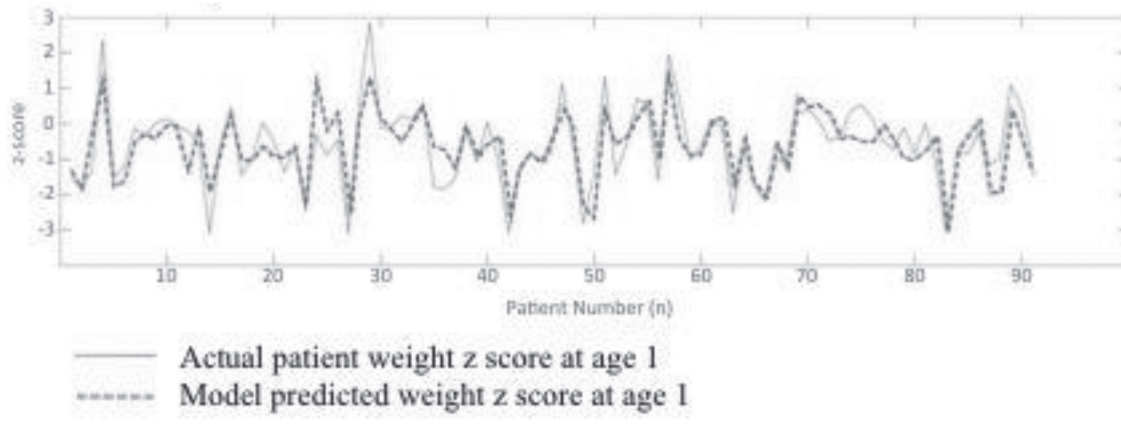

Abstract P89 Figure 1 Schematic representation of the accuracy of the model predicting weight z score at age 1

pancreatic insufficient and pancreatic sufficient children (−0.05 vs −0.36, p = 0.29) however a significant difference was observed in rate of weight gain from birth to first clinic visit (−0.1 vs −0.33, p = 0.007). Time taken for children to reach a z score of 0 for weight was 65 weeks and length was 90 weeks. Cluster analysis identified two distinct groups of children. Faecal elastase (FE) being the main determinant of class, with a cut off of 212 μg/g. Our models can predict weight z score at 1 and 2 years with a mean absolute error of 0.51 and 0.67 and length z scores at 1 and 2 years with an accuracy of 0.7 and 0.85. The most important factor when predicting future nutritional parameters was birth weight z score.

Conclusions We have developed and validated models that can provide a good estimate of weight and height z scores in the first 2 years of life for children diagnosed with CF by NBS. These models only require data available at the first clinic visit. They can potentially be used by clinicians to identify children at risk of poor nutritional outcomes thus, encouraging closer monitoring and earlier intervention.

P90 THE NORTH-SOUTH DIVIDE: REGIONAL INEQUALITIES IN DEMOGRAPHIC CHARACTERISTICS AND CLINICAL OUTCOMES IN PATIENTS WITH CYSTIC FIBROSIS IN ENGLAND–A POPULATION BASED CROSS-SECTIONAL STUDY USING UK CF REGISTRY DATA

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Background For many diseases including cancer, the inequalities in key clinical outcomes are known to be wider in the economically disadvantaged Northern England (NE) compared to the more affluent South England (SE) (Shack, *et al*, 2008). This study aimed to investigate the North-South divide in demographic characteristics and clinical outcomes in cystic fibrosis (CF) patients in England.

Methods This was a cross-sectional study of patients with CF living in the SE and NE and registered on the UK CF Registry in 2010. Clinical data from Annual Review Encounter (ARE) of that year included demographics, prescription records and clinical outcomes: FEV1%predicted and chronic infections.

Descriptive statistics were adopted to summarise categorical and continuous outcomes. Wilcoxon test and t-test was used to compare continuous outcomes, while two-sample test for equality of proportions was used to compare prevalence of infections and drug use.

Results The study cohort included 1265 children and 1752 adults from SE and 1483 children and 1917 adults from NE. For children: lung function (FEV1%), adjusted for age and sex was

Abstract P90 Table 1 Patient characteristics

Patient characteristics	Outcome/ Category	South of England N = 3017	North of England N = 3400	P-values
Sample size				
	0 – <16 (Children)	1265 (41.9)	1483 (43.62)	0.1805
	≥16 (Adults)	1752 (58.1)	1917 (56.38)	
Age (Years)	Mean ± SD	19.71 ± 13.24	18.81 ± 12.52	
Gender, n(%)				
	Female	1423 (47,17)	1578 (46.41)	0.5623
	Male	1594 (52.83)	1822 (53.59)	
Percent predicted FEV1, n(%)				
	<40	333 (11.04)	341 (10.03)	
	40–69	728 (24.13)	846 (24.88)	
	≥70	1335 (44.25)	1443 (42.44)	
Age at diagnosis, n(%)				
	<3 months; n (%)	1280 (42.43)	1590 (46.76)	<0.001
	3–12 months; n (%)	629 (20.85)	645 (18.97)	
	12 months–3 years; n (%)	416 (13.79)	474 (13.94)	
	≥3 years; n (%)	453 (15.01)	488 (14.35)	
FEV1 percent predicted				
All patients	Mean ± SD	70.98 ± 24.66	71.23 ± 24.23	0.9821
Children (Age < 16)	Mean ± SD	84.51 ± 17.99	81.57 ± 19.80	0.0061
adults (Age ≥ 16)	Mean ± SD	64.69 ± 24.81	66.73 ± 24.61	0.0422

significantly higher in SE (84.51% vs 81.57%, p < 0.01). However, rates of *Pseudomonas aeuginosa*, Burkholderia cepacia and MRSA were similar. Significantly higher proportions of patients were diagnosed before turning 3 months in the NE compared to SE (46.76% vs 42.43%). In adults: in the NE the BMI was higher 22.35 vs 21.99 (p < 0.01) as was the FEV1%p, adjusted for age and sex (66.73% vs 64.69%, p = 0.04). Patients in SE were more frequently prescribed mucolytics (Dornase Alfa and Hypertonic Saline). In NE they more frequently used chronic macrolides. There were higher rates of PA, Bcc and MRSA in NE. The rates of MSSA and NTM were higher in the SE.

Conclusions There is a north-south divide in demographic characteristics and clinical outcomes in cystic fibrosis (CF) patients in England. In SE children have higher lung function. However, adults in the NE seem to have higher lung function compared to adults in SE. A single year cohort is not sufficient to deduce if these differences affect longer-term outcomes, like survival and requires further investigation.

P91 TRYPSIN-LIKE PROTEASE ACTIVITY PREDICTS DISEASE SEVERITY AND PATIENT MORTALITY IN ADULTS WITH CYSTIC FIBROSIS

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Introduction Serine trypsin-like (TL) proteases, which are excessively active in CF airways, promote activation of the epithelial sodium channel (ENaC) and airways dehydration; a key initiating factor for CF lung disease pathogenesis. Furthermore TL-proteases enhance mucin gene expression and mucus hypersecretion, yet whether there is any relationship between the activity of these enzymes and CF pulmonary disease is unknown.

Objectives The primary objective of the current investigation was to determine whether TL-protease activity, measured in adult CF sputum sol, correlates with lung disease and patient outcome (survival). A secondary objective was to compare the strength of any relationships observed with that of neutrophil elastase (NE), an established protease biomarker.

Methods In this cross sectional retrospective study we analysed CF sputum sol collected from 30 clinically stable adult CF patients. Protease activity was measured by monitoring the hydrolysis of peptide-based substrates. Biomarkers of inflammation (IL-8 and TNF-α) were measured by ELISA. Lung function was assessed by spirometry (FEV1). Mortality data was retrospectively obtained and time in months until death or transplantation used for subsequent survival analysis.

Results TL-protease activity inversely correlated with lung function (FEV1) (r = −0.4, p = 0.031) however, no relationship with IL-8 and TNFα was observed. In contrast, NE was found to correlate with IL-8: r = 0.7, p < 0.001 and TNFα: r = 0.7, p < 0.001 but showed no relationship with lung function, indicating that these serine proteases play very distinct roles within the disease process. Kaplan-Meier analysis demonstrated significantly reduced survival for those individuals with above median TL-protease activity. Levels of NE activity showed no relationship with patient survival. Using a multivariate Cox regression analysis (adjusted for age and BMI) a significantly increased mortality hazard (HR 1.028, 95% CI: 1.007–1.049; p = 0.009) was also identified. These findings are supported by analysis of a validation cohort consisting of samples collected from a separate cohort of 33 adult CF patients.

Conclusions TL-protease activity inversely correlates with lung function and patient survival. As such tryptic activity may warrant consideration when modelling CF survivorship and should be investigated further as a biomarker of CF lung disease and as a potential therapeutic target.

P92 SYSTEMIC ALKYL QUINOLONES AS NOVEL BIOMARKERS FOR PULMONARY EXACERBATIONS IN CYSTIC FIBROSIS: A VALIDATION STUDY

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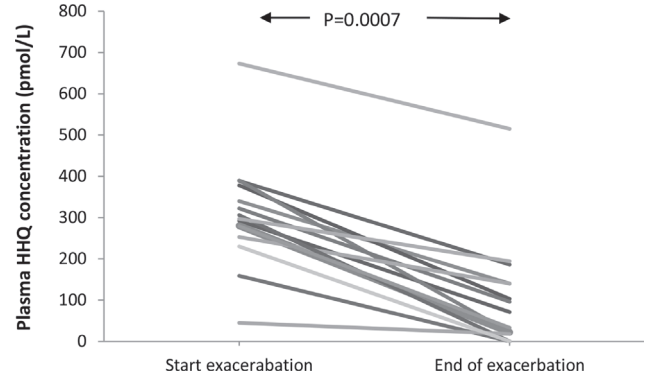
Introduction and objectives There is a clinical need to identify and validate biomarkers that are sensitive to treatment of infection in cystic fibrosis (CF). The aim of this study was to externally validate two novel biomarkers for pulmonary exacerbations in CF of the alkyl quinolone (AQ) class of quorum sensing molecules produced by *Pseudomonas aeruginosa*.

Methods Retrospective analysis of 70 plasma samples from thirteen adults with CF obtained during treatment of fifteen discrete exacerbations treated with intravenous antibiotics. Plasma samples were obtained at the start, day five, day ten, at the end of treatment, and at clinical stability. Samples were analysed using liquid chromatography-mass spectrometry. Data were analysed using Spearman's rank correlations and Wilcoxon matched pairs signed-rank tests using STATA 11 statistical software (Texas, USA). Graphs were produced in EXCEL 2011.

Results Plasma 2-heptyl-4-hydroxyquinoline (HHQ) concentration significantly decreased by a median of 221 pmol/L (IQR: 158 to 258 pmol/L) or 73% (IQR 52 to 94%; p = 0.0007) during treatment for a pulmonary exacerbation (Figure 1). In the same interval, there was no significant change in plasma NHQ (median decrease of −3 pmol/L; IQR: −35 to 10 pmol/L; p = 0.65). During treatment for a pulmonary exacerbation, percent predicted FEV1 increased by 4% (IQR: 1 to 7%; p = 0.0086). Folloing systemic antimicrobial therapy, systemic IL6 concentration decreased by a median of 2.06 pg/mL (IQR: 1.02 to 3.55 pg/mL; p = 0.0022) and systemic calprotectin



Abstract P92 Figure 1 Plasma HHQ concentrations at the start and end of 15 pulmonary exacerbations treated with systemic anti-pseudomonal antibiotics in 13 adults with CF
HHQ = 2-heptyl-4-hydroxyquinoline
pmol/L = picomoles per litre