complex, bi-directional pathways by which interactions may occur. However, few studies have explored relationships between multiple psychosocial factors and outcomes in severe asthma with these pathways in mind.

Objectives This study investigated combined and independent cross-sectional and longitudinal relationships of self-management behaviours, an index of self-management (ISM), anxiety, depression, perceived control (PC) and socio-demographic/economic characteristics with asthma control, quality of life (QoL) and severe attacks amongst asthma patients on high levels of treatment and/or with a history of admissions.

Methods Cross-sectional data from 132 adults recruited to a previously reported trial of an intervention and accompanying comparative study were subjected to multiple regression analyses. These systematically examined relationships between psychosocial factors and asthma outcomes, and were used to build final hierarchical regression models in which key clinical variables were controlled for. More limited data from a maximum of 112 patients were used to explore longitudinal relationships, primarily with asthma control.

Results Final hierarchical regression models accounted for up to 69% and 73% of the variability in asthma control and QoL respectively ($p<0.001$) and significantly predicted experience of a severe attack ($p<0.001$). Variables showing significant independent relationships to outcomes in these models are highlighted in the Abstract P175 Table 1. Some individual behaviours and the ISM showed independent and differing cross-sectional relationships to each outcome. Other psychological factors were related to subjective outcomes but not severe attacks. Relationships of some psychosocial factors (eg, depression, unemployment) to outcomes were not fully mediated by other variables, including self-management behaviours. In longitudinal analyses, there was some evidence for depression directly contributing to poorer subjective outcomes, whilst relationships of PC and anxiety with outcomes were more variable and inconsistent.

Abstract P175 Table 1 Regression

	Control (11 variables entered)	QoL (12 variables entered)	Attack (6 variables entered)
1. Clinical factors	Severity	(Sev with ISM)	–
2. Self-mgmt behs	Overusing reliever	–	Trigger avoid
3. Psych factors	Depression (PC with ISM)	Anxiety depression PC	N/A
4. Social factors	Employment age	Employment	Age
Var. acc. for (R^2):	69%	73%	app 23–31%
	(63% using ISM)	(72% using ISM)	
	All steps sig (26, 31, 9, 4%)	All steps sig (25, 19, 27, 2%)	All steps sig (~10, 6, 17%)

Conclusions Emotional and cognitive factors appear at least as important as self-management behaviours in relation to subjective outcomes in severe asthma. Along with a growing body of other research, findings suggest a particular need to identify and address depression amongst patients with severe asthma in practice, as in other chronic diseases.

P176 EVALUATING THE ROLE OF TRIAMCINOLONE IN A DIFFICULT ASTHMA SERVICE

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Introduction and Objectives 10% of patients with asthma have disease that is refractory to conventional therapy. Two important factors in this group of patients are non-adherence to prescribed treatment and steroid insensitive airway inflammation. We report on our experience using intramuscular (IM) triamcinolone to evaluate such patients.

Methods We identified 28 patients who were on BTS step 5 treatment for asthma and at risk of fatal or near fatal events, who were given IM triamcinolone in the Glenfield difficult asthma clinic. The primary reason for administration of IM triamcinolone was to evaluate whether these patients had evidence of steroid insensitivity or were potentially non adherent. Adherence was assessed objectively prior to commencing triamcinolone. Juniper asthma control questionnaire (JACQ), fraction of exhaled nitric oxide (FeNO), blood eosinophils, sputum eosinophils, FEV_1 (pre bronchodilator) were measured at baseline and whilst on triamcinolone.

Results Triamcinolone was administered monthly at a dose of 40–80 mg for a median (range) course of 4 (1–19) months. Patient demographics were: 75% (21) female, mean age 40 y, mean BMI 29.1, median dose of ICS (BDP equivalent) 2000 mcg, median dose of maintenance prednisolone 20 mg, 29% (8) had previously been ventilated. Adherence was objectively assessed in 93% (26) with non-adherence demonstrated in 77% (20), either by prescription refill check or drug assays. Significant improvements were seen whilst on triamcinolone in the mean JACQ score from 3.66 to 2.52 ($p=0.0003$), geometric mean FeNO from 52.3 ppb to 17.8 ppb ($p=0.0034$), mean blood eosinophils from 0.59×10^9/l to 0.22×10^9/l ($p=0.0032$), geometric mean sputum eosinophil count from 12.93% to 1.24% ($p<0.0001$) and in pre bronchodilator FEV_1 from 54% to 67% predicted ($p=0.0003$). Of 28 patients receiving IM triamcinolone, 68% (19) showed significant improvement in 2 or more disease markers, 7% (2) showed improvement in 1 disease marker, 18% (5) had an equivocal response and 7% (2) demonstrated no response to parenteral steroid. No significant adverse events were reported.

Conclusions This study shows that IM triamcinolone is a useful tool that may identify non-adherence in difficult-to-control asthmatic patients prescribed maintenance oral corticosteroids. Absolute steroid resistance is uncommon in this group.

P177 FLUTICASONE PROPIONATE/FORMOTEROL FUMARATE COMBINATION THERAPY IS AS EFFECTIVE AS FLUTICASONE PROPIONATE/SALMETEROL XINAFOATE IN THE TREATMENT OF ASTHMA: A RANDOMISED CONTROLLED TRIAL

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Introduction and Objectives A new asthma therapy combining fluticasone propionate and formoterol fumarate (FP/FORM) in a single pressurised metered dose inhaler has been developed. The efficacy and safety of FP/FORM and fluticasone propionate/salmeterol xinafoate (FP/SAL) therapy were compared.

Methods Adults (N=202) with mild to moderate-severe asthma were randomised 1:1 to 12 weeks of treatment with FP/FORM (100/10 μg or 250/10 μg) or FP/SAL (100/50 μg or 250/50 μg), both twice daily, in an open-label, parallel-group, multicentre study. The starting dose was based on the dose of inhaled corticosteroid the patient received before the study. Lung function and safety assessments were made during the 12-week period. The primary endpoint was mean morning pre-dose FEV_1 at Week 12.

Results FP/FORM was as effective as FP/SAL, with a least squares (LS) mean difference in morning pre-dose FEV_1 at Week 12 of −0.061 L between treatments. Non-inferiority of FP/FORM to FP/SAL was demonstrated (the lower limit of the 95% CI exceeded the acceptance limit of −0.2 L). Pre-dose FEV_1 increased in both groups

from baseline to Week 12 (FP/FORM: +0.196 L; FP/SAL: +0.257 L). The LS mean difference in change in pre-dose FEV_1 was −0.061 L between treatments (95% CI −0.161 to 0.040). Non-inferiority of FP/FORM to FP/SAL was demonstrated (the lower limit of the 95% CI exceeded the acceptance limit of −0.2 L). In total, 72.3% (73/101) patients started on FP/FORM 250/10 μg and 75.2% (76/101) on FP/SAL 250/50 μg. Eight patients (FP/FORM: n=5; FP/SAL: n=3) required an increase in dose. Similar numbers of patients treated with FP/FORM and FP/SAL discontinued due to lack of efficacy (FP/FORM: n=1; FP/SAL: n=2). Twenty-three patients (11.4%) experienced mild or moderate asthma exacerbations. Four patients (2.0%) experienced severe exacerbations (FP/FORM: n=3; FP/SAL: n=1; p=0.621). Overall, 23.8% of patients experienced at least one AE. The rate was the same in both treatment groups (24/101). Most AEs were mild or moderate. No clinically important changes in laboratory results, vital signs or ECGs were observed.

Conclusion FP/FORM and FP/SAL had similar efficacy and safety profiles.

Abstract P177 Table 1 Pre-dose FEV_1 at Week 12—per protocol set

		Pre-dose FEV_1 (L)				
		Week 12		Difference FP/FORM − FP/SAL		
	n	LS mean	95% CI	LS mean	95% CI	*P* value
FP/FORM	96	2.402	2.324 to 2.481	−0.061	−0.161 to 0.040	0.007
FP/SAL	95	2.463	2.384 to 2.543			

P178 VALIDATION OF A NOVEL SYNTHETIC ABSORPTIVE MATRIX (SAM) FOR SAMPLING NASAL MUCOSAL LINING FLUID

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Introduction An improved method for sampling nasal mucosal lining fluid (MLF), termed nasosorption, utilises a synthetic absorptive matrix (SAM) (Accuwick Ultra, Pall). Conventionally, Whatman's filter paper has been used for absorption of nasal MLF, but this natural cellulose source has the capacity to bind mediators, causing eluted fluid to have decreased and variable detectable levels of mediators. Nasal lavage has the problem of diluting MLF and this also causes detectable levels of mediators to be low. Strips of Accuwick are effective for nasosorption in adults following nasal allergen challenge and for sampling children with active rhinitis. However, Accuwick is no longer manufactured and we wished to validate an alternative SAM (Leukosorb, Pall).

Methods Sputum supernatant (40 μl) from a subject with COPD as well as a standard preparation of cytokines was spiked onto Accuwick and Leukosorb strips. Following elution by spin filter centrifugation, the MesoScale Diagnostics (MSD) multi-immunoassay platform was used to assess levels of IFN-γ, IL-10, IL-12 p70, IL-6, IL-8, and TNFα. After absorption to Accuwick and Leukosorb, elution was compared with and without buffer (PBS with BSA (1%) and Triton X (1%)), prior to immunoassay of the recovered sample.

Results Without buffer the recovery of 7 cytokines after the sputum supernatant was applied to Accuwick was a mean of 17.6% (range 1—100%), while recovery was a mean of 20.2% (range 2.9—92.5%) using Leukosorb. Addition of the buffer prior to elution of the fluid increased mean recovery to 61.8% when employing the Leukosorb system. Finally, in a direct comparison when employing Leukosorb and Accuwik for nasosorption in different nostrils after nasal allergen challenge in a single subject, Leukosorb resulted in higher detectable IL-5 levels in MLF.

Conclusion Leukosorb appears to be a superior alternative to Accuwick Ultra for nasosorption in terms of recovery of cytokines. Addition of a buffer containing detergent and protein prior to elution significantly increases recovery. SAM has the potential to be employed in the upper and lower respiratory tract to sample undiluted MLF.

P179 LUNG-BASED ASSESSMENT IN ANDERSON FABRY DISEASE (AFD) DEMONSTRATES DIFFERENTIAL α GALACTOSIDASE A ENZYME (GLA) ACTIVITY AT BLOOD AND TISSUE SITES

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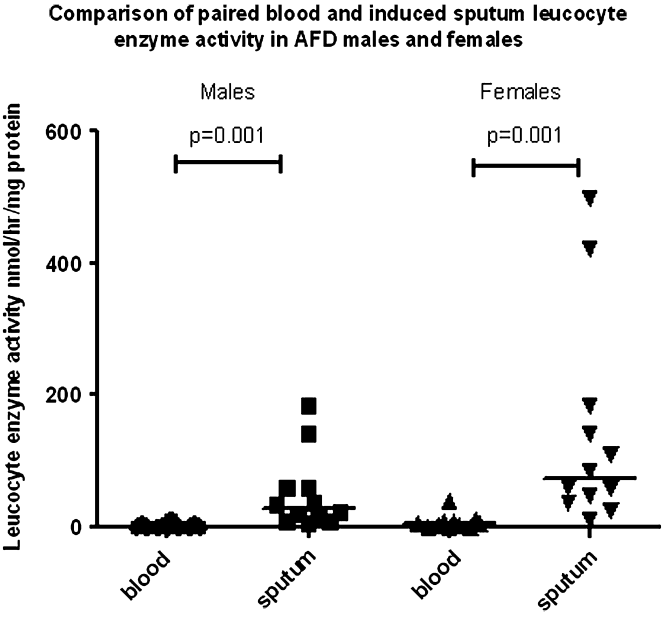
Introduction and Objectives AFD is an X-linked lysosomal storage disorder caused by mutations of the GLA gene. Lack of enzyme results in storage material accumulation within lysosomes, leading to multi-organ pathology. Airflow obstruction has been reported, though there has been no systematic assessment of lung enzyme activity in affected individuals. We therefore undertook a controlled cohort review of UK AFD patients focussing in particular on the relationship between airway and blood intra- and extracellular GLA, and lung pathology.

Methods Study subjects and controls were recruited following local Ethics Committee approval. All underwent systematic pulmonary investigation, including lung function testing and sputum induction with 40 ml of 4% hypertonic saline over 20 min via an ultrasonic nebuliser. GLA activity was measured from AFD patients and healthy controls in induced sputum (IS) cells and supernatant using a fluorometric assay. In addition, in AFD patients, GLA activity was measured simultaneously in blood leucocytes and plasma.

Results 45 AFD patients with variable severity extra-pulmonary disease were recruited (20 males, 10 smokers). The population had a mean FEV1 of 89% predicted. 20 of 45 (44%) (13 males, 6 smokers) had evidence of airflow obstruction with FEV1/FVC ratio <70%. IS intra- and extracellular GLA activity was lower in AFD affected males compared to controls (n=18 and 13, median enzyme activity 18.8 vs 41.7 nmol/h/mg protein and 0.9 vs 10.0 nmol/h/ml, p<0.001 and p<0.01, respectively). No similar difference was found in females. Paired blood and sputum data from 22 AFD patients (13 males, 18 on enzyme replacement therapy) demonstrated greater



Abstract P179 Figure 1 Comparison of paired blood and induced sputum leucocyte enzyme activity in AFD males and females.