contacts, migrants from high prevalence countries and those who are immunosuppressed. The risk of hepatotoxicity in treating LTBI is thought to be low but much of this evidence is in patients treated with 6 months of isoniazid (6H) rather than 3 months of rifampicin and isoniazid (3RH). Equally, other than age, there is limited data on other factors which may contribute to the risk of developing hepatotoxicity.

Methods A retrospective study was performed at our centre. We analysed all patients treated with chemoprophylaxis, regardless of indication, between 2009 and 2013. Demographic data, treatment regimens and adverse drug reactions, including hepatotoxicity, were recorded. Severe hepatotoxicity was defined as either a rise in ALT five times greater than the upper limit of normal, or as any change in liver function that required an interruption or alteration in treatment. Liver function tests (LFTs) were routinely measured at baseline and then again at two weeks.

Results 290 cases were identified. 84.5% of patients were treated with 3RH, 12.1% were treated with 6H. 2.1% experienced severe hepatotoxicity 2 weeks into treatment. None had symptoms which prompted blood tests prior to our standard 2 week LFTs. Gender, age, documented co-existing liver disease, regimen choice, concomitant use of hepatotoxic drugs and reason for giving chemoprophylaxis were not significantly associated with an increased risk of hepatotoxicity. LTBI treatment was case managed by TB nurses with 91.7% of patients successfully completing treatment. There was no significant difference in treatment completion and adherence rates in those who developed hepatotoxicity compared with those who did not.

Conclusions Our review demonstrates a low incidence of hepatotoxicity associated with treatment of LTBI and highlights the difficulty in predicting those in whom it will occur. If management of LTBI moves from primary to secondary care it will remain important to perform LFTs at two weeks.

Cystic fibrosis

LONGITUDINAL ASSOCIATIONS BETWEEN FEV1 AND HBA1C IN A UK COHORT OF YOUNG PEOPLE WITH CYSTIC FIBROSIS

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Objectives To interrogate the UK national data set and explore longitudinal relationships between FEV1, HbA1c and OGTT parameters in young people with CF up to the age of 23 years.

Methods The UK CF data set (2007 to 2012) recording annual measurements of height, weight, BMI,% predicted FEV1 and FVC, HbA1c and 2 h glucose (2 hrGlu) (>10 years only) was interrogated. HbA1c values >6.5% and 5.7–6.5% were used to define 'undiagnosed' diabetes and a pre-diabetic state respectively in patients not labelled as having CFRD. Data from cases with known CFRD were censored. Longitudinal models analysed %FEV1 and %FVC as dependent variables and HbA1c or 2 hrGlu, BMI SDS and age as covariates in patients with HbA1c in the pre-diabetic range.

Results 2105 patients (1097 males), 87.9% with DF508 mutations, median (range) age 13.7 (5.6–22) years, mean (SD) BMI Z score -0.11+/-1.1, %FEV1 82.1+/-20.3 at first visit were

Abstract P193 Table 1 Longitudinal relationships between lung function and glycaemia

Dependent Variable	Slope (per% higher HbA1c)	P value	95% CI
%FEV1	-2.9	0.016	-5.1 to -0.5
%FVC	-2.1	0.08	-4.4 to +0.3

included. Median range follow up was 3 (1–5) years. 2 hrGlu was available in a subgroup (n = 636). Median HbA1c (Table 1) but not 2 hrGlu (slope -0.1, p = 0.3), within the pre-diabetic range (5.7–6.5%) were inversely associated with %FEV1.

Conclusion In this large UK data set, longitudinal increases in HbA1c within the pre-diabetic range were associated with declining lung function. Our findings support the rationale for trials to intervene early to manage hyperglycaemia in young CF patients with pre-diabetes.

PREVALENCE OF UNDIAGNOSED PRE-DIABETES AND DIABETES IN A UK COHORT OF YOUNG PEOPLE WITH CYSTIC FIBROSIS

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Background In children with cystic fibrosis (CF), cystic fibrosis related diabetes (CFRD) typically develops from adolescence onwards and coincides with deteriorating lung function. Currently, diagnosis of CFRD is based on WHO oral glucose tolerance test criteria rather than HbA1c (used as part of the diagnostic criteria for diabetes mellitus).

Objective To interrogate a national data set and determine prevalence of pre-diabetes and diabetes in patients not diagnosed with CFRD as based on HbA1c.

Methods A national CF data set (2007 to 2012) recording annual measurements of height, weight, BMI,%predicted FEV1 and FVC and HbA1c was interrogated. Young people up to the age of 23 years were included. HbA1c values between 5.7–6.5% and >6.5% were used to diagnose pre-diabetes and diabetes respectively in patients not labelled as having CFRD. Prevalence of pre-diabetes, diabetes and%FEV1 were determined by age group using the first visit values for each individual.

Results 3759 patients (1627 males, 87.5% with DF508 mutations), median (range) age 14.5 years (4.5–23 years), BMI Z score -0.17 (-5.7 +/- 3.6) were included. Prevalences of known CFRD, pre-diabetes and undiagnosed diabetes are shown in Table 1. In cross sectional analyses adjusted for gender, age,

Abstract P194 Table 1 Prevalence of known CFRD, and undiagnosed pre-diabetes and diabetes by age group

N = 3759 all patients first encounter	5–10 years n = 801	10–16 years n = 1121	16–23 years n = 1837
FEV1 mean +/- SD	89.8+/- 17.0	80.9+/-18.9	70.5+/-24.1
BMI SDS mean +/- SD	+0.05+/-1.0	-0.11+/-1.1	-0.45+/-1.2
Undiagnosed CFRD n (%)	16 (2)	122 (10.9)	485 (26.4)
Undiagnosed pre-diabetes (HbA1c 5.7–6.5%) n (%)	300 (38.2)	445 (44.5)	617 (45.6)
Undiagnosed diabetes (HbA1c >6.5%) n (%)	14 (1.8)	58 (5.8)	89 (6.6)

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.