Background In contrast to findings from the Australian AREST-CF study1 infants with cystic fibrosis (CF) diagnosed by newborn screening (NBS) participating in the London CF Collaborative (LCFC) study2 were found to have relatively mild lung disease by 1 year of age when compared to healthy controls.

Hypothesis In NBS CF infants, lung function remains stable to 2 years.

Methods Lung clearance index (LCI), plethysmographic functional residual capacity (FRC) and forced expiratory volume (FEV0.5) from the raised volume technique were measured in NBS CF infants identified by 3m when compared with controls remained stable thereafter. The significant reduction in FEV0.5 (mean difference (95% CI) -1.26 (-1.73; -0.79) z score) among CF infants at 3m had improved by 1y (see Figure 1). From 1 to 2 years all 3 measurements remained stable with no significant changes in average z-scores for either the CF or control infants. On average, LCI, FRC and FEV0.5 only changed by 0.02, 0.16 and 0.06 z-scores respectively amongst CF children between 1–2 years, similar to that observed in controls. Mean (95%CI) group differences (CF-HC) in change of LCI, FRC and FEV0.5 between 1–2y were 0.02 (-0.61; 0.66), p = 0.94; 0.05 (-0.61; 0.51), p = 0.86; and 0.32 (-0.27; 0.90) p = 0.29, respectively.

Conclusions This is the first study to demonstrate stable lung function to 2y in NBS CF infants managed on standard CF therapy. These results suggest that in many of these infants novel treatments could be deferred beyond infancy when objective outcomes are more easily measured.

REFERENCES
1. Pillarietti et al. AJRCCM 2011

Abstract S7 Figure 1. Comparison of change in lung function z-scores between 3m, 1y and 2y in NBS CF infants and healthy controls. Legend: Data are expressed as mean (SD). Closed circles represent NBS CF infants; open circles represent healthy controls. Lung function outcomes were expressed as z-scores which adjusted for age and body size as appropriate. Dashed lines indicate limits of normality (+/-2 z-scores).
SIFT-MS ANALYSIS AS A NON-INVASIVE DETERMINANT OF LUNG CLEARANCE INDEX (LCI) AND PSEUDOMONAS AERUGINOSA INFECTION IN PATIENTS WITH CYSTIC FIBROSIS

Background There is evidence that Pseudomonas aeruginosa (Pa) produces volatile organic compounds (VOCs) such as hydrogen cyanide (HCN) and 2-aminoacetophenone (2-AA). VOCs in exhaled breath are therefore proposed as potential biomarkers of infection. We hypothesised that selective ion-flow mass spectrometry (SIFT-MS) breath analysis might allow discrimination of CF patients with (CF + Pa) and without Pa (CF-Pa).

Methods 79 adults (31 CF + Pa, 22 CF-Pa and 26 healthy controls) provided starved, single tidal exhalation breath samples. Quantification of 15 VOCs was performed within two hours on SIFT-MS. All results are presented as (median parts-per-billion by volume [IQR]).

Results 2-AA was significantly higher in CF + Pa than CF-Pa (5.0 [3.4–7.1] vs. 1.3 [0.0–3.2], p < 0.01). However, there was significant overlap and median co-efficient of variation was 35.41%; clinical utility is therefore questionable.

Dimethyl disulphide was also significantly higher in CF + Pa (95.2 [41.3–211.2] vs. 35.5 [22.1–79.8], p < 0.01). When combined with 2-AA, area under ROC curve was 0.867.

Counter to our sputum results, there was no difference in HCN between CF + Pa and CF-Pa (8.1 [5.0–11.9] vs. 6.9 [4.4–11.0], n/s) or between all CF patients and healthy controls (7.8 [4.9–11.5] vs. 7.0 [4.6–11.5], n/s).

Our early in vitro data showed decreased butanol over Pa cultures, suggesting consumption. This was replicated in breath with lower levels in CF + Pa vs. CF-Pa (37.4 [24.3–87.6] vs. 91.7 [46.9–143.7], p < 0.05).

Of VOCs likely to be of host origin, isoprene was increased in CF vs. controls (108.0 [83.4–195.5] vs. 69.6 [46.9–89], p < 0.01) with no difference between CF + Pa vs. CF-Pa. Acetone was reduced in CF (269.9 [161.9–356.4] vs. 324.9 [236.7–598.9], p < 0.01).

Conclusions 2-AA is a potential biomarker of Pa infection but clinical applicability is uncertain. Dimethyl disulphide and butanol also show promise. Mouth-exhaled HCN assessed by SIFT-MS does not appear to fulfil its promise as a Pa biomarker. Other VOCs assessed were either similar between Pa groups or different between healthy controls and CF, but unable to differentiate between Pa status. This study provides proof-of-concept for the development of a non-invasive tool with which to screen for lower airway bacterial infection in CF though a clinically applicable test remains some way off.

S10 LUNG CLEARANCE INDEX (LCI) AND PSEUDOMONAS AERUGINOSA IN ADULTS AND CHILDREN WITH CYSTIC FIBROSIS (CF)

Introduction LCI obtained from multiple breath washout (MBW) is a sensitive measure of ventilation inhomogeneity in CF. Persistent colonisation with P. aeruginosa is associated with a decline in LCI in children (Kraemer et al. 2006). Further research is required to investigate the relationship between airways infection and LCI in adults.

Objective To investigate the sensitivity of LCI to P. aeruginosa in adults and children compared with FEV1%pred and FEF25–75% pred.

Methods Stable CF patients from adult & paediatric Northern Ireland CF centres were recruited. LCI was derived from MBW, using 0.2% SF6, and a modified InnocorTM device. P. aeruginosa status was determined from routine culture of a spum sample or deep throat swab. Patients categorised as having P. aeruginosa infection met the Leeds criteria for chronic infection defined by the Leeds criteria (Lee et al. 2003).

Analysis Receiver-operator characteristic (ROC) curves and area under the receiver operating curves (AUCROC) indicate the level of sensitivity and specificity where "SF" = perfect discrimination considering sensitivity and specificity.

Results Sixty-seven adults were recruited (39M), median (IQR) age 27 (16) years. Mean (SD) FEV1%pred 71.8 (23.0), median (IQR) FEF25–75%pred 40.0 (46.7) and mean (SD) LCI 10.3 (3.0) lung volume turnovers. 49% had P. aeruginosa infection.

Forty-three children were recruited (24M), mean (SD) age 11.7 (3.4) years. Mean (SD) FEV1%pred 85.2 (16.6), median (SD) FEF25–75%pred 66.0 (27.6) and mean (SD) LCI was 7.8 (1.8) lung volume turnovers. 16% had P. aeruginosa infection.

Compared to FEV1%pred and FEF25–75%pred, LCI had the greatest sensitivity and specificity to discriminate between CF patients with and without P. aeruginosa in both adults and children. Adult AUCROC (SE) for LCI = 0.82 (0.05), p < 0.0001, compared with FEV1%pred = 0.66 (0.07), p = 0.021 and FEF25–75%pred = 0.64 (0.07), p = 0.044 (Figure 1). Child AUCROC (SE) for LCI = 0.85 (0.10), p = 0.004, compared with FEV1%pred = 0.80 (0.12), p = 0.014 and FEF25–75% pred = 0.67 (0.13), p = 0.152.

Conclusion LCI is more sensitive and specific to the presence of P. aeruginosa airways infection across the age groups in CF compared with spirometry.

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S8 Hyperpolarised 3He MRI is superior to lung clearance index in detection of ventilation abnormalities in young children with mild CF

H Marshall, A Horsley, L Smith, D Hughes, F Horn, L Armstrong, J Parra-Robles, S Cunningham, I Aldag, C Taylor and JM Wild

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