Supplementary data:

Study design and participants: Sample size calculation to measure reliability of tablet and web-based audiometry using intraclass correlation with a 95% confidence interval indicated a minimum of 57 patients with hearing loss would be required. Using an estimated prevalence of hearing loss of 40% and an expected drop-out rate of 15%, study recruitment target was 170. Following interim analysis as the primary endpoint was met, recruitment was stopped at 156 participants with 126 participants completing audiology test follow-up. Blood samples for mitochrondrial SNP analysis was collected from 124 participants.

Study recruitment was not targeted to those with pre-existing risk factors. The only exclusion was current use of 'hearing aids' which may have reduced overall prevalence of hearing loss in our cohort. 11 study subject had audiometric testing (web, tablet and formal audiometry) performed during administration of intravenous antibiotics.

Demographic data collection:
Total days of intravenous antibiotic use over previous 10 year period was collected through a manual data query from the United Kingdom Cystic Fibrosis registry. This would include the administration of **any** intravenous antibiotic (regardless of number of doses) at hospital and/or at home given for an infective exacerbation of cystic fibrosis (e.g. aminoglycoside, cephalosporin etc) in a single day. Chronic macrolide prophylactic use was also collected through registry analysis but was an independent variable. Given the purpose of the study was to examine the use of easily accessible data for screening stratification purpose, retrospective hand-written prescription charts were not analysed or examined.

Specific antibiotic prescription data was available and collected through electronic health record data searches from the Royal Brompton hospital for the preceding 5 year period. Data was collected for intravenous aminoglycoside and amikacin. During this period only once daily aminoglycoside dosing was used with a combination of once or twice daily amikacin dosing. During this period data was also collected for retrospective inhaled tobramycin and amikacin dosing. No other inhaled antibiotic dosing was analysed.

Mitochondrial SNP analysis: The primers, which were used for both PCR and sequencing were as follows: RNR1-aF ACTTTTAACAGTCACCCCCCA, RNR1-aR TGAGGTTGATCGGGGTTTAT, RNR1-bF ACAATAGCTAAGACCCAAACTGG and RNR1-bR TATCTATTGCGCCAGGTTTC; and resulted in two fragments of 819 bp and 729 bp spanning from m.470 to m.1727. The variant allele frequency (% in each cohort) of the 42 mtDNA variants identified in the 124 CF patients, was calculated in the total study cohort and in the cohort classified with 'normal' or 'abnormal' hearing based on formal sound-booth audiometry. Variants with rs numbers had been previously reported in dbSNP (https://www.ncbi.nlm.nih.gov/snp/). Pathogenicity classification was derived from Clinvar, MitoMap and MitoTIP (in silico prediction of pathogenicity of novel tRNA variants).

Audiometry: For all pure-tone audiometry performed regardless of device, the tones were presented for 1–2 s, with varying intervals between tone presentations. The test level of each succeeding presentation was determined by the preceding response. After each failure to respond to a tone, the

level was increased in 5dB steps until a response occurred. After this response, tone intensity was decreased 10 dB, and another ascending series begun. Thresholds were defined as the lowest dB HL at which responses occurred in at least one-half of a series of ascending trials. The minimum number of responses needed to determine thresholds of hearing was two responses out of three presentations at a single level. A threshold of greater than 25dB hearing loss at one or more audiometric frequencies was considered to be outside the normal hearing range as per current National Guidelines for Classification of Hearing Loss.

Health economic modelling:
Given the clear increase in hearing loss seen above the age of 40, we performed a Monte Carlo simulation to compare the cost-efficiency between universal screening with formal sound-booth or tablet audiometry or limiting tablet screening to adults <40 years old given the increased probability of hearing loss above that age. With tablet screening, in the first scenario, all CF adults will be screened with tablet audiometry and those with abnormal tests will have a confirmatory formal sound-booth audiometry test afterwards. The second scenario assumes that all CF adults ≥40 years old will proceed straight to formal sound-booth audiometry testing with those <40 years old following the first scenario. The simulation was conducted in R 3.6.0. The package fitdistrplus was used to obtain the parameters for the distribution of age and total exacerbations. The age distribution was calculated from all adults with CF at the Royal Brompton and Harefield NHS Foundation Trust (539 adults). The distribution of the sensitivity and specificity of the iPad test were generated using beta distributions. The parameters for these distributions were calculated using the package epiR based on the estimated mean and confidence intervals from the analysis. We simulated the true status of 539 patients based on the multivariate model presented in the methods. The true prevalence was obtained from the simulated individual true status and the apparent prevalence (AP) was generated with the formula:

$$AP = Se*TP + (1-Sp)*(1-TP)$$

Finally, we included the cost of each test. We approximated a £2000 cost per year for the software license to conduct all iPad tests. The current NHS tarrif cost for formal sound-booth audiometric testing per adult is ~£150. 10,000 iterations of the algorithm were run.

Usability questionnaires: The UEQ was used to model people experience with each version of the test. UEQ is composed of 26 pairwise comparisons, where each item is presented as a 7-point Likert. The answers are scaled from -3 (fully agree with the negative term) to +3 (fully agree with the positive item) and measures 6 main factors: i) Attractiveness, intended as the overall impression of the product; ii) Perspicuity intended as an ability to get familiar with the product i.e., learnability); iii) Efficiency, intended as the ability of users to solve their tasks without unnecessary effort; iv) Dependability, intended as ability of users to feel in control of the interaction; v) Stimulation, intended as the ability of the product to excite and motivate end-users to use; vi) Novelty intended as the perceived level of innovation of the product. The UEQ manual offers a toolkit for the interpretation of the results and enables benchmarking of the outcomes of a new product against a validation sample developed on 246 product evaluations with the UEQ with a total of 9905 participants.

The UMUX was applied to assess the satisfaction of use i.e., perceived usability. This short scale is composed of four items on a Likert scale from 1 strongly disagree to 7 strongly agree. UMUX offers one single metric to capture perceived usability on a scale from 0 to 100 which were regressed to a standard with a regression formula. [28,29] The benchmarked results of the regressed scores of UMUX were used to model the perceived usability of each product using the following grading scales proposed by Sauro and Lewis.[30]

Finally, the NPS was applied to evaluate the likelihood to promote the use of each product. In tune with previous research [31-33], the intention to promote is a key element to evaluate innovation and new products or services. The NPS presents a result from -100 (all end-users are detractors) to +100 (all end-users are promoters). This one item tool 10 *(Extremely likely)* to 0 *(Not at all likely)* is usually adopted in usability studies to model the likelihood of adoption of a product after its release. Results of NPS can be benchmarked against scores obtained about other products from different domains.[34,35]

Supplementary Table 1

Average threshold 0.5-4kHz	Sex	Age	FEV1 % pred	eGFR ml/min	BMI	Recent microbiology	Mycobacterial disease (abscessus treated)	Chronic rhinosinusitis	Total IV antibiotic days in last 10 years	IV Tobramycin	IV amikacin	Inhaled Amikacin	Inhaled Tobramycin	Azithromycin
32.5	F	62	59	46	40.5	MRSA, pseudomonas aureginosa	N	N	38	3	0	0	0	N
26.9	M	57	35	90	22.0	Pseudomonas aureginosa	Y	N	222	0	15	168	596	Y
31.9	M	34	23	>90	18.9	Burkholderia multivorans	N	N	208	211	0	0	534	Y
27.5	M	30	33	>90	15.9	Pseudomonas aureginosa	N	Y	566	523	0	0	2222	Y
26.9	M	57	62	71	27.5	Staphylococcus aureus	N	N	56	0	0	0	224	Y
30.6	M	37	32	>90	20.8	Pseudomonas aureginosa	N	Y	164	0	0	0	0	Y
28.1	M	69	31	>90	23.5	Pseudomonas aeruginosa	N	N	182	172	0	0	168	N
28.1	M	21	68	>90	26.3	Pseudomonas aureginosa	N	Y	49	18	0	0	0	N
26.9	F	45	90	27	24.0	Nil	N	Y	0	0	0	0	0	Y
35.6	F	72	122	61	28.5	Pseudomonas aureginosa	N	Y	0	0	0	0	0	Y

FEV1 – Forced Expiratory volume in 1 second; eGFR – estimated glomerular filtration rate; IV – intravenous; BMI – Body mass index

Supplementary Table 2

Mitochondrial variants	Pathogenicity classification (ClinVar/MitoMap)	Frequency (%)			Univariate analysis P-value
		All	Normal Hearing	Abnormal Hearing	
m.477T>C rs41442247	not in ClinVar/ no classification in MitoMap	2.42	2.99	1.75	1.000
m.489T>C rs28625645	not in ClinVar/ no classification in MitoMap	8.87	14.93	1.75	*0.011*
m.497C>T rs28660704	not in ClinVar/ no classification in MitoMap	4.03	4.48	3.51	1.000
m.499G>A rs3901846	not in ClinVar/ reported (Endometriosis)	2.42	2.99	1.75	1.000
m.508A>G rs113683159	not in ClinVar/ no classification in MitoMap	0.81	0.00	1.75	0.460
m.512A>C (No rs no. but reported in MitoMap)	not in ClinVar/ no classification in MitoMap	0.81	0.00	1.75	0.460
m.514_524delAC rs78907894	not in ClinVar/ no classification in MitoMap	9.68	7.46	12.28	0.382
m.514_523dupCA (No rs no. but reported in MitoMap)	not in ClinVar/ no classification in MitoMap	0.81	0.00	1.75	0.460
m.514_523dupCACA (No rs no. and not reported in MitoMap)	not in ClinVar/ no classification in MitoMap	1.61	1.49	1.75	1.000
m.517A>T (No rs no. but reported in MitoMap)	not in ClinVar/ no classification in MitoMap	0.81	1.49	0.00	1.000
m.520C>T (No rs no. but reported in MitoMap)	not in ClinVar/ no classification in MitoMap	0.81	0.00	1.75	0.460
m.568_573dupC/CC/CCC/... rs1556422469	not in ClinVar/ dupCCC: reported (Absence of Endometriosis)	4.03	1.49	7.02	0.179
m.629T>C rs201031012	not in ClinVar/ MitoTIP: likely-benign	0.81	1.49	0.00	1.000
m.669T>C rs879005843	not in ClinVar/ reported (Deafness)	1.61	0.00	3.51	0.209
m.709G>A rs2853517	not in ClinVar/ no classification in MitoMap	8.87	10.45	7.02	0.546
m.710T>C rs28358568	not in ClinVar/ no classification in MitoMap	0.81	0.00	1.75	0.460
m.721T>C rs1556422479	not in ClinVar/ reported (possibly LVNC-associated)	0.81	1.49	0.00	1.000
m.723A>C rs386828878	not in ClinVar/ no classification in MitoMap	0.81	1.49	0.00	1.000
m.723A>G rs386828878	not in ClinVar/ no classification in MitoMap	0.81	0.00	1.75	0.460
m.750A>G rs2853518	not provided/ no classification in MitoMap	98.39	98.51	98.25	1.000
m.769G>A rs2853519	not in ClinVar/ no classification in MitoMap	0.81	0.00	1.75	0.460
m.794T>A	not in ClinVar/ no classification in MitoMap	0.81	1.49	0.00	1.000

rs1569483796					
m.825T>A rs2853520	not in ClinVar/ no classification in MitoMap	0.81	0.00	1.75	0.460
m.827A>G rs28358569	Pathogenic/ conflicting reports (deafness)	0.81	1.49	0.00	1.000
m.851A>G rs28502491 【not in ClinVar】	not in ClinVar/ no classification in MitoMap	0.81	0.00	1.75	0.460
m.930G>A rs41352944	not in ClinVar/ no classification in MitoMap	0.81	1.49	0.00	1.000
m.951G>A rs200887992	likely-benign/ no classification in MitoMap	0.81	1.49	0.00	1.000
m.956_960dupC/CC/CCC/… rs111033185 (likely benign)	likely-benign/ dupC: reported (possibly DEAF-associated)	1.61	2.99	0.00	0.499
m.961T>C rs3888511 (benign)	benign/ unclear (deafness, possibly LVNC-associated)	1.61	2.99	0.00	0.499
m.961T>G rs3888511	likely benign/ unclear (possibly deaf-associated)	0.81	0.00	1.75	0.460
m.1018G>A rs2856982	benign/ no classification in MitoMap	0.81	0.00	1.75	0.460
m.1187T>C rs111033320 (UVS)	uncertain significance/ no classification in MitoMap	0.81	1.49	0.00	1.000
m.1189T>C rs28358571	benign/ no classification in MitoMap	4.03	4.48	3.51	1.000
m.1193T>C rs111033321	likely benign/ no classification in MitoMap	0.81	1.49	0.00	1.000
m.1243T>C rs28358572	benign/ no classification in MitoMap	3.23	4.48	1.75	0.624
m.1290C>T rs1556422517	likely benign/ no classification in MitoMap	0.81	1.49	0.00	1.000
m.1406T>C rs111033322	benign/ no classification in MitoMap	0.81	1.49	0.00	1.000
m.1438A>G rs2001030	benign/ no classification in MitoMap	95.97	97.01	94.74	0.660
m.1462G>A rs111033326	benign/ no classification in MitoMap	0.81	1.49	0.00	1.000
m.1692A>T (No rs no. but reported in MitoMap)	not in ClinVar/ no classification in MitoMap	0.81	1.49	0.00	1.000
m.1719G>A rs3928305	not in ClinVar/ no classification in MitoMap	8.06	2.99	14.04	*0.043*
m.1721C>T rs200626438	not in ClinVar/ no classification in MitoMap	3.23	1.49	5.26	0.333

Supplementary Table 3 - Usability analysis of sound-booth, tablet and web based audiometry

Scales	**Formal Audiometry**	**Tablet audiometry**	**Web-based audiometry**
UMUX and grade	77.5 (B+)	78 (B+)	72(C+)
NPS	+62	+68	+11
UEQ	**Figure 4A**	**Figure 4B**	**Figure 4C**
Attractiveness	Above Average (1.36)	Above Average (1.39)	Below average (0.92)
Perspicuity	Excellent (2.49)	Excellent (2.32)	Excellent (1.92)
Efficiency	Excellent (1.85)	Good (1.69)	Above Average (1.23)
Dependability	Above Average (1.38)	Below average (0.93)	Below average (0.82)
Stimulation	Below Average (0.93)	Above Average (1.00)	Below average (0.68)
Novelty	Bad (0.02)	Above Average (0.80)	Below average (0.57)

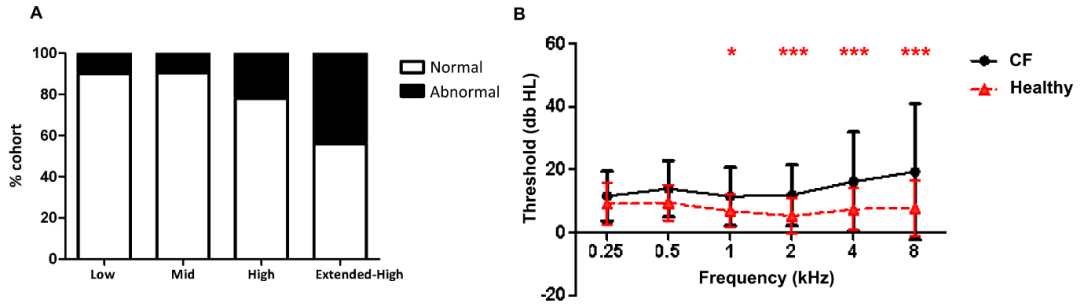
Supplementary Figure Legends:

Supplementary Figure 1: A) A breakdown of hearing loss detected through sound-booth audiometry is shown by Frequency range: Low (0.25 and 0.5kHz); Mid (1 and 2kHz); High (4 and 8kHz) and Extended-High Frequency (10 and 12,5kHz). **B)** Hearing (average threshold per frequency (0.25-8kHz) in sound-booth audiometry) in our 20-29 study population (n=38) is compared to a large published cohort study of healthy 20-29 year olds (n=92). Significant increase in average thresholds is seen in our CF cohort. (* - $p<0.05$; *** - $p<0.001$)

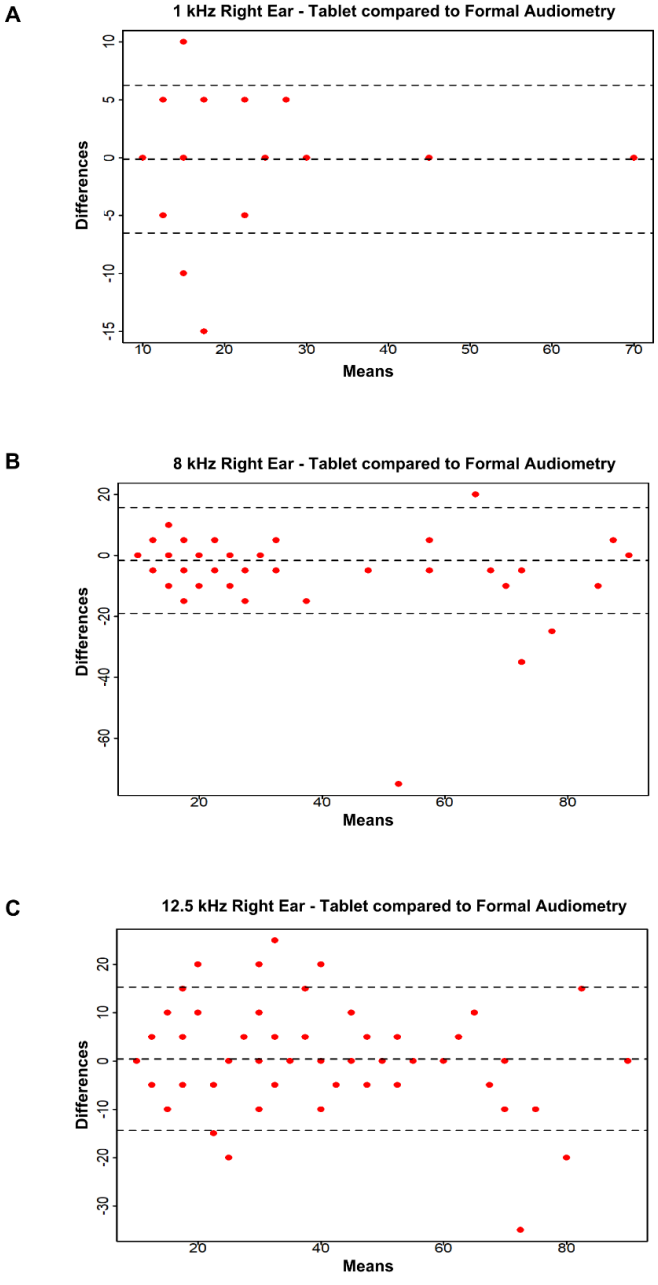
Supplementary Figure 2: Representative Bland Altmann plots seen at **A)** low (1kHz), **B)** high (8kHz) and **C)** extended high frequency (12.5kHz) comparing tablet audiometry to formal sound booth audiometry.

Supplementary Figure 3: Audiogram showing significant aminoglycoside related ototoxicity detected by tablet-based audiometry in individual with CF. Red line shows audiogram post intravenous aminoglycosides.

Supplementary Figure 1



Supplementary Figure 2



Supplementary Figure 3