school attendance and quality of life. Identifying the child at increased risk of future asthma attacks could inform clinical management and targeting of care. We aimed to systematically review the literature to identify and weight factors associated with increased risk of attacks in children with asthma aged 5–12 years.

Methods Using Cochrane methodology, we systematically searched six databases and undertook forward and backward citation searches, with no date/language restrictions. Two reviewers independently selected studies for inclusion, assessed methodological quality, and extracted data. An expert panel of four clinicians independently assessed each factor for both magnitude of risk and degree of confidence in that assessment, based on study quality, effect sizes, biological plausibility, and consistency of Results Consensus was achieved by discussion and agreed at a multidisciplinary workshop.

Results From 16 109 records, we included 69 papers (29 cohort, 4 case-control, 36 cross-sectional studies) providing data on 32 potential factors associated with an increased risk of asthma attacks. The panel had high confidence that previous asthma attacks were associated with greatly increased risk of future attacks. Poor access to care and persistent symptoms were associated with moderately/greatly increased risk. A moderately increased risk of attack was associated with sub-optimal drug regimen (low controller/total therapy ratio), comorbid atopic/allergic disease, African-American ethnicity (US studies), poverty, and vitamin D deficiency. Environmental tobacco smoke (ETS) exposure, younger age, and obesity were associated with slightly increased risk. Gender, urban residence, and Hispanic ethnicity (US studies) were not associated with risk. The evidence for other factors was inconclusive.

Conclusions Assessment of clinical and demographic features (especially persistent symptoms, previous attacks, and sub-optimal drug regimen) may help clinicians to ‘spot the child’ at increased risk of asthma attacks and focus appropriate management. Population level factors (poverty, poor access to care) may be used by health service planners and policymakers to target healthcare initiatives.

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DO THE ROYAL COLLEGE OF PHYSICIANS ‘THREE QUESTIONS’ PREDICT SYMPTOM CONTROL IN PAEDIATRIC ASTHMA?

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Introduction and Objectives The UK Quality Outcomes Framework (QOF) rewards primary-care practices for completing the Royal College of Physicians “Three Questions” (RCP3Q) score for all patients listed on their asthma register. Almost no validation data currently exists, however, to support its use in

children. This study aimed to investigate the performance of the RCP3Q to predict asthma control in children, by comparing it with the validated Asthma Control Test (ACT) or Childhood Asthma Control Test (C-ACT).

Methods This was a prospective, observational study involving 8 primary-care practices. Children aged 5–16 on the QOF asthma register and/or receiving asthma medication were invited to self-complete the ACT (age 12–16, n=96) or C-ACT (age 5–11, n=223) questionnaire immediately prior to a primary-care asthma review, where responses to the RCP3Q were collected. RCP3Q scores were compared with ACT or C-ACT data to assess performance of the RCP3Q in predicting asthma control. The RCP3Q scoring system is summarised in figure 1.

Results Questionnaire and RCP3Q data was completed for 319 participants. RCP3Q scores correlated moderately with C-ACT and ACT data (Spearman’s rho –0.49 and –0.52 respectively, $p < 0.001$). A RCP3Q score of ≥ 2 predicted uncontrolled asthma (C-ACT or ACT ≤ 19) with a sensitivity of 57% and specificity of 81%. A lower threshold RCP3Q score of ≥ 1 gave a specificity of 55%, resulting in a high false positive rate. A RCP3Q score of 0 predicted well-controlled asthma (C-ACT or ACT ≥ 20) with a sensitivity of 55% and specificity of 81%. Using thresholds of RCP3Q ≥ 2 for uncontrolled asthma and RCP3Q = 0 for good control resulted in 25% participants unclassified (RCP3Q = 1) and 18% of participants scoring 0, 2 or 3 incorrectly classified. Binary logistic regression showed that individual positive answers to RCP questions 1 and 2, but not 3, significantly increased the likelihood of uncontrolled asthma.

Conclusions Our data in ≥ 300 participants does not support use of the RCP3Q to classify asthma control in children. Our findings support current BTS/SIGN guidelines, which recommend use of validated asthma control questionnaires, such as C-ACT, when conducting a paediatric asthma review.

Asthma: infection and inflammation

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CLINICAL AND TRANSCRIPTOMIC PROFILES OF SEVERE ASTHMATICS WITH HIGH OR LOW EXPRESSION OF THE GLUCOCORTICOID RECEPTOR AND IMPORTIN-7

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Introduction and Objectives The majority of asthmatics can be well-controlled using inhaled corticosteroids (ICS) and long-acting β_2 -agonists (LABAs). However, approximately 5% have a severe, refractory form of the disease and are often difficult to treat. Corticosteroid (CS) Insensitivity is the defining feature of these asthmatics known as “severe” asthmatics. The

In the last month:

1. Have you had difficulty sleeping because of your asthma symptoms (including cough)?
2. Have you had your usual asthma symptoms during the day (cough, wheeze, chest tightness or breathlessness)?
3. Has your asthma interfered with your usual activities (e.g. housework, work, school etc)?

Score 1 for each yes answer, with total score ranging from 0 and 3.

Abstract S63 Figure 1

molecular mechanisms underlying CS insensitivity are not fully known. Here, we hypothesise that reduction in the expression of the Glucocorticoid receptor (GR) and Importin 7 are related to CS insensitivity. This aims project were to compare the gene expression of GR and Importin 7 between severe asthmatics and mild/moderate asthmatics or healthy controls of the U-BIOPRED cohort. We then investigated whether changes in their expression, correlated with changes in clinical features and expression of other genes.

Methods The U-BIOPRED database contains data on mRNA expression, lung function, medication usage, blood, urine and sputum samples for their subjects (n=611). Using an unbiased approach to analyse the data we will initially used Gene Set Variation Analysis (GSVA) to look for differences in expression of GR and Importin 7 between the severe asthma, mild/moderate asthma and healthy volunteer cohorts. We then characterised the asthmatics into subjects with high (top 25%, compared to healthy controls) or low (bottom 25%) expression of GR or Importin 7 and then compared clinical characteristics and gene expression profiles between the high and low expressing GR or Importin-7 groups.

Results Severe and non-severe asthmatics had reduced GR expression in endobronchial biopsy and brushings samples compared to healthy controls. There were no significant differences in lung function, blood analytes or exacerbation rates between high or low GR expression groups. Severe non-smoking asthmatics had reduced Importin 7 expression in sputum compared to mild/moderate asthmatics and healthy controls. Low Importin 7 group had lower means in FEV1%, FEV1/FVC, higher means in blood and sputum neutrophils%, IL-6 and hCRP.

Conclusions Reduced Importin-7 expression in sputum samples of asthmatics correlated with reduced lung function scores, increased neutrophilic inflammation and more oral CS use.

S65 QUANTIFICATION OF 'WHOLE LUNG' PULMONARY EOSINOPHILIC INFLAMMATION USING RADIOLABELLED AUTOLOGOUS HUMAN EOSINOPHILS

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Background Eosinophils are key mediators of allergic inflammation. The ability to localise and quantify eosinophilic inflammation *in vivo* would facilitate patient endotyping and evaluation of eosinophil-targeted therapeutics. We aimed to quantify eosinophil distribution and organ-specific uptake in healthy subjects, asthmatics, and patients with focal pulmonary eosinophilic inflammation.

Methods We injected autologous radiolabelled eosinophils into 8 healthy volunteers, 15 asthmatics (7 obese and 7 non-obese), and 3 patients with focal eosinophilic inflammation and monitored eosinophil distribution (planar imaging, single photon emission computed tomography – SPECT)/CT). Lung accumulation of technetium-99 m-labelled eosinophils was quantified (Patlak-Rutland analysis). Whole body indium-111-labelled eosinophil distribution and loss were further assessed in 5 healthy volunteers and 7 asthmatics using a whole body counter.

Findings Pulmonary eosinophil clearance was increased in patients with focal eosinophilia (0.0033 ml/min/ml; 95% CI -0.005-0.011; p=0.02) compared to asthmatics (0.0007 ml/min/ml; 95% CI 0.0003-0.0010; p=0.14) and controls (0.0003 ml/min/ml; 95% CI -7.5 × 10⁻⁵-0.0008). Absolute lung eosinophil migration was elevated in patients with focal inflammation (5932 eosinophils/min/ml; 95% CI -14351-26215, p=0.01) and asthma (364 eosinophils/min/ml; 95% CI 38-689; p=0.03) versus healthy volunteers (38 eosinophils/min/ml; 95% CI -11-87). Stratification of asthmatics based on BMI revealed increased pulmonary eosinophil clearance in obese (0.001 ml/min/ml; 95% CI 0.0007-0.001; p=0.02) versus non-obese asthmatics (0.0003 ml/min/ml; 95% CI -0.0002-0.0009).

Interpretation Eosinophil radiolabelling can quantify pulmonary eosinophilic inflammation, with the potential for patient endotyping and testing eosinophil-targeted treatments.

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S66 LONG-TERM AZITHROMYCIN THERAPY IMPROVES CLINICAL OUTCOMES IN AN INFECTIVE PHENOTYPE OF SEVERE ASTHMA

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Introduction Azithromycin is a macrolide with antibiotic and anti-inflammatory properties, which may reduce exacerbations and improves clinical outcomes in severe asthma. However, the target population and clinical utility of azithromycin in real life setting remain uncertain.

Aim To determine the efficacy and safety of long-term azithromycin treatment in severe asthma in real life setting.

Methods Patients attended a tertiary severe asthma between 2013 to 2016 were clinically characterised using pre-designed protocol and data were recorded on the dendrite system. The clinical outcomes of patients treated by long-term azithromycin (≥4 months) were compared for the 12 months before and 12 months on treatment using parametric and non-parametric analysis.

Results Out of a total number of 259 patients entered on the registry, 46 (17.7%) patients had long-term azithromycin treatment. The mean age of this group was 50 years. (range 25-72), 33 (66%) females, mean BMI 32±8.4 kg/M², 41 (80%) had infective phenotype (≥4 LRTI per annum and/or chronic productive cough), 13 (23%) had CT-scan confirmed bronchiectasis, mean ICS 1620 mcg/day and 13 (26%) were on maintenance OCS. The mean FEV1=1.96 L±0.73, %predicted FEV1=69.4±24.3, mean FEV1/FVC ratio 64.6±16.5, mean FeNO 26±27.2 ppb, mean blood eosinophil 0.3*10⁹/l, and mean blood neutrophil was 6.2±2.2*10⁹/l. We observed significant reduction in the mean number of OCS requiring exacerbation in the 12 months on treatment compared to the 12 months pre-treatment (figure 1). There was also significant reduction in LRTI frequency from median=4.5 per annum to 1.0 (p<0.00001) and hospital admissions from mean of 1.17±2.4 to 0.24±0.7 (p=0.01). Also statistically non-significant improvement in ACQ-7 mean 3.5±1.26 to 3.18±1.3 (p=0.09) and FEV1 1.72 to 1.91 (p=0.36). The treatment was generally well tolerated with 35 (76%) of patients had positive