were in close proximity on the ward to the index case became infected, as did 1 patient at other end of ward. Influenza B infection was followed by an average reduction in FEV_1 of 10.54% (SD 11.25) at the time of infection (p=0.0124). Follow-up data demonstrated a persistent FEV_1 reduction of 10.50% (SD 5.95) 3 months post infection (p=0.0034). 70% of patients on the ward and 62% of staff had received the seasonal influenza vaccine. Further investigation revealed this to be a trivalent influenza vaccine that did not cover the strain B/Brisbane/60/2008. A ward ventilation survey identified that ventilation measurements in affected patient rooms ranged from 1.75 to 2.10 air changes/hour, well below DOH recommendations of 6 air changes/hour for single patient rooms.

Conclusion The influenza B outbreak at the MACFC had a detrimental effect on patients' lung function, which was still present after 3 months. Inadequate ward ventilation and a lack of protection from the influenza vaccine given to patients and staff may have contributed to the spread of the virus.

P246 THE IMPACT THE INTRODUCTION OF A UNIVERSAL PAYMENT BY RESULTS ANNUAL TARIFF CF CENTRES UPON THE NORTH SOUTH DIVIDE IN ENGLAND

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Background Our preliminary work demonstrated inequalities in key demographic characteristics, clinical outcomes and medication use in Cystic Fibrosis (CF) patients between the relatively economically disadvantaged North of England compared to the South. The analyses presented here aimed to assess if this North-South divide has been closed following the introduction of a new and equal CF payment policy ("banding") in 2012.

Methods We compared the cross-sectional data from Annual Review Encounter in 2010 and 2015 for patients registered on the UK CF Registry. The data for each year were analysed separately and the North/South Results compared. We used Wilcoxon and t-tests to compare continuous outcomes, and the chi-squared test to compare proportions.

Results The 2010 and 2015 cohorts included 6417 and 8007 patients, respectively (Table 1). There were no significant gender differences. Mean age of the populations increased, the significantly higher age in the South in 2010 levelled out by 2015. A new gap in overall lung function emerged in 2015: 72.24% vs 73.5% (p=0.041), the significantly higher FEV_1 in children in the South remained, although the gap narrowed from 3.27% to 1.7%. The better FEV_1 in adults in the North disappeared post banding. More patients in the North were diagnosed before turning 3 months. Prescription of key medications (DNase and Hypertonic saline) increased overall between 2010 and 2015 but higher use in the South remained (p<0.001). Rates of chronic *Pseudomonas aeuginosa* fell but remain significantly higher in the North. Rates of MSSA and NTM remain higher in the South.

Conclusions There appears to be a closing of the North-South gap in some key areas such as FEV_1 and age, this may suggest improved outcomes although survival analysis is not possible on small cohorts such as these. The higher use in the South of the high cost drug DNase must now be down to clinician preference rather than funding problems. These markers of overall improvements (higher mean age, higher FEV_1, lower *Pseudomonas*) may be associated with the introduction of equality of funding in England but could equally represent improved care in general with similar improvements seen in other international registries.

Abstract P246 Table 1 Patient characteristics

	Pre Banding (2010 Annual Review Encounter)		Post Banding (2015 Annual Review Encounter)	
Outcome	**South of England/North of England (n=3017/3400)**		**South of England/North of England (n=3887/4120)**	
	Summary statistics	p-value	Summary statistics	p-value
Age: Mean±SD	19.71±13.24/18.81 ±12.52	0.0052	20.82±14.23/20.3 ±13.78	0.0967
Median	18/18		19/19	
Gender, n(%) Female	1423 (47.17)/1578 (46.41)		1870 (48.11)/1894 (45.97)	
Age at diagnosis, n (%)				
<3 months; n (%)	1280 (42.43)/1590 (46.76)	0.0052	1852 (47.65)/2121 (51.48)	<0.001
≥18 years; n (%)	188 (6.23)/191 (5.62)	0.2296	295 (7.59)/258 (6.26)	0.0216
FEV1 percent predicted				
(Overall) Mean±SD	70.98±24.66/71.23 ±24.23	0.7172	73.5±24.53/72.24 ±24.84	0.041
Age<16 Mean±SD	84.51±17.99/81.57 ±19.80	0.0022	87.78±17.37/86.08 ±17.66	0.0361
Age≥16 Mean±SD	64.69±24.81/66.73 ±24.61	0.0153	67.6±24.63/66.6 ±25.13	0.1754
Hypertonic Saline (n (%))	433 (14.35)/311 (9.15)	<0.001	1319 (33.93)/860 (20.87)	<0.001
Dornase Alfa (n(%))	1394 (46.2)/1393 (40.97)	<0.001	2572 (66.17)/2274 (55.19)	<0.001
Chronic macrolides (n (%))	1284 (42.56)/1445 (42.5)	0.9822	1498 (38.54)/1607 (39.00)	0.6856
Asthma (n(%))	534 (17.7)/393 (11.56)	<0.001	685 (17.62)/538 (13.06)	<0.001
CFRD (n(%))	528 (30.14)/623 (32.5)	0.1325	838 (53.51)/957 (57.34)	0.0389
NTM (n(%))	116 (3.84)/55 (1.62)	<0.001	297 (7.64)/193 (4.68)	0.001
Pseudomonas (n(%))	1058 (35.07)/1359 (39.97)	<0.001	1100 (28.3)/1332 (32.33)	0.0269

P247 LUMACAFTOR/IVACAFTOR IS ASSOCIATED WITH HIGH DISCONTINUATION RATES IN PATIENTS WITH BASELINE SEVERE LUNG FUNCTION BUT ALSO BENEFITS IN THOSE WHO TOLERATE THERAPY

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Lumacaftor/ivacaftor (LUM/IVA) is a combination CFTR modulator which is licensed for patients with cystic fibrosis homozygous for the Phe508del mutation. In clinical trials, use of LUM/IVA resulted in modest improvements in lung function, a reduction in pulmonary exacerbations and small increases in nutritional parameters. Although these trials excluded patients with FEV1 <40%, licensing does not restrict therapy on this basis. In the UK, LUM/IVA is only available on a managed access programme for patients with low lung function. We aimed to examine the safety, tolerability and effectiveness of LUM/IVA in patients with severe lung disease. 32 patients were admitted to commence LUM/IVA and 8 (25%) permanently discontinued therapy. One patient successfully recommenced therapy after discontinuation. Adverse event rate was 88%, with 87% related to respiratory symptoms. Therapy initiation was associated with significant relative falls in both FEV1 (−14±11.6%) and FVC (−11.6±13.1%) at 24 hours. A significant increase in CRP (mg/L) was identified at both day 3 [18 (7 -40) p<0.001] and day 7 [16.5 (5–49), p=0.038] compared to baseline [7.5 (4–18.8)]. Those patients who discontinued therapy had a higher increase in CRP at day 3 (p=0.01), a lower baseline pO2 (p=0.013) in the preceding year, and were more likely to complain of dyspnoea (p=0.017). For those who continued therapy, FEV1 increased compared to day 0 values (32.0%±6.9% v. 29.5%±6.7%, p=0.01) but not compared to best FEV1 in the preceding 3 months (31.1%±6.5%, p=0.23). A 2 kg increase in weight from day 0 was identified in those who continued LUM/IVA (p<0.001). In 14 patients who had at least 6 months therapy there was a reduction in the annualised rate of pulmonary exacerbations requiring iv antibiotics compared to the preceding year (3.2±2.8 v. 5.2±2.5, p=0.001) and days on iv antibiotics (47±33 v. 69±39, p=0.026). We report a very high adverse events rate associated with the initiation of LUM/IVA which was associated with adverse changes in objective markers. In those who tolerate therapy benefits may be similar to those reported in clinical trials.

P248 CFRD IS NOT AN INDEPENDENT RISK FACTOR FOR STENOTROPHOMONAS MALTOPHILIA ACQUISITION – 5 YEAR ANALYSIS OF UK CF REGISTRY DATA

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Introduction Recently, *Stenotrophomonas maltophilia* (SM) has been shown to have an increased prevalence in the sputum of people with CF-related diabetes (CFRD), raising the question as to whether CFRD is a risk factor for its acquisition. We investigated this at a population level by looking at UK CF Registry data.

Methods We analysed national UK CF Registry data for 2011–2015, looking at demographics, lung function and sputum microbiology, using descriptive and multivariable strategies to establish independent predictors for SM culture and associated outcomes. 6234 people with CF older than age 12 (mean 26 years, CFRD 26%, SM 15%, 54% male) with more than 3 years complete sputum microbiology and lung function data were included.

Results Although on univariate analysis those with SM were more likely to have CFRD (odds ratio [95% CI] 1.18 [1.01–1.39] p<0.0001), lower lung function (mean FEV1 [% predicted] 66.6 vs. 74.15, p<0.001) and more IV days (24 vs. 10, p<0.0001), multivariate logistic regression analysis showed no independent association for CFRD or Hba1c but IV antibiotic use and *Aspergillus* culture independently demonstrated an increased likelihood of SM growth (see Table 1). Furthermore, longevity of SM growth showed weak but statistically significant correlations with poorer FEV1 (rho −0.2, p<0.0001) and more IV days (rho=0.1, p<0.0001) but no association with CFRD (OR 1.09 [0.98–1.21]) or Hba1c (rho=-0.001, p=0.94).

Conclusion Our data suggests CFRD is not an independent risk factor for SM growth in CF. The increased prevalence of SM in CFRD may be explained by increased intravenous antibiotic pressure in this group.

Acknowledgement We would like to thank the CF Registry Research Committee for releasing the data used in this analysis.

Abstract P248 Table 1 Multivariate analysis of potential predictors of SM growth

Variable	Odds Ratio (95% CI)	
Age	0.99 (0.98–1.00)	NS
(years)		
>18		
FEV1	1.22 (0.92–1.64)	NS
(% predicted)	1.28 (0.82–2.01)	NS
<50		
<30		
IV antibiotics	0.41 (0.31–0.52)	***
(days/year)	1.46 (1.05–2.02)	***
0	1.64 (1.06–2.23)	**
>0		
>14		
Dysglycaemia	1.08 (0.80–1.46)	NS
CFRD	0.98 (0.62–1.58)	NS
Hba1c>48		
Microbiology		
Pseudomonas aeruginosa	0.69 (0.55–0.87)	**
Aspergillus	3.76 (2.93–4.82)	***
Burkholderdia Cepacia Complex	0.59 (0.34–1.03) 1.46 (1.18–1.83)	NS **
Staphylococcus aureus		

NS=not statistically significant *=<0.05 **=<0.01 ***=<0.001

P249 IT IS POSSIBLE TO DETECT ACTIVE NEUTROPHIL ELASTASE IN EXHALED BREATH CONDENSATE OF PATIENTS WITH CYSTIC FIBROSIS

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Introduction CF is characterised by chronic progressive respiratory decline punctuated with periods of acute pulmonary exacerbations (PEx). Given the relationship between PEx number and chronic rate of decline and that ~25% of PEx patients fail to regain their baseline FEV_1, there remains a need for a reliable biomarker to predict PEx and/or monitor responses to treatment. Several biomarkers have been explored, including sputum Neutrophil Elastase (NE). However, any sputum-based biomarker will only be suitable for patients able to expectorate, whereas significant disease begins earlier in life. Previously, our group (Thorax 2013;68: 532–9) reported the change of physiological, functional and structural markers over a PEx within which we collected exhaled breath condensate (EBC). These samples were analysed with a newly-developed immunoassay; detection of NE would offer the potential to detect airway inflammation in non-expectorating subjects.

Methods EBC was collected using an Ecoscreen condenser, stored at −80°C, and then analysed using the ProteaseTag® Active Neutrophil Elastase Immunoassay (ProAxsis Ltd).

Results 35 EBC samples from 19 participants were available. Participants were 12–44 years; 10 female. Median FEV_1% predicted was 52.5% (IQR 43.75%–74.8%). All had chronic *Pseudomonas aeruginosa* infection apart from 1 who had chronic *Burkholderia cepacia* complex infection. NE could be detected (≥LLD 7.2 ng/ml) in 28 of 35 samples (80%). For the whole group, median concentration was 15.45 ng/ml (IQR 10.36–19.02 ng/ml).

Discussion This was a small, pilot study seeking to demonstrate the feasibility of measuring active NE in EBC and successfully reporting, for the first time to our knowledge, detectable levels of this inflammatory marker. However, levels were near the lower end of detection of the immunoassay; therefore development of a more sensitive assay could be helpful. Further work is needed to establish CF/non-CF differences and the relevance of levels to accepted measures of airway disease. The use of EBC could allow monitoring of airway inflammation at the early stages of CF lung disease when patients cannot expectorate sputum, and during a period in their disease progression when the potential impact of interventions on long term outcomes may be greatest.

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P250 A NATIONAL STUDY OF NON-INVASIVE VENTILATION AND CLINICAL OUTCOMES IN CYSTIC FIBROSIS

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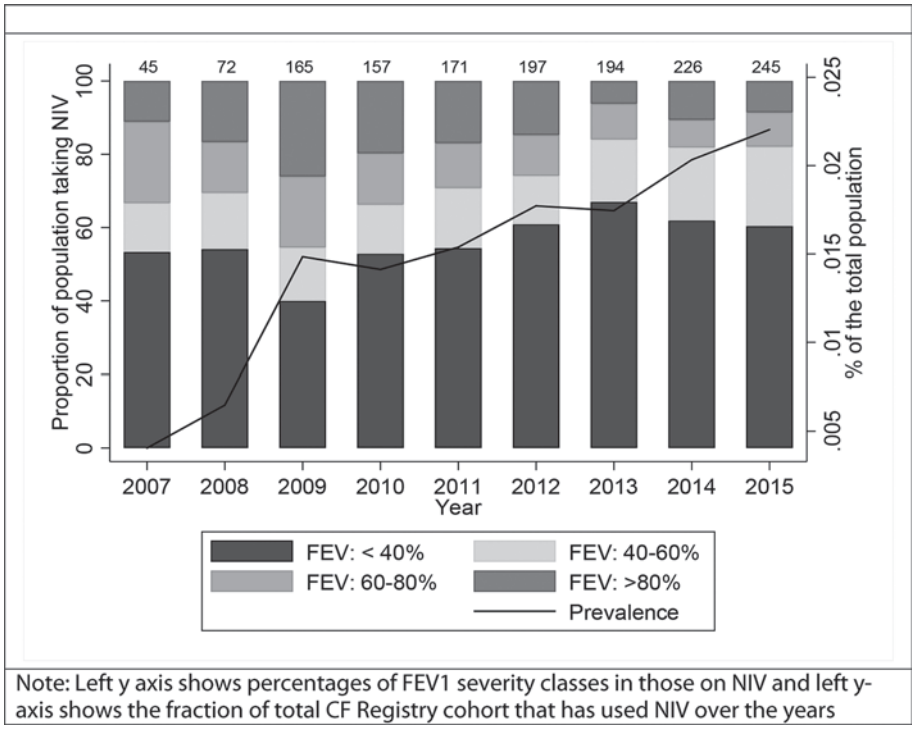
Introduction/Objectives Non-invasive ventilation (NIV) is often used as a 'bridge' to transplantation, for symptom control or as an adjunct to physiotherapy. Whether or not NIV is being appropriately used in UK patients with CF, successfully targeting those who will benefit most, is unknown; nor is there information on the life expectancy of those who start on NIV.

Methods The present study is part of the CF-Epidemiological Network (CF-EpiNet project) and uses data from the UK Cystic Fibrosis Registry to describe the patterns of NIV use by



Abstract P250 Figure 1 Lung function distribution across years and prevalence of NIV use.