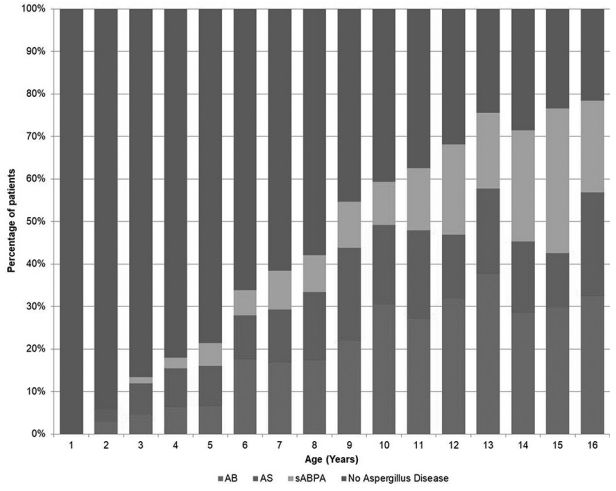
Methods Longitudinal annual review data were retrospectively collated for all children with CF from two centres within a large regional network. Using an algorithm agreed by the investigators prior to the study and based on Aspergillus fumigatus specific IgE and Aspergillus specific IgG (or aspergillus precipitins), children with CF were classified serologically as having no aspergillus disease, serological allergic bronchopulmonary aspergillosis (sABPA), aspergillus sensitisation (AS) or aspergillus bronchitis (AB). Additional parameters collected included respiratory culture of aspergillus within the last year, total IgE, BMI, lung function (FEV1) and whether an episode of clinical ABPA (cABPA) had occurred.

Results Analysis of 1267 years of longitudinal annual review data was undertaken for 137 children. Serological evidence of AB increased from 0% over childhood to 32% by 16 years (figure 1). Serological evidence of AS and sABPA was between 10%–30% and 5%–22% respectively for most years. In contrast, No aspergillus disease decreased over childhood and adolescence from 100% to 22% at 16 years. Nineteen (14%) children had at least one episode of cABPA. Serological evidence of AS or sABPA was present in ~70% at annual review the year before a first episode of cABPA.



Abstract S139 Figure 1 Prevalence of each serological class in patients with CF aged between 1–16 years old. *Key:* sABPA=Serological Allergic Bronchopulmonary Aspergillosis, AS=Aspergillus Sensitisation, AB=Aspergillus Bronchitis

Conclusions We have shown in a large cohort of children and adolescents with CF, that serological evidence of AB appears to increase over childhood and adolescence. We have also shown that most first episodes of cABPA are preceded by serological evidence of AS or sABPA at the last annual review. Future work should investigate further the temporal relationships between aspergillus serology and the development of cABPA and AB in childhood.

REFERENCE

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S140 INTERIM RESULTS FROM A PROSPECTIVE STUDY OF TABLET AND WEB- BASED AUDIOMETRY TO DETECT OTOTOXICITY IN ADULTS WITH CYSTIC FIBROSIS

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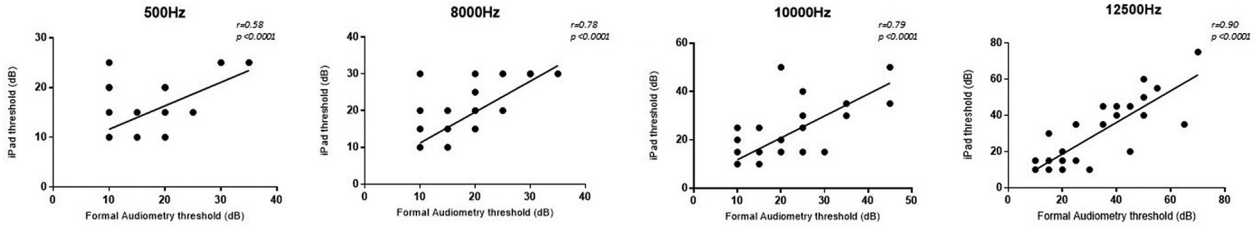
Introduction Individuals with Cystic Fibrosis (CF) often receive frequent, prolonged anti-infective therapy including aminoglycosides which result in ototoxicity. There are, however, no current national or international screening recommendations. Although high-frequency audiometry has increased sensitivity for early detection of drug-induced hearing loss, formal audiometry is costly and requires further outpatient visits. We analyse the validity of an interactive Apple-iPad app-based high-frequency audiometer (*Shoebox MD*) that can be used by non-audiologists to test hearing in an outpatient setting to screen for ototoxicity in an adult CF population.

Methods Adults with CF at the Royal Brompton and Harefield or Kings College Hospital NHS Foundation Trusts are being recruited over an 8 month period. Hearing was analysed with an iPad app in an outpatient setting by non-audiologists followed by formal audiometry. A threshold of $\geq$25 dB hearing loss at one or more audiometric frequencies was considered to be outside the normal hearing range. Correlation analysis was used to determine reliability of iPad compared to formal audiometry at individual frequencies. Sensitivity and specificities were analysed to determine efficacy of iPad audiometry as a screening tool. Demographics are currently being collected to determine risk factors for hearing loss development and genomic sequencing performed to analyse mitochondrial mutations associated with aminoglycoside related hearing loss.

Results Interim results of the first 28 participants show an overall prevalence of hearing loss in our cohort of 39%. Significant positive correlation between the iPad interactive and formal audiometry was seen at high frequencies (see figure 1) but relatively poor correlation at low frequencies where hearing loss is however uncommon in our cohort. iPad interactive audiometry showed a sensitivity of 91%, specificity of 82%



Absatrct S140 Figure 1

and negative predictive value of 93% to identify adults with hearing loss, highlighting its potential use for ototoxicity screening in this population.

Conclusion We present interim results highlighting for the first time, the use of novel app-based audiometry as a screening tool for aminoglycoside induced hearing loss in adult CF with potential application in other chronic lung disease cohorts. Full results will be presented at the conference.

Guilt by association: ILD genetics and co-morbidities

S141 A NOVEL DIMETHYLARGININE DIMETHYLAMINOHYDROLASE 1 (DDAH1) GENETIC VARIANT ASSOCIATED WITH LOWER ASYMMETRIC DIMETHYLARGININE (ADMA) LEVELS PREDICTS ACCELERATED LUNG FUNCTION DECLINE AND MORTALITY IN IDIOPATHIC PULMONARY FIBROSIS

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Background Increased nitric oxide (NO) and its generating enzyme, inducible nitric oxide synthase (iNOS), are observed in experimental models of idiopathic pulmonary fibrosis (IPF). Asymmetric dimethylarginine (ADMA) competitively inhibits iNOS and is hydrolysed by dimethylarginine dimethylaminohydrolase (DDAH) 1 and 2. Modulation of NO bioavailability via pharmacological/genetic knock-out of DDAH1 attenuates bleomycin-induced fibrosis *in vivo*. Using a candidate gene approach with an *a priori* hypothesis, we investigated the impact of *DDAH1* variants associated with lower ADMA (thus indicative of *DDAH1* over-activity) on lung function decline and survival in IPF.

Methods Consecutive patients with a new diagnosis IPF were recruited from a tertiary UK ILD centre (n=70). Only Caucasian individuals were included, patients on anti-fibrotic agents were excluded. Clinical end points were: time to first FVC decline (≥10% relative change in FVC from baseline) and survival (months survived following presentation). *DDAH1* tSNPs were identified in Caucasian individuals genotyped in the International HapMap Project. Those with minor allele frequency >40% in the IPF cohort and an association with lower ADMA levels in a normal cohort were selected – rs530006 and rs6576765. Survival curves and stepwise multivariate Cox proportional hazards analyses were performed.

Results Baseline pulmonary function did not vary between genotypes. FVC decline differed between rs530006 genotypes (p<0.0039*, median months: GG 34.5; GT 38.6; TT 13.7) [figure 1], with minor homozygote carriage (p<0.0009*, HR 4.68, 95% CI 1.88 to 11.65) and remained significant on multivariate analysis (p<0.001*). Survival differed between rs530006 genotypes (p<0.0418*, median months: GG 42.4; GT 57.2; TT 26.0), with minor homozygote carriage (p<0.0118*, HR *2.43, 95% CI 1.22 to 4.86) and trended towards significance* on multivariate analysis (p<0.054). FVC decline differed between rs6576765 genotypes (p<0.0249*, median months TT 20.7; TA 38.6; AA 33.4), with major homozygote carriage (p<0.0075*, HR 2.58, 95% CI 1.29 to 5.15) and on multivariate analysis (p<0.014*). Survival did not significantly differ between rs6576765 genotypes.

Conclusion Minor homozygote carriage of *DDAH1* variant rs530006 was associated with accelerated disease progression and mortality in IPF. These findings require validation in a larger, replicate cohort of IPF patients. Identification of aggressive disease phenotypes may allow risk stratification and earlier therapeutic intervention in IPF.

S142 NEUTROPHIL LYMPHOCYTE RATIO (NLR) AS A PREDICTIVE BIOMARKER IN IDIOPATHIC PULMONARY FIBROSIS (IPF)

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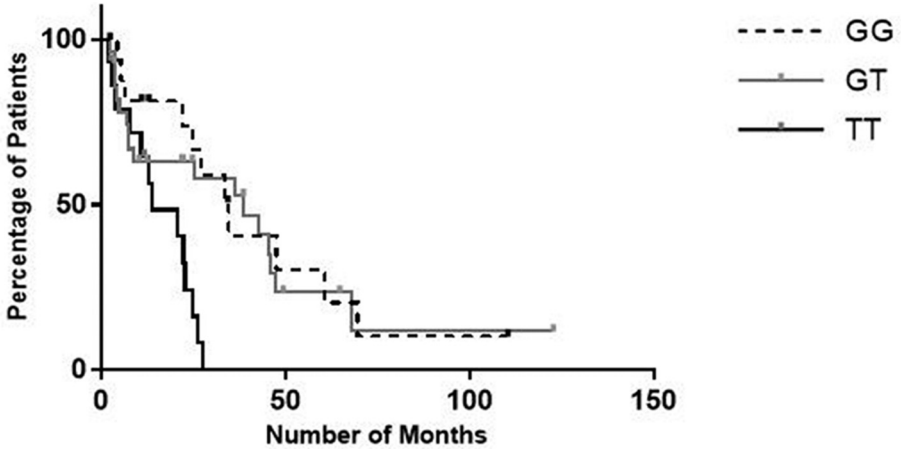
Introduction IPF is a heterogeneous disease, and, due to the absence of predictive biomarkers, prognostic estimates rely on clinical scoring systems such as GAP (Gender, Age,



Abstract S141 Figure 1 Time to first FVC decline (months taken for ≥10% relative change in FVC from baseline) by carriage of *DDAH1* variant rs530006 genotypes; p<0.0039* (Mantel-Cox log-rank test)

Correction: *S140 Interim results from a prospective study of tablet and web- based audiometry to detect ototoxicity in adults with cystic fibrosis*

Vijayasingam A, Shah A, Simmonds N, *et al*. S140 Interim results from a prospective study of tablet and web- based audiometry to detect ototoxicity in adults with cystic fibrosis. *Thorax* 2018;73:A87–8. doi: 10.1136/thorax-2018-212555.

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