genotype and BMI, FEV1 was inversely associated with HbA1c, B=-5.0 (95% CI -6.0–3.0, p < 0.0001).

Conclusion In this large UK data set, an additional 6.6% of CF patients aged 16–23 years would be diagnosed with diabetes based on HbA1c values. Furthermore, the prevalence of undiagnosed pre-diabetes was high across all age groups and associated with lower %FEV1.

P195 PROSPECTIVE EXAMINATION OF THE EFFECTS OF IVACAFTOR ON GLYCAEMIC HEALTH

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Background The clinical benefits of the novel cystic fibrosis transmembrane conductance regulator (CFTR) have now been well established for patients carrying the G551D mutation through both phase 3 and real world clinical studies. Modulation of CFTR alters intestinal pH, which may assist in the function of pancreatic enzymes and which theoretically might have an impact on the absorption of nutrients in cystic fibrosis (CF). This may have significant impact on the glycaemic health of patients and early reports from a phase 2 study suggested a significant risk of hyperglycaemia in a patient with pre-existing diabetes.

Aim We aimed to prospectively assess the impact of ivacaftor on glycaemic health

Methods We conducted a prospective observational cohort study of subjects who commenced ivacaftor following NHS approval. Baseline measures were recorded including spirometric measures, weight and sweat chloride. Glycaemic control was assessed using HbA1c and repeated measures were recorded at 1, 3 and 6 months.

Results 24 subjects were included in the study. 17 subjects had normal glucose handling as defined by oral glucose tolerance test, 4 subjects had a pre-existing diagnosis of CF-related diabetes and 3 subjects had impaired glucose tolerance prior to ivacaftor commencement. Ivacaftor significantly increased FEV_1 and BMI at 1,3 and 6 months compared to baseline, and decreased sweat chloride at 2 months, all indicating effective CFTR modulation.

There was a significant reduction in HbA1c from baseline to 6 months in the total cohort, (median 42.5 mmol/L versus 39.5 mmol/L, p = 0.004), but not at other time points. In the diabetic or IGT subgroups, there were no clinically significant changes in HbA1c.

Conclusion Ivacaftor is an effective treatment for CF patients carrying the G551D mutation. In normoglycaemic patients, Ivacaftor significantly reduces HbA1c at 6 months. There was no adverse effect on glucose control noted in diabetic or impaired glucose tolerance subgroups. This may be attributable to improved insulin secretion by CFTR related mechanisms or improved insulin sensitivity. These results are important and reassuring when commencing patients with diabetes on CFTR modulators.

P196 THE EFFECT OF IVACAFTOR THERAPY ON THE MICROBIAL DIVERSITY OF CYSTIC FIBROSIS LUNG INFECTION

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Introduction and objectives Ivacaftor is a CFTR potentiator which is licensed for cystic fibrosis (CF) patients with the G551D mutation. Ivacaftor has led to significant benefits in lung function and weight, a reduction in pulmonary exacerbations and a decrease in time spent on intravenous antibiotics. This impact on exacerbations may be secondary to qualitative or quantitative change in the airway microbiome. The aim of this study was to investigate whether partially restoring CFTR function using Ivacaftor is associated with early changes in airway microbiology.

Methods Paired sputum samples were obtained from 13 adult CF patients immediately prior to Ivacaftor therapy, and after 1 and/or 3 months of treatment. FEV_1 was measured at each visit, and sweat chloride was assessed pre-treatment and at 2 months. Samples underwent routine microbiology and extraction of total nucleic acids using a standardised automated method. Ribosomal Intergenic Spacer Analysis (RISA) qualitatively investigated sputum bacterial diversity and 16s rRNA gene pyrosequencing was used to investigate bacterial diversity semi-quantitatively.

Results All subjects had samples at baseline and at either 1 or 3 months post Ivacaftor therapy. 4 subjects had samples at all three time points. Mean FEV1 percent predicted improved from 56 to 63% at 1 month (p < 0.01). Mean sweat chloride improved from 115 to 54 mmol/L (p < 0.01). Culture and pyrosequencing analysis showed 11 out of 13 patients had a single dominant infecting pathogen.

These techniques demonstrated no major changes in microbial diversity, especially with regards to the dominant pathogen, pre- and post-treatment (see Figure 1). 10 patients had a reduction in the number of pyrosequencing reads attributable to *Streptococcus* on follow-up samples (p < 0.05).

Conclusions Ivacaftor resulted in significant clinical improvements in this group of adult patients within the first 3 months of therapy. Airway microbiology in these patients was largely unaltered in the 3 months after starting Ivacaftor. The preliminary finding of a reduction in *Streptococcus* reads requires quantitative follow up to evaluate its significance. These findings suggest that potentiation of CFTR function using Ivacaftor does not significantly alter the lung microbiome and clinical improvements witnessed are likely secondary to a different mechanism.

P197 THE INCIDENCE OF NEW PSEUDOMONAS AERUGINOSA INFECTION IN CHILDREN WITH CYSTIC FIBROSIS

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Introduction Pseudomonas aeruginosa (PA) is one of the most important pathogens in cystic fibrosis (CF). Although there is a wealth of data about the prevalence of chronic PA infection, there is a paucity of evidence about the incidence of new PA infection.

Methods The SPACE (Sensitivity and specificity of PA detection using the hydrogen Cyanide concentration of Exhaled breath) study investigated if exhaled breath hydrogen cyanide is an early marker of PA infection in children with CF. Breath samples, clinical data and microbiology samples were collected at each outpatient appointment from a large cohort of children with CF who had not isolated PA for >12 months. This abstract reports the PA acquisition data.

Results 233 children were followed for a median of 2.0 (1.7–2.3) years. The median (IQR) age was 8.0 (5.0–12.2) years. 71 children isolated PA during the study period. The incidence rate (95% CI) of new PA infections was 0.15 (0.10–0.22) cases per patient year for those that had never previously isolated PA and 0.19 (0.13–0.27) cases per patient year for those that had been free from PA for >12 months. This rate varied between 0.08 (0.04–0.18) and 0.28 (0.14–0.49) cases per patient year at the 8 recruiting centres. 42% of children were asymptomatic at the time of PA acquisition. The median (IQR) number of antibiotic courses per patient year varied between the centres: 0.6 (0.2–1.3) to 3.6 (3.1–4.2) for oral and 0.0 (0–0) to 0.4 (0–1.2) for intravenous.

Conclusions This is the first prospective study to report the incidence of new PA infection in a large cohort of children with CF, considered to be free of PA airway infection. Incidence rate was higher in children who had isolated PA previously. The variation between centres is not easily explained and needs further investigation.

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P198 NEW APPROACHES TO THE CULTURE OF MYCOBACTERIUM ABSCESSUS COMPLEX FROM PATIENTS WITH CYSTIC FIBROSIS

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Introduction M.abscessus complex (Mab) are Rapid Growing Mycobacteria (RGM) that can cause severe infection. Prevalence is increasing and a recent study using whole genome sequencing showed cross infection between Cystic Fibrosis patients. Frequent surveillance for Mab infection may allow earlier diagnosis and prevent spread.

Automated broth (e.g. MGIT), is a sensitive rapid method for mycobacterial culture. Decontamination is needed to kill other bacteria and yeasts before culturing CF sputa in MGIT, but decontamination may reduce Mab numbers.

Other possibilities include chlorhexidine decontamination which yields more Mab but is incompatible with MGIT. Some mycobacteria grow directly from sputum on *Burkholderia cepacia* selective agar (Bcc) after extended incubation, without prior decontamination.

The aim of this study was to improve Mab culture from CF sputum.

Methods We compared MGIT culture of CF sputa with extended incubation of Bcc used in the routine laboratory. We compared growth of 30 known Mab on 3 formulations of Bcc and 2 Middlebrooke selective agars. We took 12 sputa from 9 CF patients with Mab infection and compared MGIT with culture on selective agars or chlorhexidine decontamination followed by culture onto non selective agar. Mycobacteria were identified by the National Mycobacterium Reference Laboratory and an in house PCR.

Results Eighteen of 515 CF sputa grew RGM (9 on Bcc agar and MGIT, 3 MGIT alone, 4 Bcc alone and 2 on Bcc with no MGIT culture). Contamination with other bacteria and fungi made it extremely difficult to see RGM on the routine Bcc.

Thirty sequenced M.abscessus abscessus, M.bolletii and M. massilliense all grew on the 3 commercial Bcc and 2 Middlebrooke agars.

One Bcc and one Middlebrooke agar successfully cultured RGM from all 12 sputa with fewest contaminants. Chlorhexidine decontamination and blood agar was effective but labour-intensive. Only 8 of 12 MGIT cultures grew RGM.

There was no difference in time to positive culture between agar and MGIT.

Conclusion Culture onto selective agar may be more sensitive than MGIT. It is quantitative and provides pure culture for identification, typing and susceptibility testing.

This may be a sensitive cost-effective way to screen sputa from patients at risk.

P199 MOLECULAR ANALYSIS DEMONSTRATES SHARED STRAINS OF MYCOBACTERIUM ABSCESSUS ISOLATES IN CYSTIC FIBROSIS PATIENTS ATTENDING A SINGLE CENTRE

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Introduction and objectives The *Mycobacterium abscessus* complex is an emerging group of pathogens in cystic fibrosis (CF), which may cause cross infection. The aim of this study was to determine whether CF patients infected with M.abscessus attending a single UK adult CF centre harboured unique or shared strains of M. abscessus.

Methods Isolates were from 12 patients attending a single adult CF centre, who yielded one or more positive sputum cultures for *M. abscessus* complex during the period January 2010 to August 2013. Isolates were identified to subspecies level using hsp65-rpoB concatenated sequence cluster analysis. Variable Number Tandem Repeat (VNTR) analysis was used to compare these isolates and determine whether two or more patients were infected with the same strain.

Results 11 isolates were identified as *M. abscessus susbp. abscessus*. VNTR analysis demonstrated 2 clusters of 6 and 2 patients carrying the same strains of *M. abscessus susbp. abscessus*, both

Abstract P199 Table 1 Mycobacterium abscessus cluster sequence analysis and Variable Number Tandem Repeat profiling results

Patient	*M.abscessus* subspecies	VNTR Profile
1	*abscessus*	2+, 5+, 3, 6, 2, 5, 1+, 2+, -
2	*abscessus*	2+, 5+, 3, 6, 2, 5, 1+, 2+, -
3	*abscessus*	2+, 5+, 3, 6, 2, 5, 1+, 2+, -
4	*abscessus*	2+, 5+, 3, 6, 2, 5, 1+, 2+, -
5	*abscessus*	2+, 5+, 3, 6, 2, 5, 1+, 2+, -
6	*abscessus*	2+, 5+, 3, 6, 2, 5, 1+, 2+, -
7	*abscessus*	3+, 4+, 3, -, 4, 3+, 2+, 2+, 2
8	*abscessus*	3+, 4+, 3, 2, 4, 3+, 2+, 2+, 2
9	*abscessus*	2+, -, 3, 4, 2, 5, 1+, 2+, -
10	*abscessus*	-, 5+, 2, 2+, 4, 5, 1+, 3, 2
11	*abscessus*	1+, 4+, 2, 2, 4, 3+, 2+, 2+, 2
12	*bolettii*	2+, -, 5, 5, 4, 3+, 1+, 2, 1+