cals and diagnostic (or staging) tests, more than offset by cost savings related to lower consumption of other health care resources.

PRS73

SYSTEMATIC REVIEW OF THE GUIDELINES ON THE PREVENTION OF ALLERGIC MANIFESTATIONS IN CHILDREN

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OBJECTIVES: A systematic review of the literature was performed to gather all official recommendations on the prevention in infants of allergic manifestations (AM), and, more specifically, atopic 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 in case of disagreement. Of interest were recommendations pertaining to the prevention of AM issued by national or regional associations of medical professionals. **RESULTS:** This review yielded 11 sets of guidelines published for Australia, France, Germany, Spain, Switzerland (all n=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. Hence, recent evidence regarding the preventive efficacy of a specific brand of PHF, NAN-HA®, should provide the basis for new recommendations.

Respiratory-Related Disorders – Research On Methods

PRS74

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 clinically 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 supposedly relevant allergens. We parallely 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 concomitant skin conditions, and 17 were unchanged despite elimination of the alleged relevant allergens. The likely diagnoses of patients whose test results were negative/non-relevant were: non-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.

PRS75

HEALTH TECHNOLOGY APPRAISAL OF NEW DRUGS: ARE WE GETTING IT RIGHT?

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OBJECTIVES: A particular challenge for economic evaluation of new pharmaceuticals is to address the potential for conflict between 1) the available evidence that informs decisions about reimbursement coverage, and 2) the reality of how products are used in clinical practice. The aim of this study is to explore the issue of divergence between actual and evaluated drug pathways and resultant consequences for the appropriateness of technology appraisals and reimbursement coverage decisions. **METHODS:** We develop a generic decision analytic model to illustrate the issue of divergence between actual and evaluated drug pathways arising from a new product changing the number of lines of therapy available to patients, rather than displacing existing therapies. Under this generic model, incremental costs and effects are potentially affected by response to therapy and the clinical decision to maintain or switch treatment. The potential effects on the estimated cost-effectiveness of new drugs from the misspecification of the drug pathway are illustrated using COPD as a case study disease area and prescription utilisation data from Australia. **RESULTS:** In the case of treatments for COPD, cost-effectiveness of new therapies is overestimated when displacement is assumed, but the real-world utilisation of new products involves additions to reimbursement schedules without displacement and when effect size decreases with therapy line. We define this as *pathway misspecification bias* and consider that it may arise in all disease areas and drug classes. We demonstrate that the size of the bias is positively related to the proportion of non-responders. **CONCLUSIONS:** We demonstrate that without provision to withdraw funding from existing lines of therapy, cost-effectiveness analysis to inform reimbursement decision-making should be expanded to include further routine modelling of the likely use of products in clinical practice. We demonstrate that providing for the withdrawal of funding for existing technologies may provide for more efficient funding decisions.

PRS76

SYSTEMATIC LITERATURE REVIEW OF CONCEPTUAL MODELS TO INFORM ECONOMIC MODELLING IN COPD

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OBJECTIVES: To identify evidence gaps for future economic modelling of Chronic Obstructive Pulmonary Disease (COPD) by reviewing published Conceptual Models and studies reporting associations between end-points and disease outcomes. **METHODS:** A systematic literature search was undertaken to identify English language publications since 2000 in Medline and Embase describing Conceptual Models of COPD and studies reporting associations between end-points and disease outcomes. Studies were reviewed against inclusion/exclusion criteria and those including therapeutic interventions were excluded at screening. **RESULTS:** Forty-one published papers were identified: 7 conceptual models of COPD and 34 articles on associations between endpoints and disease outcomes. Of the 7 conceptual models, 6 described single aspects of COPD (cognitive function, dyspnoea, brain function, design of patient related interventions, activity and functional performance). Only 1 described a broader set of determinants of health status in COPD patients (physiological functioning, patient complaints, functional impairment and quality of life.) 2 review papers on cognitive function 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 symptoms (mainly dyspnoea), health status, exercise, lung function, exacerbations, quality of life, biomarkers, co-morbidities, mortality and healthcare utilization 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 diagnosis, disease progression and outcomes needed for a comprehensive disease based economic model in COPD.

PRS77

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 INVOLVE (indacaterol 300μg and 600μg vs 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 treatment effects in terms of SGRQ Symptom scores 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 -8 for all patients; INVOLVE 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.