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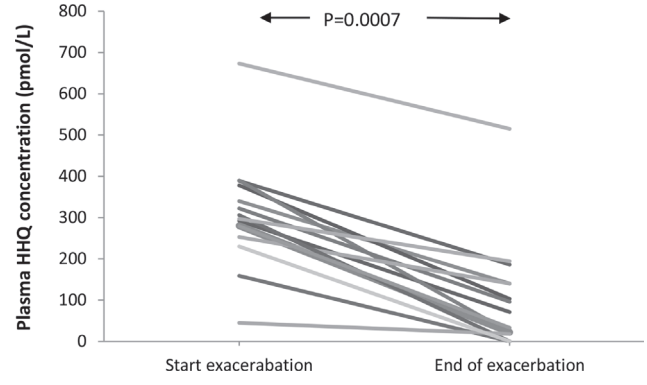
Introduction and objectives There is a clinical need to identify and validate biomarkers that are sensitive to treatment of infection in cystic fibrosis (CF). The aim of this study was to externally validate two novel biomarkers for pulmonary exacerbations in CF of the alkyl quinolone (AQ) class of quorum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

decreased by 1687 ng/mL (IQR: 291 to 3992 ng/mL; p = 0.0229).

There was no significant association between change in plasma HHQ and change in FEV1 during treatment of a pulmonary exacerbation (Spearman's correlation co-efficient, r = −0.42; p = 0.15).

Conclusions Plasma HHQ declined significantly during treatment of a pulmonary exacerbation and merits further investigation as a biomarker for measuring treatment response in CF. There was no significant decline in plasma NHQ during systemic antimicrobial therapy.

P93 IN- VITRO ACTIVITY OF SEVEN HOSPITAL BIOCIDES AGAINST MYCOBACTERIUM ABSCESSUS

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Introduction and objectives *Mycobacterium abscessus* pulmonary infection in patients with cystic fibrosis (CF) is associated with significant morbidity, and the prevalence is increasing. The cause of the apparent increase is unknown. Contributing factors may include the ageing CF population, and the potential for patient-to-patient transmission. To date, there is a paucity of data describing the activity of common hospital biocides against this organism.

Methods *M. abscessus* isolates (n =13) were recovered from CF and non CF respiratory specimens. Seven commonly employed hospital biocides (Steri-7™, Difficile-S™, Hydrex™, Cutan™, Stellisept™, Rely^{+}On™ PeraSafe™, Distaclor™) were assayed for their biocidal activity against *M. abscessus*. Fresh cultures of NTM were exposed to biocide in liquid medium as per manufacturers instruction and were immediately plated following the completion of the contact period. The mean concentration of NTM plated was 9.82×10^6 colony forming units (CFU) (range: $1.63 \times 10^5 - 1.12 \times 10^8$). Additionally, the remaining bacteria/biocide solution was enriched non-selectively in Mueller Hinton broth (37 ° C/1 week). Following this, growth of surviving bacteria was assessed with broth turbidity.

Results After appropriate exposure of NTM to biocide, all NTM isolates survived in Steri-7™, Hydrex™, Stellisept™ and Rely^{+}On™ PeraSafe™. One out of 13 NTM cultures was killed by Difficile-S ™ and 1 by Distaclor™, representing a 5 log kill. Two isolates were killed by Cutan™ again representing a 5 log kill. Following enrichment, Stellisept™ showed the greatest biocidal activity with 11/13 isolates, whereas 2/13 cultures were killed by Distaclor™. All other biocide/culture combinations yielded growth.

Conclusions These data indicate that *M. abscessus* may persist after exposure to several commonly employed hospital biocides. Given the importance of effective infection prevention and control, further work is urgently needed to define unequivocal biocide contact treatments to ensure successful eradication.

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P94 THE MANAGEMENT OF RESPIRATORY TRACT FUNGAL DISEASE IN CYSTIC FIBROSIS – A UK SURVEY OF CURRENT PRACTICE

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Aspergillus fumigatus is commonly found in the airways of patients with Cystic Fibrosis, (CF). Allergic Bronchopulmonary Aspergillosis, (ABPA), is the most recognised clinical condition associated with *Aspergillus*. The most widely used diagnostic criteria are from the Cystic Fibrosis Foundation Consensus Conference 2003. However, diagnosis remains challenging due to the overlap of classical symptoms and radiological features of ABPA and CF. There are a lack of clinical trials with clear outcomes to guide management of fungal disease, leading to variability between CF centres.

The aim of this survey was to assess the variability in current practice across the UK in diagnosis and management of fungal lung disease in CF patients.

A 21 question anonymous online survey was sent to 94 paediatric and adult CF consultants in the UK.

The response rate was 60.6% with 55 full and 2 partially completed surveys. Thirty-two respondents were adult physicians and twenty-five paediatricians. For a first diagnosis of ABPA 20 (35.1%) treat with Prednisolone alone, 19 (33.3%) use Prednisolone with Itraconazole capsules, 19 (33.3%) use Prednisolone with Itraconazole liquid and 2 (3.5%) choose Voriconazole.

Only 5 (8.8%) treat with Prednisolone alone for a 1st relapse, preferring Prednisolone with Itraconazole Liquid (33.3%) or with Itraconazole capsules (24.6%).

To reduce treatment, 21 (36.8%) decrease steroids to zero over time and maintain azole therapy, 18 (31.6%) stop the azole and steroid after a fixed time and 5 (8.8%) stop azole after a fixed time and maintain a small steroid dose. Variations in specific therapies were reported, including the use of pulsed Methylprednisolone, Posaconazole, nebulised Amphotericin and Omalizumab.

Thirty-eight (66.7%) respondents believe *Aspergillus* colonisation of the airway can cause clinical deterioration and 37 (66.1%) would treat this. *Scedosporium apiospermum* infection has been diagnosed and treated by 35 (61.4%) of respondents.

Results of this survey highlight significant differences in treatment regimes for ABPA, with increasing variation seen in the management of subsequent relapses. Respondent comments showed a wide range of opinions. This survey highlights the lack of evidence currently available to guide the management of CF fungal disease.

P95 EXPLORING THE TIMING OF HYPERTONIC SALINE (HTS) AND AIRWAYS CLEARANCE TECHNIQUES (ACT) IN CYSTIC FIBROSIS (CF): A CROSS OVER STUDY

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