Results All four biomarkers were positive in smear-positive TB, but SAA and CRP were less sensitive in smear-negative TB (see attached table). Even in the control group, there were positive tests for the four biomarkers. None of those with latent TB developed active disease, even though a proportion had a positive test.

Conclusion These four biomarkers did not distinguish between active and latent disease, and did not predict the development of active disease in those with latent TB infection.

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Clinical trials and outcome measures in paediatric lung disease

S64

EOSINOPHIL CATIONIC PROTEIN AND CYTOKINE ANALYSIS IN EXHALED BREATH CONDENSATE IN PAEDIATRIC ASTHMA

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10.1136/thoraxjnl-2014-206260.70

Background Sputum eosinophil counts are unstable in childhood asthma.¹ This makes sputum induction to quantify sputum eosinophils an unsuitable test to guide anti-inflammatory therapy.² While eosinophils may be cleared following apoptosis, free eosinophil granules, containing effector proteins, may persist in the airway lumen. We speculated that inflammatory mediators in exhaled breath condensate, released by eosinophils (such as eosinophil cationic protein (ECP)) could aid risk-profiling in children with asthma. We therefore sought to assess whether ECP is present in EBC from asthmatic children, alongside an assessment of pro-inflammatory cytokines.

Methods Children with asthma aged 7–15 and age matched healthy controls underwent spirometry, sputum induction, collection exhaled breath condensate (EBC), and completed the childhood asthma control test. Exhaled breath was tested for eosinophil cationic protein (ECP) using an immunoassay. A cytokine analysis of the exhaled breath condensate was also carried out in addition to a sputum leucocyte differential.

Exhaled breath condensate (EBC) was collected in an R-tube following manufacturer protocol, over 10 min.

Results Sputum leucocyte counts were performed in 33 children with asthma. Suitable samples (visible airway plugs) were obtained from 14 children at baseline who concurrently

provided EBC samples. Of these, 7/14 (50%) were eosinophilic and 7/14 (50%) were non-eosinophilic. The cytokine analysis showed that IL-4 did not differ between groups. IL-13 was raised in children who had sputum eosinophilia (2.54 ± 1.18 vs. 0.87 ± 1.49 pg/ml, mean $\pm$ sd, $p = 0.0387$, unpaired t-test).

Exhaled breath condensate was collected in 26 asthmatic children and 10 controls. ECP was detected in EBC from 5/26 asthmatic children and 0/10 healthy children. In 2 asthmatic children, detectable ECP was associated with sputum eosinophilia ($>2.5\%$). In one child ECP was detectable with no induced sputum eosinophils. (Table 1).

Discussion ECP may be identified in EBC from children with asthma, and is not exclusively associated with concurrent sputum eosinophilia. Eosinophilia may be identified non-invasively by measuring Th2 cytokines in EBC. These techniques may provide additional insights into underlying airway inflammation and identify children who may benefit from specific anti-Th2 cytokine monoclonal antibody therapies.

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S65

URINARY PROSTAGLANDINS AS INFLAMMATORY MARKERS FOR CHILDHOOD ASTHMA EXACERBATIONS

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10.1136/thoraxjnl-2014-206260.71

Background Measuring inflammation (inflammometry) may assist decisions regarding preventative anti-inflammatory therapies in asthma.¹ Prostaglandin metabolites, which reflect airway inflammation, may be measured in urine samples.² We sought to prospectively assess associations between urine prostaglandins and subsequent asthma exacerbations in children, and to compare these markers to current markers that aim to predict future risk.

Methods Children with asthma aged 7–15 underwent spirometry, sputum inductions, completed the childhood asthma control test (C-ACT) and provided urine samples at baseline. Urine was also provided by healthy (non-atopic) controls. Urine PGD, PGE and PGJ metabolites were measured using HPLC-MS. At 3 months, sampling was repeated, data was collected on exacerbations (unscheduled medical attendance or day missed from school due to asthma symptoms) and the receiver operator characteristic was calculated for the baseline assessment.

Results 73 children (asthma $n = 25$, controls $n = 48$) were included. Urine PGD₂, PGE₂ and PGJ₂ metabolites were increased in asthma in comparison to controls, and 15-dPGJ₂ predicted subsequent asthma exacerbation (PPV=75%, NPV=90%, ROC AUC 0.858, $p = 0.005$). Sputum eosinophils, spirometry and C-ACT did not predict subsequent exacerbations after correction for multiple comparisons, and sputum phenotypes were unstable. Change in C-ACT score was associated with interim control ($p = 0.04$).

Conclusions Urinary prostaglandin metabolites are increased in children with asthma in comparison to controls. Urine 15-dPGJ₂ is a biologically plausible, non-invasive marker for inflammometry in childhood asthma, and is superior to assessment of sputum eosinophils, C-ACT, or spirometry.

Abstract S64 Table 1 Eosinophil cationic protein (ECP) assay using exhaled breath. The threshold for detection in the assay was 50.7 pg/ml

Patient	Mean ECP (pg/ml)	Sputum Eosinophils (%)
Child 1	65	(unknown)
Child 2	505	18.96
Child 3	134	6.2
Child 4	1113	0.21
Child 5	1307	0.0

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Abstract S65 Figure 1 (A) Urine 15dPGJ₂ at baseline is significantly lower in children who have an asthma exacerbation within 3 months. (B) ROC curve for 15dPGJ₂. ROC AUC=0.858, p=0.005. PG:prostaglandin. Bar represents median, comparison by Mann-Whitney test. *p<0.01.

S66

THE GLI SPIROMETRY REFERENCE EQUATIONS INFLUENCE THE APPARENT RATE OF DECLINE IN FEV₁ AMONG CHILDREN AND ADOLESCENTS WITH CYSTIC FIBROSIS

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10.1136/thoraxjnl-2014-206260.72

Background In patients with cystic fibrosis (CF), interpretation of cross-sectional FEV₁ data is greatly influenced by choice of spirometry reference equation, particularly during childhood (Stanojevic; J Cyst Fibros 2014). We hypothesised that availability of the Global Lung Function Initiative (GLI) spirometry reference equations (Quanjer; ERJ 2012) will also affect the apparent rate of decline in lung function over time, thereby potentially altering our understanding of disease progression in CF.

Abstract S66 Figure 1 Average FEV₁ decline in people with cystic fibrosis according to three spirometry reference equations

Methods Data were extracted from two patient registries: the UK CF Registry (n = 6043 subjects; 20,013 test occasions over a period of 5 years) and the Toronto CF database (n = 1023 subjects; 27,868 test occasions over a period of 23 years). Spirometric outcomes were interpreted using %predicted FEV₁ calculated from GLI, Knudson (as currently used by the UK CF Registry), and Wang-Hankinson (as used by the US CF Foundation) reference equations. Patients >30 yrs or with FEV₁ > 130% predicted were excluded. We used a non-linear mixed effects model to describe the average change in FEV₁ with age. To illustrate the importance of reference equation in evaluating risk factors, FEV₁ decline according to patient gender was also explored.

Results The pattern of lung function decline at the population level differed according to selected equation (Figure). Average rate of decline was steeper with Knudson or Wang-Hankinson than GLI. Importantly, GLI equations showed a steady decline in FEV₁ starting at 6 yrs, whereas the other equations suggest greater decline during adolescence. Similar patterns were observed in both UK and Toronto populations. When analysed according to gender, the rate of lung function decline was steeper in females during early adolescence compared with males where the decline was steady.

Conclusions In both datasets, Knudson and Wang-Hankinson reference equations suggest relative preservation of spirometry in childhood followed by rapid decline in adolescence. However using the more robust GLI equations, steady decline throughout childhood with a less dramatic acceleration during adolescence is seen, with differences in pattern of change over time according to patient gender. Accurate identification of critical periods of lung function decline offers novel opportunities to target care.

Funded by the UK CF Trust.

S67

LUNG CLEARANCE INDEX (LCI) IS A SENSITIVE PREDICTOR OF HIGH RESOLUTION COMPUTED TOMOGRAPHY (HRCT) SCORES IN CHILDREN WITH NON-CF BRONCHIECTASIS

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10.1136/thoraxjnl-2014-206260.73

Introduction and objectives LCI is a sensitive predictor of early cystic fibrosis (CF) lung disease, and correlates with HRCT better than spirometry (Thorax. 2008;63:129–134). The same is true in adults with non-CF bronchiectasis (Am J Respir Crit Care Med. 2014;189:586–592.), but by contrast, in PCD there were no relationships between LCI, HRCT or spirometry (Am J Respir Crit Care Med. 2013;188:545–549). It is unclear whether these differences reflect primary versus secondary ciliary dyskinesia, or CFTR versus non-CFTR disease. We hypothesised that in children with non-CF bronchiectasis, relationships between spirometry, LCI and HRCT will be similar to those in CF children and non-CF bronchiectasis adults, rather than PCD patients.

Methods 12 children with non-CF bronchiectasis performed LCI and spirometry and underwent thoracic HRCT. HRCT scans were scored quantitatively (Thorax. 2013;68:532–539). Results were compared with those from large CF (n = 125) and PCD (n = 38) cohorts.

Results In non-CF bronchiectasis there was a correlation between first second forced expired volume (FEV₁) and LCI (p = 0.009, r=-0.6), similar to that seen in CF (p < 0.0001,