real-world Canadian setting.

and characteristics of patients with ME secondary to branch RVO (BRVO) and cen-

The annual incidence of VI due to ME secondary to BRVO and CRVO was 0.056% and 0.021%, respectively. More RVO patients had hypertension (68 vs. 18%) or dyslipidemia (16 vs. 10%) than control cohort (p<0.05). One-quarter of RVO patients had a history of vascular disease, primarily MI and stroke. CONCLUSIONS: In a real-world setting, the annual incidence of VI due to ME secondary to BRVO and CRVO was 0.056% and 0.021%, respectively. RVO is associated with several vascular comorbidities.

PSS4

CURRENT CLINICAL PATIENT BENEFITS OF POLYQUAD® PRESERVATIVE INSTEAD OF BENZALKONIUM CHLORIDE IN PROSTAGLANDIN EYE DROPS: A MICROSIMULATION MODEL IN OCULAR HYPERTENSION AND OPEN-ANGLE GLAUCOMA

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OBJECTIVE: The presence of the preservative benzalkonium chloride (BAC) at 0.02% in prostaglandin (PG) eye drops is known to increase the risk of ocular surface disease (OSD), which worsens with the extent of exposure to BAC. We aimed to estimate longer-term clinical outcomes with travoprost preserved with Polyquad® 0.001% instead of BAC. METHODS: A Markov microsimulation model was developed. Treatment strategies include the development of OSD and disease progression (Mean Defect [MD], in db) over 10 years, in patients initiating travoprost with Polyquad® followed by travoprost/beta-blocker fixed combination vs. the same sequence using BAC-preserved drops. Initial patient’s characteristics came from distributions on age (normal), sex, OSD, disease stage (uniform) and anticipated progression rates (triangular). The risk of developing OSD in aging population was derived from a US incidence study, multiplied by independent risk factors (age, sex, duration and amount of BAC-containing drops received). Rates of disease progression (db/year) came from landmark studies in OHT/glaucoma, multiplied by independent acceleration factors (disease stage, treatment line, OSD severity, non-compliance). Compliance was expected by experts to be 20% (absolute) better with Polyquad® vs. BAC-preserved drops.

RESULTS: Using 3000 trials (mean age 57 years, 57% female, 14% with initial OSD, mean MD -4db), 47.6% [41.5-53.6%] of patients receiving in first and second line BAC-preserved travoprost treatments are expected to have OSD at 10 years versus 31.7% [28.5-35.1%] with Polyquad®. In OHT/early glaucoma patients, the model predicted the progression to advanced glaucoma (MD<-12db) of 13.2% [12.0-14.4%] with BAC-preserved drops versus 18.1% [16.7-19.5%] with BAC. Also, patients initiating with moderate glaucoma, 1.9% [1.4-2.4%] versus 5.6% [4.8-6.4%] progressed to blindness (MD<-24db) respectively. CONCLUSIONS: The model estimated that OSD incidence was reduced by 33% and glaucoma disease progression was significantly less frequent after 10 years of use of Polyquad® versus BAC-containing travoprost eye drops.

PSS5

VISUAL FIELD EVOLUTION IN GLAUCOMA PATIENTS PRESENTING WITH DIFFERENT DISEASE STAGES: RESULTS FROM AN OBSERVATIONAL STUDY

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OBJECTIVES: The progression of glaucoma is measured by a Mean Defect (MD) of the perimeter in decibels (db), from an early disease stage (~6db loss), until moderate (~6-12db loss), advanced stages (12-24db loss) and eventually blindness (~24db loss). The rate of disease progression is highly variable between individuals and hard to predict. The objective of this study was to analyze the change in MD of glaucoma patients in a real-life setting in Germany. METHODS: We analyzed patient-level data from a German observational study in ocular hypertension (OHT) and glaucoma, with retrospective collection of MD measures (db). Descriptive statistics were derived on the rate of disease progression (db loss/year, obtained by dividing the change in MD by the duration of observation). The change in MD in best eye between the time of first treatment until last MD measure was included in a general linear model, regressing for age, sex, presence of cataract, time since first treatment, initial MD and initial glaucoma stage (OHT, early/moderate or advanced). RESULTS: MD data was available for 57 patients (53% female, mean age 67 +/-12 years). The mean (SD) time from first treatment until last MD measure was 6.7 (3.7) years. The mean (SD) MD was 4.5db (4.7) at first treatment and 0.6db (6.8) at last assessment (i.e. average rate of progression of -0.21db/year, all stages). In 12 OHT patients, 50% had no MD worsening, while 50% lost on average -0.26db/year. Based on the adjusted analysis, the initial diagnosis was significantly associated with the amount of db loss over time (early/moderate glaucoma -0.15db/year +/-0.13, advanced -0.66db/year +/-0.22, p=0.038). CONCLUSIONS: The rates of disease progression measured over more than 7 years in glaucoma patients was...