

environment if anything predisposes to airways dysfunction. Exhaled nitric oxide is a promising non-invasive means of assessing eosinophilic airways inflammation in all elite athletes.

S133 EOSINOPHILIC AIRWAY INFLAMMATION IS ASSOCIATED WITH FEV₁ DECLINE IN SEVERE ASTHMA

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Background Severe asthma is a multidimensional disease, with recent evidence supporting the notion that eosinophilic airway inflammation (EAI) is an important driver for exacerbations. In addition EAI has been shown to be associated with airflow limitation in cross sectional studies. However, it remains to be established whether EAI may drive FEV₁ decline.

Methods The severe asthma registry at Glenfield hospital, Leicester, was screened for patients with a physician diagnosis of asthma and at least 5 years of longitudinal data recording sputum eosinophils, pre- and post-bronchodilator spirometry, inhaled corticosteroid usage as well as standard demographic indices during stable scheduled follow-up visits. Linear mixed effects models were used to investigate the effect of log sputum eosinophils as a time varying covariate on decline of post bronchodilator FEV₁. Models were iteratively compared and refined using standard information criteria. Other fixed effects in the final model were, time and the interaction terms for time * log sputum eosinophils and time * daily dose of inhaled corticosteroids and pack years smoked. Individual variations in the slopes and intercepts of time and time*log sputum eosinophils were considered by adding them iteratively as random effects. A first-order autoregressive correlation structure was used to model covariance of random effects.

Results 92 patients, 46% male with severe asthma were identified from a registry cohort of 686 between 2000 and 2009. The mean (sem) age was 54(12.9) years and age of onset 23 (2.1) years. The mean (range) duration of follow-up and number of visits were 6 years (4.6–10.5), 2.7/year. We found a significant interaction between sputum eosinophils, time and post bronchodilator FEV₁. Indicating a net decline (95% CI) of –16.8 mls(25.8–7.8 mls)/annum/log unit increase in sputum eosinophils (F(1, 43.4); p<0.0001). In contrast there was a net decline 95%CI of –0.015 mls (0.029 to 0.0014 mls)/annum/mcg of inhaled beclomethasone dipropionate daily (F(1,726); p=0.031).

Conclusion Eosinophilic airway inflammation is associated with a significant decline in FEV₁ in severe asthma.

S134 WITHDRAWN

S135 CAN YOUR MOBILE PHONE IMPROVE YOUR ASTHMA?

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Background It is recognised that some 45% of the population exhibit poor asthma control. Over 90% of the population possess a mobile phone (>70% over 60 years of age). Mobile technology potentially

Abstract S135 Table 1

ACQ6 score	Group 1(n=110)	Group 2(n=99)	Between group p value
Baseline, median (IQR)	2.17 (1.67–2.67)	2.33 (1.67–2.67)	0.441
6 months, median (IQR)	1.25 (0.67–1.83)	1.17 (0.67–1.83)	0.995
Median difference (IQR)	0.83 (0.17–1.50)	0.83 (0.33–1.33)	0.586
Within group p value (Wilcoxon)	<0.001	<0.001	
Mean difference (95% CI)	0.84 (0.67 to 1.02)	0.94 (0.77 to 1.11)	0.434
Within group p value (t-test)	<0.001	<0.001	
MID*, n (%)			0.652
Improvement = MID	74 (67.3)	73 (73.7)	
Improvement < MID	20 (18.2)	16 (16.2)	
Deterioration < MID	6 (5.5)	5 (5.5)	
Deterioration = MID	10 (9.1)	5 (5.1)	

addresses the barriers of low expectations and poor concordance which are factors in poor asthma control.

Hypothesis Using mobile phone recording of symptoms, lung function and medication use with instant feedback of asthma control, would improve control compared to using paper diaries.

Trial design A 6-month researcher-blinded randomised controlled trial

Setting UK primary care

Method Using central randomisation, we allocated patients ≥12 years of age with poorly controlled asthma (ACQ>1.5) to either mobile phone or paper-based monitoring. Clinical care was provided by practice asthma nurses in accordance with SIGN/BTS guidelines. Patients were reviewed monthly until control was achieved. A researcher, blinded to allocation assessed outcomes at 3 m and 6 m. Primary outcome measure: change in Asthma Control Questionnaire score between baseline and 6 months.

Results We randomised 288 patients from 32 practices (209 completed). Baseline characteristics of both groups were similar. Intention to treat analysis, before breaking the randomisation code, showed that control in both groups improved significantly and to a similar extent. ACQ: Group 1 (n=110) Baseline 2.17, 6m 1.25; Group 2 (n=99) Baseline 2.33, 6m 1.17. Mean (95% CI) improvement in ACQ: Group 1 (n=110) 0.84 (0.67, 1.02), Group 2 (n=99) 0.94 (0.77, 1.11) both p<0.001. Between group p=0.434 ns. Approximately 70% in each group improved by ≥0.5 (minimal clinically important difference).

Conclusion Both groups demonstrated significant improvement in asthma control from baseline. Use of mobile phone technology provided no additional benefit over paper diaries.

S136 FUNGAL SPUTUM CULTURE IN PATIENTS WITH SEVERE ASTHMA IS ASSOCIATED WITH A REDUCED POST BRONCHODILATOR FEV₁

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Introduction and objectives IgE sensitisation to fungal allergens is common in severe asthma, but the clinical relevance of this, and the relationship to airway colonisation with fungi, is not known. Many of the fungi that can grow at body temperature are filamentous moulds from the genera *Aspergillus* and *Penicillium*. We report here the

relationship between lung function and fungal sputum culture in patients with severe asthma.

Methods We recruited 126 patients attending a tertiary referral centre with a diagnosis of asthma and 18 healthy volunteers. 93% of patients were on GINA treatment step 4 or higher. At a single stable visit subjects underwent: spirometry with reversibility to 200 µg salbutamol; sputum fungal culture and a sputum cell differential count; skin prick testing to both common aeroallergens and an extended fungal panel (+ve ≥3 mm); specific IgE to *Aspergillus fumigatus* by CAP (positive >0.35 kU/l). Fungi were identified by morphology and species identity confirmed by sequencing regions of the nuclear ribosomal operon.

Results Patients had a mean age of 56 years (21–84 years); 48% were males with median ICS dose of 800 µg Fluticasone equivalent. 60% were atopic to common aeroallergens, 45% were IgE sensitised to one fungal allergen and 27% to ≥2 fungal allergens. 64% of patients cultured a mould in their sputum, 7% more than one species. This compared with three healthy subjects (17%) culturing any mould ($p < 0.01$). *Aspergillus* species were most frequently cultured ($n=58$) followed by *Penicillium* species ($n=15$) and *Thermoascus* species ($n=2$), others ($n=8$). Four fungal genera were cultured from healthy volunteers sputum, *Aspergillus*, *Penicillium*, *Coprinus* and one other. Post bronchodilator FEV₁% predicted was 71% in those with a positive fungal culture vs 84% in those who were culture negative, ($p < 0.01$). There were no differences in the sputum cell differential between culture positive and negative patients.

Conclusions In addition to IgE fungal sensitisation, sputum culture focused towards detection of moulds is frequently positive and associated with impaired post-bronchodilator FEV₁. Colonisation of the airways with mould in asthma could be responsible for the development of fixed airflow obstruction.

S137 THE AT-RISK REGISTERS IN SEVERE ASTHMA (ARRISA) STUDY: A CLUSTER-RANDOMISED CONTROLLED TRIAL IN PRIMARY CARE

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Objectives To evaluate the effectiveness of using electronic registers to identify and improve management of high-risk asthma patients in primary care.

Design Cluster-randomised controlled trial with stratification by high/low deprivation scores and 1-year follow-up.

Participants 29 GP practices in Norfolk, UK with suitable software systems used electronic searches and clinical knowledge to identify 911 patients aged 5+ years at high risk from their asthma as defined by British asthma guidelines (severe asthma plus adverse psychosocial characteristics, including poor adherence).

Intervention Intervention practices established registers of high-risk asthma patients and used an electronic alert to identify these patients at all practice encounters. This allowed reception staff to prioritise appointments and facilitate patient access to clinicians and clinical staff to review patients' asthma at all opportunities. Practice staff received a 1-h tailored training session on the use of alerts and actions to be taken from a GP (MN) and nurse (JW). Control practices continued with routine care.

Outcomes A composite measure of moderate–severe exacerbations (primary outcome, see Abstract S137 Table 1 for definition), disaggregated exacerbation-related events, consultations and medications

Abstract S137 Table 1

Events per person per year	Intervention (N=14 pracs, 457 patients)	Control (N=15 pracs, 454 patients)	Rate ratio (95% CI)	p Value
Median (IQR) rate of moderate–severe exacerbations (composite of below*)	1 (2)	0 (2)	1.21 (0.95 to 1.55)	0.13
No. (%) of patients hospitalised for asthma*	15 (3.3)	29 (6.4)	0.52 (0.28 to 0.98)	0.04
No. (%) of patients attending A&E for asthma*	29 (6.4)	37 (8.2)	0.73 (0.41 to 1.30)	0.28
No. (%) of patients attending out-of-hours for asthma*	26 (5.7)	32 (7.1)	0.84 (0.46 to 1.51)	0.56
No. (%) of patients prescribed courses of oral prednisolone for exacerbations*	247 (54.1)	213 (46.9)	1.24 (0.99 to 1.54)	0.06
No. (%) of patients prescribed nebulised short-acting β-agonists	36 (7.9)	63 (13.9)	0.56 (0.37 to 0.84)	0.005
Median (IQR) no. inhaled short-acting β-agonists prescribed	6 (10)	7 (12)	1.03 (0.89 to 1.19)	0.70
Median (IQR) dose of inhaled corticosteroids prescribed (µg/day)	658 (1036)	658 (1036)	1.14 (1.00 to 1.30)	0.04
Median (IQR) no. inhaled long-acting β-agonists prescribed	8 (9)	6 (9)	1.24 (1.08 to 1.42)	0.003
Median (IQR) no. primary care consultations for any reason	9 (11)	8 (11)	1.08 (0.93 to 1.25)	0.34
No. (%) of patients who 'did not attend' primary care consultations for any reason	81 (17.7)	102 (22.5)	0.53 (0.31 to 0.90)	0.02

(secondary outcomes) were derived from anonymous clinical data extracted from practice-based patient records for the year before and after implementation of registers.

Results See Abstract S137 Table 1 for results of unadjusted analyses. After adjustment for relevant covariates at baseline similar effects were observed but only the effect on nebulised β-agonists prescriptions remained significant.

Conclusions Use of at-risk registers had no significant effect on the overall rate of moderate–severe exacerbations. However, they were associated with increases in prescriptions of oral steroids, inhaled steroids and long-acting β-agonists, coupled with reductions in asthma hospitalisations, prescriptions of nebulised short-acting β-agonists and in failures to attend primary care appointments. Together these are suggestive of improved asthma management in the intervention group.

Mechanisms of fibrosis in respiratory disease

S138 CLARA CELLS INHIBIT ALVEOLAR EPITHELIAL WOUND REPAIR THROUGH A TRAIL-DEPENDENT APOPTOSIS MECHANISM

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Introduction Alveolar bronchiolization, a hyperproliferation of ciliated and non-ciliated (Clara) bronchiolar cells and their extension into the alveolar region, is a common feature of idiopathic pulmonary fibrosis. The role of this bronchiolization process in alveolar wound repair is controversial. Clara cells are also believed to be progenitors for ciliated bronchiolar epithelium but their influence in repair processes is unclear.