Understanding CF lung disease and its consequences

P82 EFFECT OF A RATIONAL CROSS-INFECTION CONTROL POLICY ON THE SPREAD OF A TRANSMISSIBLE PSEUDOMONAS AERUGINOSA STRAIN

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Background Strategies to prevent chronic lung infection with *Pseudomonas aeruginosa* (Psa) in cystic fibrosis (CF) include early eradication and the prevention of cross-infection by patient segregation. However, cohorting patients into those with and without Psa infection does prevent superinfection by transmissible strains and is illogical since, by definition, unique strains pose no threat to non-Psa infected patients. We have a large cohort of patients infected with the Liverpool Epidemic Strain (LES), inherited from the paediatric sector, but no cohorts of other transmissible strains. In 2003 we introduced a rational cross-infection policy where those infected with transmissible strains are segregated from those with unique strains who are not separated from patients without chronic Psa infection. To ensure that cross-infection/superinfection does not occur, Psa genotypes are regularly analysed. We now report 6 years' experience of this cross-infection policy.

Methods Individual Psa genotypes are identified using PCR (polymerase chain reaction) from sputum samples obtained from all our patients with CF (every 3 months for LES negative and yearly for LES positive). We looked at the prevalence and cross-infection/superinfection rates between LES-infected patients and the remainder between 2003 and 2008.

Results There was a decline in the proportion of patients with LES infection (from 71% to 56%) and an increase in those with unique strains (from 23% to 27%) and without Psa infection (from 8% to 33%), all due to a decrease in the proportion of Psa-infected patients from the paediatric sector (table 1). Superinfection is rare, all due to contact outside the healthcare environment, and there have been no new cases of chronic Psa infection in those who were previously uninfected.

Conclusions This study demonstrates that our rational segregation policy has controlled the spread of the commonest highly transmissible strain in the UK (LES) in our clinic, without endangering patients who were not previously infected with Psa. It confirms that it is unnecessary to segregate patients infected with unique strains from those without Psa infection. In future, segregation policies should concentrate on preventing the spread of chronic infection with transmissible strains in the CF community.

P83 INCREASING RESISTANCE OF THE LIVERPOOL EPIDEMIC STRAIN OF PSEUDOMONAS AERUGINOSA TO ANTIBIOTICS IN CF: A CAUSE FOR CONCERN?

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Background Transmissible *Pseudomonas aeruginosa* (Psa) strains in the cystic fibrosis (CF) community increase the risk of chronic infection which, in turn, confers a poor prognosis and is difficult to treat, often requiring the use of multiple toxic intravenous antibiotics. The most important of these, the Liverpool Epidemic Strain (LES), is now widespread throughout UK CF clinics. Its antibiotic resistance pattern is therefore important. To look at this further, we compared such patterns of Psa strains in our CF clinic over 5 years, where we have a large cohort of patients infected with LES. Our clinic regularly checks Psa genotypes and we have no cohorts of patients harbouring other transmissible strains.

Methods The antibiograms of all sputum samples collected in 2004–8 from patients attending our large regional centre (currently 250 patients) were included. Isolates were tested against ciprofloxacin, ceftazidime, tobramycin, colomycin, tazocin and meropenem by disc diffusion method (total 9200 sensitivity patterns). We looked at overall resistance and the number of isolates which were resistant to all antibiotics, comparing LES with non-LES and also trends over time.

Results There was an increase in antibiotic resistance in both LES and non-LES over time (mean increase 25.6% (range 0–58.1%) and 8.5% (range 0–20.7%), p<0.001) respectively. Furthermore, there was an increase in the number of isolates that were resistant to all antibiotics tested (LES: mean change 18.9% to 34.0%; non-LES: 7.2% to 11.3%), p<0.001), with LES isolates becoming the most resistant (p<0.001). Overall, the antibiotics to which the most increase in resistance occurred were tobramycin (from 10% to 35%), meropenem (from 30% to 45%), ceftazidime (from 38% to 58%) and ciprofloxacin (from 5% to 34%). Furthermore, colistin resistance has occurred in LES isolates over the last 2 years.

Conclusion This study shows a worrying trend in antibiotic resistance in the Psa isolates in the CF population, particularly among transmissible strains. This highlights the need to prevent cross-infection through rigorous segregation and also the need to develop new strategies to treat these difficult organisms.

Abstract P82 Table 1

Psa status	2003 (n = 133)	2004 (n = 149)	2005 (n = 161)	2006 (n = 183)	2007 (n = 195)	2008 (n = 204)
LES	95 (71%)	105 (70%)	109 (68%)	116 (63%)	115 (58%)	115 (56%)
Non-LES	30 (23%)	31 (21%)	37 (23%)	45 (25%)	48 (25%)	56 (27%)
Other	8 (6%)	13 (9%)	15 (9%)	22 (12%)	32 (17%)	33 (17%)
Superinfection	–	2 (4.5%)	2 (3.8%)	1 (1.4%)	2 (2.8%)	0 (0%)
Conversion to Psa	0	0	0	0	0	0
LES new transfers	–	11	10	10	7	6
Non-LES new transfers	–	7	11	13	8	14
Other new transfers	–	5	3	7	12	9

LES, Liverpool Epidemic Strain; Psa, *Pseudomonas aeruginosa*.

P84 RETICULAR BASEMENT MEMBRANE THICKENING IN END-STAGE CYSTIC FIBROSIS LUNG DISEASE

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Introduction and Objectives Lung disease accounts for over 95% of morbidity and mortality in cystic fibrosis (CF). CF lung disease is characterised by airflow obstruction, neutrophilic inflammation and chronic endobronchial infection. Apparent thickening of the subepithelial reticular basement membrane (RBM) due to collagen matrix deposition is a characteristic feature of airway remodelling seen in people with asthma. Airway remodelling has also been implicated in the pathogenesis of CF lung disease and RBM thickening has been reported in endobronchial biopsies from children with CF.[1] Changes in airway dimensions have been described in explanted CF lungs but RBM thickness has not been investigated in end-stage disease to our knowledge. The objective of this study was to quantify RBM thickness in the airways of people with CF requiring lung transplantation.

Methods Blocks of intermediate to large airway were dissected from the explanted lungs of 16 people with CF, median age 28 years (14.7–57.7) and fixed in 10% formalin and embedded in paraffin before 5 μm sections were stained with haematoxylin and eosin. RBM thickness was evaluated objectively by measuring the distance between two demarcating lines in five high-power fields using image analysis software. Comparison was made with RBM thickness measured in an earlier study of 22 healthy adults[2] and previously published normal measurements.[3]

Results RBM thickness for each individual is displayed in fig 1. Median RBM thickness in CF airways was 9.58 μm (7.15–13.56). This compares with 7.7 μm (5.2–9.6) in healthy subjects in the earlier study ($p = 0.0008$).[2] Other published normal measurements for RBM in formalin-fixed tissue range from 2.9 to 6.7 μm.[3]

Conclusions RBM thickness is significantly increased in end-stage CF lung disease. This agrees with results in children and provides evidence of airway remodelling in advanced CF lung disease.

1. Hilliard, et al. Thorax 2007;62:1074–80.
2. Ward, et al. Thorax 2002;57:309–16.
3. Wilson, et al. Clin Exp Allergy 1997;27:363–71.
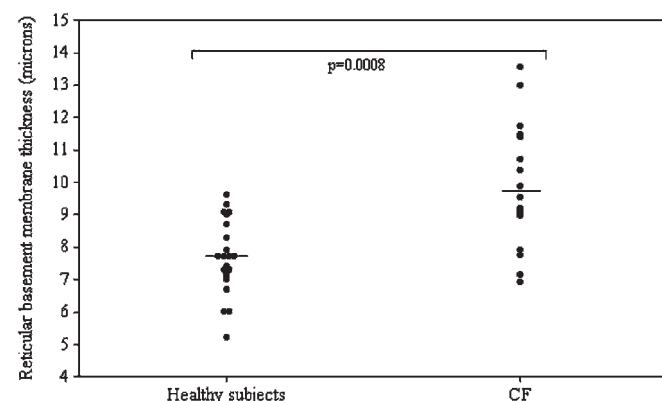
Abstract P84 Figure 1 Reticular basement membrane measurements.

P85 SUCCESS AND UTILITY OF SPUTUM INDUCTION IN NON-EXPECTORATING CF SUBJECTS: DATA FROM THE UK CF GENE THERAPY RUN-IN STUDY

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Microbiological surveillance is the mainstay of cystic fibrosis (CF) clinical monitoring. Prompt recognition allows tailored treatment and may prevent chronic infection. Many patients cannot expectorate sputum spontaneously. Alternatives include throat swabs, cough swab (CS) or cough plates, but there are concerns about sensitivity.

The UK CF Gene Therapy Run-in study involves patients from London and Edinburgh aged ≥10 years. Patients are seen at regular intervals during periods of clinical stability for measurement of biomarkers being assessed as end-points for our clinical programme. Any patient that is either non-productive or produces <1.1 ml sputum undergoes sputum induction with 3.5–7% NaCl and CS culture at the same visit, affording an unique opportunity to address the success and utility of sputum induction.

534 study visits have been completed, involving 191 patients. Expectoration status divides patients into three groups: (a) sufficient spontaneous sputum (52% of visits; group 1); (b) some produced but induction required (9% of visits; group 2); (c) no spontaneous sputum, induction required (39% of visits; group 3). In those unable to expectorate (group 3) but producing sputum after induction with a full dataset available (n = 41), cultures from induced sputum (IS) and CS were fully concordant in 41% (n = 17: 10 both negative; 7 both positive for the same organisms). In a further 15% (n = 6), both samples were positive but incompletely concordant: 4 had an additional organism (*S maltophilia* (Sm), *A fumigatus* (Af), *S aureus* (Sa), *H influenzae* (Hi)) in IS which was not detected on CS; 2 patients had only Af in sputum, but Pa (n = 1) and Sa, Hi and Sm (n = 1) on cough swab. Importantly, samples in 44% of cases (n = 18) were completely discordant and in all of these a significant pathogen was grown only from IS while CS culture was negative. Similarly, in group 2 (n = 16), 56% had a negative CS despite one or more significant pathogens in sputum; only one patient had a negative sputum culture with a positive CS (*P stutzeri*).

Culture of IS provides additional clinically-relevant information compared with CS in non/poorly-expectorating CF patients. We suggest that IS should be considered more routinely in the clinical setting and could save patients from more invasive investigation.

P86 EXPLORING THE PHENOTYPE OF THE LYMPHOCYTIC INFILTRATE IN THE CF AIRWAY: DO IL-17+ CELLS PLAY A ROLE IN DISEASE PATHOGENESIS?

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In contrast to the neutrophilic inflammation in the airway lumen, lymphocytes predominate in the airway wall of patients with cystic fibrosis (CF). The phenotype and function of these lymphocytes has not been explored. It is postulated that the Th17 pathway could play an important role in CF as interleukin (IL)-17, secreted by Th17 lymphocytes, is proinflammatory and regulates granulopoiesis as well as neutrophil recruitment. We hypothesised that the lymphocytic infiltrate in the CF airway wall could consist of Th17

cells. We aimed to characterise the lymphocytes in the submucosa of endobronchial biopsies of patients with CF, non-CF bronchiectasis (Bx) and healthy controls, staining for CD4 (T helper cells), CD8 (cytotoxic T cells) and IL-17.

Immunohistochemistry was performed on endobronchial biopsies obtained from four groups of children: newly diagnosed CF (N = 4, median age 2.7 years (range 1.5–4.3)), established CF (N = 24, 9.3 years (1.2–16.8)), non-CF Bx including PCD (N = 14, 9 years (5.7–14.8)) and controls without airway disease (N = 8, 8.8 years (0.2–16.4)). There was a significant difference in CD4 counts between groups (Kruskal-Wallis (KW), p = 0.03), with the highest counts observed in patients with non-CF Bx (median 232 cells/mm² (IQR 194–505)) and established CF (223 (135–389)). Controls and newly diagnosed CF counts were 154 (76–179) and 162 (109–319), respectively. CD8 counts were similar across the four groups. IL-17 cell counts were significantly different across disease groups (KW, p = 0.01); patients with established CF (205 (118–531)) and non-CF Bx (245 (177–448)) had levels significantly higher (p<0.05 for both) than controls (54 (24–106)). Counts in the newly diagnosed CF group (195 (128–268)) appeared increased compared with controls, but the small sample was underpowered; further samples are being analysed. Double staining of CD4 and IL-17 has demonstrated that the majority of the IL-17+ cells are CD4+, implying they are Th17 lymphocytes.

There are significant differences between disease groups in T helper (CD4+) cells but not cytotoxic (CD8+) T cells. Double staining for phenotype and cytokine confirmed there are Th17 lymphocytes in the submucosa of endobronchial biopsies from these children. Both established CF and non-CF Bx samples had higher numbers of IL-17+ cells, suggesting that this is not a CFTR-specific phenomenon.

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Introduction Co-ordinated clinical care has led to improved lung health and a reduction in prevalence of respiratory failure in childhood cystic fibrosis (CF). A recent randomised crossover study in adults with CF has suggested improved daytime functioning following nocturnal non-invasive ventilation (NIV).[1] The use of NIV in paediatric CF is not yet fully established.
Aims To quantify NIV use across UK, Australian and New Zealand (NZ) paediatric CF centres, to ascertain if practice differs between centres and to elucidate factors leading to NIV initiation in childhood CF.
Methods A semi-structured questionnaire was sent to the CF consultant and physiotherapist of the 41 paediatric specialist CF centres in UK, Australia and NZ.
Results 35 of 41 (85%) centres responded, representing 5499 children with CF. 21 patients (0.4%) of the UK, Australia and NZ childhood CF population were reportedly using NIV, with a median (range) age of initiation of 14 (6–17) years and a median (range) NIV usage of 6 (3–10) h per night. 16/35 (45%) centres undertook sleep studies varying from oximetry studies alone to full polysomnography, with centres performing 3–52 studies/year. The most common indications for NIV initiation were as a bridge to transplantation, as an adjunct to physiotherapy or during an acute exacerbation. Bi-level ventilation (BiPAP) was the most commonly used mode in the 25 centres (71%), with single-level ventilation used in 7 centres (20%). 11/35 centres (31%) have a protocol for initiating NIV, with set-up being variously undertaken by doctors, nurses, physiotherapists and sleep technicians. There were 17 reported NIV failures from 9 centres, with reasons varying from poor tolerance and non-adherence to adverse events. Three NIV-associated adverse events were reported.
Discussion NIV is rarely used in Australasian and UK CF children. There is heterogeneity both to assessment of respiratory failure and use of NIV. There is no agreed definition of hypoxia and hypercapnia, modes of NIV used differs, and few institutions have an NIV initiation protocol. Guidelines for NIV use in children with CF are needed.

1. **Young AC**, et al. Thorax 2008;**63**:72–7.

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Introduction and Objectives It is now widely accepted that specialist input is of significant benefit in the management of paediatric cystic fibrosis (CF). In the UK all children with CF have regular access to a specialist team, in accordance with CF Trust guidelines. This is delivered in either a centralised only non-shared care (NSC) format at a Specialist CF Centre (SCFC) or in a shared care (SC) arrangement with a local CF clinic. Published evidence comparing the benefits of centralised and shared care is limited and ambiguous. The objective of this study was to compare the clinical characteristics of children with CF who are managed solely at a SCFC with those whose care is shared. We hypothesised that children having shared care would have poorer lung function and growth.
Methods Retrospective cross-sectional study of all children attending the SCFC for annual assessment in 2007. Children were categorised according to the pattern of care received in the review year as either NSC or SC. Demographic data (age, sex, genotype), primary characteristics (height and weight, and pulmonary function for children >6 years) and secondary characteristics (treatment and CF-related complications) were examined.
Results No significant differences in demographic, lung function or growth data were found between the SC and NSC groups (table 1). Rates of allergic bronchopulmonary aspergillosis were significantly higher in the NSC group (p = 0.04). A significantly greater proportion of subjects in the SC group received at least one course of intravenous antibiotics in the review year (p = 0.025).
Conclusions In this study, children following a SC arrangement did not have significantly poorer lung function or growth compared with those in NSC. SC may therefore be an acceptable pattern of care for children with CF. Longitudinal studies examining lung function and growth decline in children following centralised and the various subcategories of shared care are required to determine the efficacy of shared care.

Abstract P88 Table 1

	NSC	SC	p Value
	N = 52	N = 163	
Height z-score (SD)	−0.43 (1.22)	−0.13 (1.09)	0.10
Weight z-score (SD)	−0.15 (1.12)	−0.12 (1.11)	0.83
	N = 36	N = 116	
FEV₁ % predicted (SD)	86.7 (13.7)	84.3 (15.9)	0.40
FVC % predicted (IQR)	94.0 (88.0–99.3)	91.0 (84.8–103.0)	0.43

FEV$_1$, expiratory volume in 1 s; FVC, forced vital capacity; NSC, non-shared care; SC, shared care; SD, standard deviation; IQR, interquartile range.

P89 | RECURRENT SEVERE HAEMOPTYSIS IN CYSTIC FIBROSIS

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Introduction and Objectives Severe haemoptysis is a serious complication of cystic fibrosis (CF), associated with a high morbidity and mortality. Bronchial artery embolisation (BAE) is recommended in the management of massive haemoptysis as it is relatively safe and effective. However, a significant number of patients have recurrent haemoptysis following BAE, requiring re-embolisation. Few studies have looked at outcome in patients with recurrent severe haemoptysis who have undergone multiple BAE. A retrospective case note review of patients with severe haemoptysis was undertaken to identify factors associated with recurrence and outcome following repeat BAE.

Method All CF patients with severe haemoptysis, occurring between May 2004 and April 2009, were identified from the database held of all patients at our adult centre. Severe haemoptysis was defined as >100 ml blood over 3–7 days, >240 ml blood in a day or life-threatening compromise secondary to bleeding. BAE were performed over this time period by the same radiologists.

Results There were 22 patients identified with severe haemoptysis (13 (59%) men, 9 (40%) women; median age 29.5 years, range 18–44) and 34 embolisations were performed. Twelve (55%) patients died during the study period (11 during an admission with severe haemoptysis, 3 due to massive haemoptysis). Four patients had no BAE, 9 patients had one BAE and 9 (41%) patients had two or more; one patient required five embolisations. Recurrent severe haemoptysis was significantly associated with use of non-invasive ventilation (NIV)/long-term oxygen therapy (LTOT) (p = 0.012) and with a worse forced expiratory volume in 1 s (FEV_1) (p = 0.016). The time to re-bleed following embolisation for 50% of patients was 128 days. Patients who had a second or subsequent severe haemoptysis following BAE prior to discharge home were significantly more likely to die during the admission (p = 0.005).

Discussion Severe haemoptysis is associated with a high mortality. Patients with advanced CF (low FEV_1 or on NIV/LTOT) are more likely to have a subsequent severe haemoptysis following BAE and to die. Patients who have recurrent severe bleeds as an inpatient following BAE are unlikely to survive, irrespective of the number of BAEs performed, suggesting that repeated re-embolisation in a patient with recurrent haemoptysis may be unhelpful.

P90 | RELATIONSHIP BETWEEN HBA1C AND LUNG DISEASE IN PATIENTS WITH CYSTIC FIBROSIS NOT KNOWN TO HAVE DIABETES

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Introduction Cystic fibrosis-related diabetes (CFRD) and impaired glucose tolerance (IGT) are associated with accelerated pulmonary decline. This study aims to explore the relationship between HbA_{1C}, a marker of glucose intolerance, and disease severity in CF.

Methods Unselected adult outpatients (≥16 years) were recruited from a single tertiary CF centre when clinically stable. Participants were assessed at baseline and clinical information was collected and
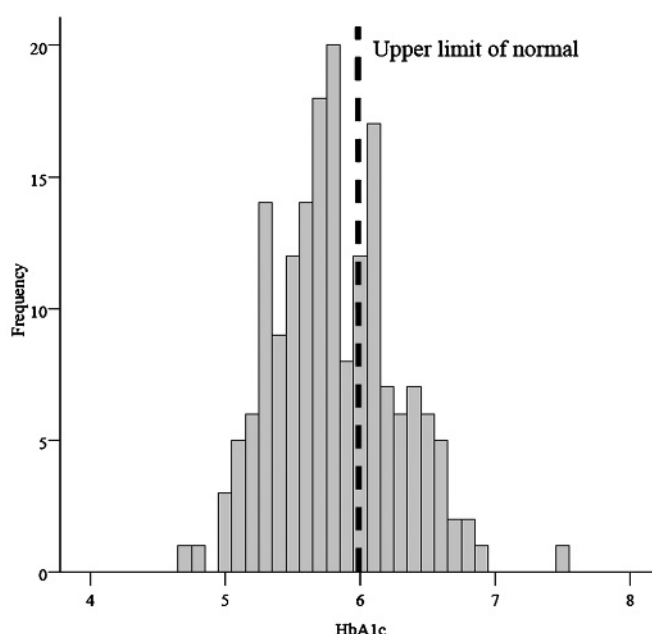
Abstract P90 Figure 1 Histogram of HbA_{1C} in patients with cystic fibrosis without cystic fibrosis-related diabetes or impaired glucose tolerance.

HbA_{1C} measured. Patients were designated as CFRD if established on treatment or by oral glucose tolerance test (OGTT); IGT by OGTT or fasting hyperglycaemia; or "not known to be diabetic" if not clinically suspected on selective screening policy[1] or normal OGTT. Participants were followed for 52 weeks to determine exacerbation frequency, defined as a change in symptoms or lung function. All participants gave written informed consent and the study had ethical approval.

Results Of 254 participants, 17% had CFRD (blood glucose (BG) 9.6±3.4 mM, HbA_{1C} 8.1±1.8%), 10% had IGT (BG 6.3±1.6 mM, HbA_{1C} 6.5±0.4%) and 73% had no known diabetes (BG 5.4±1.6 mM, HbA_{1C} 5.8±0.5%) (p = 0.000). Of the 177 CF patients without known CFRD/IGT, HbA_{1C} was significantly correlated with oxygen saturations (R = −0.317, p = 0.000); body mass index (R = −0.234, p = 0.002); white cell count (R = 0.200, p = 0.008); and exacerbation number by 52 weeks (R = 0.199, p = 0.026, fig 1). HbA_{1C} was higher in patients taking oral corticosteroids (prednisolone 6.1±0.6%, no prednisolone 5.8±0.4%, p = 0.007); with *Ps aeruginosa* or *B cepacia* on sputum culture (*Ps cepacia* 5.9±0.4%, no *Ps cepacia* 5.7±0.5%, 0 = 0.015) and with pancreatic insufficiency (PI) (PI 5.9±0.5%, no PI 5.7±0.4%, p = 0.032). On univariate analysis of variance, only oxygen saturations independently predicted HbA_{1C}. In 166 patients not taking oral prednisolone, HbA_{1C} was independently associated with forced expiratory volume in 1 s (FEV_1) (partial eta squared 0.072, p = 0.007) and chest radiographic abnormalities assessed by Northern score (partial eta squared 0.040, p = 0.049).

Conclusion One-third of CF patients without CFRD/IGT have elevated HbA_{1C}. HbA_{1C} is independently associated with FEV_1 and chest radiographic abnormalities. Oxygen saturations are negatively correlated with and independently predict HbA_{1C}. Hypoxia has been shown to impair glucose tolerance in volunteers[2] and patients with chronic obstructive pulmonary disease,[3] and underlying mechanisms need further investigation.

1. **Yung**. *Thorax* 1999;**54**:40–3.
2. **Oltmans**. *Am J Respir Crit Care Med* 2004;169:1231–7.
3. **Hjalmarsen**. *Diabetes Metab* 1996;**22**:37–42.

P91 CHRONIC RESPIRATORY DISEASES STRONGLY INFLUENCE MAJOR LIFE-CHANGING DECISIONS

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Introduction Major life-changing decisions (MLCD) are influenced by chronic skin conditions,[1] but the effect of other chronic conditions such as respiratory disease has been less explored. We studied the influence of cystic fibrosis (CF) and chronic obstructive pulmonary disease (COPD) on MLCD.

Methods Survey packs were posted or given at outpatient appointments to adult patients who had CF (n = 100) or COPD (n = 100) for more than 1 year. Patients were asked to write down any ways in which their long-term disease had influenced their MLCD. Qualitative software Nvivo 8 was used for detailed data analysis. Different life-changing decisions were grouped into core decisions.

Results Of the 200, 110 (55%) survey forms were returned (CF = 61, COPD = 49). Of these, 91 patients (58% male, mean age: CF = 27 years (range 18–53), COPD = 65 years (range 53–84)) reported the impact of their chronic condition on MLCD. 81 patients (CF = 50, COPD = 31) reported there was an influence on at least 1 MLCD (range 1–9), 10 patients (CF = 3, COPD = 7) reported no influence, 17 patients (CF = 8, COPD = 9) declined to take part and 2 patients had died (COPD). MLCD affected by CF and COPD were job (n = 39), having children (n = 36), career (n = 31), early retirement (n = 32), education (n = 24), relationships (n = 19), moving abroad (n = 15), change of profession (n = 10), separation (n = 9), moving to another house (n = 9), marriage (n = 6), buying a house (n = 4) and moving to another city (n = 4). Decisions related to holidays (n = 21) and life style change (n = 4) were also regarded by patients as life changing. The most prevalent influential factors of the condition for both CF and COPD are shown in table 1.

Conclusions This study demonstrates that respiratory conditions such as CF and COPD influence MLCD which impact on patients' lives significantly over time. Appropriate and timely advice and support may help patients to cope better with long-term illnesses. In parallel, greater understanding by clinicians might enhance health outcomes. Targeted help at an early stage may improve patients' future health and lives.

1. **Bhatti ZU**, Finlay AY, Salek S. Chronic skin diseases influence major life changing decisions: a new frontier in health outcome research. Br J Dermatol 2009;**161**(Suppl 1):58–9.

Abstract P91 Table 1 Factors influencing major life-changing decisions (MLCD)

Factors	% CF (n = 53)	% COPD (n = 38)
Ill health and severity of disease	64.1	71
Stress, fear and anxiety	33.9	31.5
Frequent hospital visits and treatment	32	18.4
Physical disability	11.3	42.1
Reliance on family members	5.6	21
Proximity to hospital, home and family	28.3	–
Future children's health and social life	26.4	–
Working conditions	18.8	–
Genetic counselling/advice	18.8	–
Risk to health	15	–
Insurance cost	15	–
Disease explanation and embarrassment	15	–
Employers understanding to illness	13.2	–
Infertility/IVF treatment	11.3	–

P92 MEAN 3-DAY GLUCOSE IS CLOSELY LINKED TO HBA1C IN ADULTS WITH CYSTIC FIBROSIS

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Introduction and Objectives Cystic fibrosis-related diabetes (CFRD) is common, causing increased morbidity and mortality. Optimal methods of assessing glycaemic control in CF are unclear due to insulin deficiency, variable insulin resistance and unique glucose kinetics. Glycosylated haemoglobin (HbA1c) is a marker of glycaemic control in non-CF for prevention of diabetic complications, but its relevance in CF is undetermined. It is proposed that greater red blood cell turnover, anaemia, iron deficiency and different glycation mechanisms may affect validity of HbA1c in CF. Continual glucose monitoring studies (CGMS) are being investigated as a more relevant measure of real life glycaemia than conventional markers—for example, the oral glucose tolerance test (OGTT), HbA1c and capillary blood glucose (CBG) monitoring. Our aim is to explore whether the mean CGMS 3-day glucose level is linked to HbA1c level in stable adults with CF.

Methods In an ongoing observational study, 30 clinically stable adults with CF underwent concurrent CGMS, OGTT and HbA1c recording. All participants recorded four daily CBG measurements for calibration of CGMS sensors.

Results 30 adults completed the protocol: mean (SD) age 31.5 (12.9) years, 15 (50%) men. Solutions (Medtronic, USA) and SPSS 15.0 software were used for analysis (table 1). Pearson's correlation coefficient (two-tailed, 5% significance level) showed mean CGMS glucose level correlated with HbA1c level (r = 0.814, p<0.001).

Conclusions In our CF study population, mean 3-day glucose by CGMS correlated strongly with HbA1c. Recent research in CFRD found no correlation between HbA1c and mean glucose by repeated CBG profiles. CGMS may capture glucose excursion more accurately than CBG profiles, resulting in a strong correlation with HbA1c. CGMS may therefore be useful in evaluating glycaemic control and preventing complications in CFRD. Work is ongoing to fully and robustly validate CGMS in our adult patients.

Abstract P92 Table 1 Mean (SD) continual glucose monitoring studies (CGMS) glucose value and HbA1c by oral glucose tolerance test (OGTT) result

	Glucose tolerance category by OGTT			
	All n = 30	Normal n = 12 (40.0%)	Impaired n = 7 (23.3%)	Diabetic n = 11 (36.7%)
HbA1c (%)	6.3 (1.0)	5.6 (0.4)	6.0 (0.7)	7.2 (1.1)
CGMS glucose (mmol/l)	6.9 (1.7)	6.0 (0.7)	6.4 (2.1)	8.0 (1.6)

P93 ASSOCIATION OF NOCTURNAL HYPOXIA AND CLINICAL STATUS IN CHILDHOOD CYSTIC FIBROSIS

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Hypoxia in cystic fibrosis (CF) occurs with sleep, exercise, chest exacerbations and air travel. Hypoxia may modulate growth, the pulmonary circulation, quality of life and also lung inflammation, which may in turn affect lung function and exercise capacity. The study aimed to delineate the association of nocturnal hypoxia and clinical status in childhood CF.

41 children (21 girls) with CF each underwent home oximetry. Hypoxia was defined as SaO_2 <93% for >10% sleep time. Spirometry, exercise testing with oxygen uptake ($\dot{V}O_2$) measures, bone densitometry of lumbar spine (BMAD), quality of life assessment using the CFQ-UK questionnaire, Chrispin-Norman (CNS) scoring of chest radiographs and measurement of inflammatory markers (full blood count, serum interleukin 8) were performed. Mann-Whitney tests were used for intergroup comparisons.

Hypoxia was detected in 9/41 subjects. Hypoxic subjects were older with median (IQR) age of 14.9 (12.4, 15.6) vs 12.2 (10, 13.7) in normoxic subjects (p<0.05) and had lower body mass index (−1.1 (−2, −0.6) vs −0.2 (−0.7, +0.3); p<0.01). Hypoxic subjects had lower forced expiratory volume in 1 s (−3.9 (−3.3, −4.7) vs −1.7 (−2.5, −0.4); p<0.001) and forced vital capacity (−2.6 (−3.8, −1.8) vs −0.6 (−1.8, +0.1); p<0.001) z-scores, increased residual volume/total lung capacity ratio (0.5 (0.45, 0.64) vs 0.32 (0.24, 0.45) p<0.001), higher CNS (16 (12, 19) vs 10 (7, 13); p = 0.002), lower peak $\dot{V}O_2$ (28.8 (24, 34.2) vs 35.3 (33.3, 43.2) ml/kg/min; p = 0.01) and reduced CFQ-UK scores (62 (45, 70) vs 74 (66, 88); p = 0.03). Hypoxic subjects had higher neutrophil counts (8.3 (4.8, 13) vs 3.2 (2.5, 4.6) $\times 10^9$/ml; p<0.001) and interleukin 8 levels (10.8 (4.4, 25.7) vs 5.1 (3.6, 9) pg/ml; p<0.05), more intravenous antibiotic courses in the preceding year (4 (2.5, 4) vs 0 (0, 1); p<0.001) and reduced BMAD z-scores (−1.4 (−1.8, −0.4) vs −0.3 (−1, +0.7); p = 0.03).

While hypoxia may be a casual mechanism for worsening clinical and inflammatory status, it may simply be a surrogate marker of disease severity. Future research should aim to delineate the role of hypoxia in CF, elucidating effector mechanisms by which hypoxia mediates CF lung disease and also the extent to which restoration of normoxia (by oxygen therapy or non-invasive ventilation) impacts on the CF lung.

COPD exacerbations

P94 USE AND UTILITY OF A 24-HOUR INFORMED TELEPHONE SUPPORT SERVICE FOR "HIGH-RISK" PATIENTS WITH COPD

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Introduction The "epidemic" of chronic obstructive pulmonary disease (COPD) requires innovative service developments to improve outcomes. It is particularly important to prevent hospitalisations. Successful chronic care models in COPD have been described. We present the first evaluation of an Early Presentation and Intervention in COPD (EPIC) service focused on "informed" 24/7 telephone support for high-risk NHS COPD patients. The service was funded by a Clinical Innovations competition at Royal Free Hampstead NHS Trust.

Method 74 "high-risk" patients were recruited over 6 months (defined as GOLD stage IV or those with previous hospitalisation) from inpatient and outpatient settings, representing 32% of patients admitted over that period. After a recruitment interview to record key patient and COPD information, patients were contacted every 2 months by a nurse and reviewed in clinic 6-monthly. Patients were invited to use the telephone service "when you need any advice about your chest and particularly if you think you are having a flare-up". We present the use and utility of the service over 1 year.

Results The 74 patients were high-risk (eg, mean (SD) age 70.3 (9.1) years, forced expiratory volume in 1 s 44.2 (16.5)%). 30% were on long-term oxygen therapy and 46% lived alone. 70% of patients completed 1 year, 23% died and 7% left. Follow-up was for a total of 22074 days. 76% of patients used the service or it was used on their behalf, generating 258 calls (mean duration 7.9 min) at a rate of 1 call/100 patients/day. 76% of calls were between 08.00 h and 17.00 h. The proportion of calls in response to possible exacerbation did not vary by day, but was higher overnight and at weekends. There were very few overnight calls, most of which required further assistance from emergency services. To avoid one hospital assessment overnight, the service would require 7359 patients. The 52 patients completing 1 year had a reduced number and duration of hospitalisations while on the service compared with the previous year (31 vs 56 admissions and 289 vs 461 days, both p = 0.002). The patients valued the service.

Conclusion A telephone advice line for high-risk COPD patients reduces hospitalisation and is valued by patients, but is unlikely to be cost-effective 24/7 at a local level given the low volume of overnight calls.

P95 EFFECT OF TELEPHONE WEATHER ALERT SYSTEM ON EMERGENCY COPD ADMISSIONS AND HEALTHCARE UTILISATION IN PATIENTS WITH MILD TO MODERATE AIRFLOW OBSTRUCTION

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Introduction Exacerbations are a major cause of morbidity and mortality in patients with chronic obstructive pulmonary disease (COPD). They have a great impact on patients' health, as well as having a large impact on healthcare utilisation (HCU) including emergency hospital admissions. They are more frequent in the winter months, and it has been hypothesised that they are positively linked with a sudden drop in temperature.

Aims To evaluate the effectiveness of a telephonic alert system (the Met Office project) to warn patients with COPD of severe weather changes on hospital admissions and HCU.

Methods All patients with mild to moderate airflow obstruction from three primary care practices were invited to participate. The project ran between 1 November 2008 and 28 March 2009. Weather alerts were delivered to patients via automated message by the Met Office. The primary outcome was number of emergency COPD admissions. Secondary outcomes were hospital bed-days, general practice consultations (surgery visits and telephone advice), home visits, visits to A&E, visits by COPD early supported discharge (ESD) team and out-of-hours service were measured during the project and compared (for the same patients) with the same data between 1 November 2007 and 28 March 2008 (12 months earlier).

Results A total of 435 patients were invited to participate and 157 (34%) patients took part in the project. Mean (SD) age 71 (9.7) years, forced expiratory volume in 1 s (FEV_1) 1.4 (0.5) l and 59.1 (16.5)% predicted. During the project five weather alerts were generated (first alert reached 150 patients; second reached 146; third reached 138 patients; fourth reached 137 patients; and the fifth reached 125 patients). Data on hospital admissions and HCU are