SUPPLEMENTARY DATA

Title: Diagnostic agreement among experts assessing adults presenting with possible Cystic Fibrosis: need for improvement and implications for patient care.

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Contributions: ANF conceptualized the study, designed the questionnaire, performed data analysis, and wrote the manuscript. AT contributed to case identification and selection, data collection and edited the manuscript. JG and PGW participated in study design, questionnaire proofing and manuscript editing. GS performed internal review and editing of the manuscript. AF, NGM and DGD participated in distribution, internal review, and editing of the manuscript. BSQ contributed to study and questionnaire design, manuscript editing and is the senior author.

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Supplement contents:

Response rates.

Surveys were distributed via third party collaborators (CF Canada in Canada, the CF Foundation in the USA, the ECFS – Clinical Trials Network for UK sites, and the Irish Thoracic Society in Ireland). Of these, only the US CF Foundation adopted a tracking system which allowed estimation of the number of addresses, link clicks and completion rates. Our summary metrics from the USA suggest that the survey link was issued to 399 addressees, with 29 full completions of the survey. In Canada we estimate 40-45 actively practicing adult-CF specialist clinicians, of 15 of whom provided full responses (~30-35%). In the UK, the CF trust lists 69 active adult-CF specialists across England, Wales, Scotland and Northern Ireland with 9 responses. This means estimate a response rate of approximately 13% of the UK clinicians was achieved. Finally, at the time of survey distribution, there were 9 adult-CF specialists practicing in the Republic of Ireland, with 2 providing responses (~20%). In total if we estimate a possible population of 520 respondents based on survey distribution, we estimate a response rate (67 survey accessions) representative of 12.9% of the eligible population, and a completion rate of 10.6%.

Supplementary tables

Supplemental table 1. Predictors of Recommending further testing vs making a diagnosis

	Reduced model			Expanded model		
Predictors	***Odds Ratios***	***95%CI***	***p***	***Odds Ratios***	***95%CI***	***p***
(Intercept)	0.19	0.07 – 0.55	**0.002**	0.17	0.06 – 0.50	**0.001**
Location of practice						
Canada	*Reference*			*Reference*		
UK & Ireland	3.16	1.37 – 7.32	**0.007**	2.75	1.16 – 6.53	**0.022**
USA	0.65	0.31 – 1.34	0.244	0.55	0.26 – 1.17	0.122
Experience						
<5y CF-practice	*Reference*			*Reference*		
5-10y CF-practice	3.74	1.32 – 10.58	**0.013**	3.3	1.14 – 9.54	**0.028**
>10y CF-practice	2.87	1.17 – 7.06	**0.022**	2.57	1.01 – 6.55	**0.048**
Cases						
Case 1	*Reference*			*Reference*		
Case 2	0.75	0.32 – 1.76	0.506	0.75	0.32 – 1.77	0.51
Case 3	0.54	0.22 – 1.32	0.177	0.54	0.22 – 1.33	0.18
Case 4	0	0.00 – Inf	0.991	0	0.00 – Inf	0.971
Case 5	0.83	0.36 – 1.92	0.659	0.83	0.35 – 1.94	0.663
Case 6	0.75	0.32 – 1.76	0.506	0.75	0.32 – 1.77	0.51
Case 7	0.28	0.10 – 0.75	**0.011**	0.28	0.10 – 0.75	**0.012**
<5 adults assessed annually				*Reference*		
5-10y adults assessed annually				1.83	0.84 – 3.96	0.126
>10 adults assessed annually				1.53	0.70 – 3.33	0.285
Random Effects						
σ^2	3.29			3.29		
τ_{00}	0.24 $_{\text{ResponseId}}$			0.20 $_{\text{ResponseId}}$		
ICC	0.07			0.06		
N	55 $_{\text{ResponseId}}$			55 $_{\text{ResponseId}}$		
Observations	385			385		
Marginal R^2 / Conditional R^2	0.919 / 0.924			0.923 / 0.927		

Model comparison metrics

	npar	***AIC***	***BIC***	***logLik***	***deviance***	***Chisq***	***Df***	***Pr(>Chisq)***
Reduced model	12	374.19	421.63	-175.1	350.19	39.7195	4	4.95E-08
Expanded model	14	375.78	431.13	-173.89	347.78	2.4102	2	0.2997
Model excluding Cases as fixed effects (coefficients not shown above)	8	405.91	437.54	-194.96	389.91			

Generalized mixed effects logistic regression model.
Reduced model = excludes annual referral numbers as a predictor
Expanded model = includes annual referral numbers as a predictor

CFTR – Survey document

Start of Block: Introduction

Q1.1 Thank you for taking the time to participate in this 15-minute survey. This survey is intended for clinicians practicing in **adult** CF services.

You will be presented with 7 real-world clinical vignettes and a series of follow up questions.
After, you will be asked to rate the significance of various clinical findings in the diagnostic workup of CF.
Finally, you will be asked to rate your agreement with a series of statements.

All answers will be automatically de-identified (no metadata or linked email information will be collected) prior to review by the survey team.
Study results may be submitted for publication in journals or conference abstracts.

- ○ I understand that by proceeding with this survey I consent to having my anonymized answers collected and analyzed by the study team, for possible inclusion in academic publications. (1)

End of Block: Introduction

Start of Block: Country

Q2.1 In which country do you currently practice as an adult CF specialist?

▼ Afghanistan (1) ... Zimbabwe (1357)

Q2.2 How long have you been practicing in CF clinical care?

- ○ < 5 years (1)
- ○ 5 to 10 years (2)
- ○ > 10 years (3)

Q37 On average, how many adults (CF specific diagnostic work-up starting at or after 18 years of age) do you personally assess for a possible diagnosis of Cystic Fibrosis each year?

- ○ <5 (1)
- ○ 5 to 10 (2)
- ○ >10 (3)

End of Block: Country

Start of Block: Case 1

Q3.1
CASE 1

A 65-year-old Caucasian female is referred for assessment following two successive sweat chloride levels of 80 and 72 mmol/L.

The **indication for CF testing** was a 30 year history of rhino-sinusitis and post-nasal drip (deviated septum, septoplasty in 2020, no nasal polyposis, morphologically normal sinus anatomy on CT) in conjunction with a family history of CF with 3/4 first-degree cousins reportedly passing away in childhood (approx 50 years ago). Extended CF genetics (Whole Gene Sequencing) in this patient reveal no CFTR variants.

Respiratory: No childhood issues. Reports recurrent physician-diagnosed pneumonia treated in the community in her 30s and 40s. Developed daily cough productive of clear low volume (<1 teaspoon) phlegm in her late 30s. No antibiotics were required for chest infections in the past 15 years. CT chest reveals minimal bronchiectasis isolated to the antero-medial segment of the left lower lobe. Spirometry reveals an FEV1 of 95% predicted. Sputum culture reveals methicillin sensitive *Staphylococcus aureus* (MSSA).

GI: No GI symptoms or relevant history. Morphologically normal liver and pancreas on Ultrasound. Fecal elastase normal at 320 µg/gram (assay defines "insufficiency" as <200 µg/gram). No liver disease. No history of bowel obstruction.

Other: HbA1c 5.6% (no OGTT performed), 25-OH Vit D low, Vit A/E - normal. DXA suggestive of low bone mass. No fertility issues.

Neonatal/infantile history: suggests no relevant issues.

Q3.2 Based on the available information I believe the most appropriate diagnosis is:

- ○ CF (1)
- ○ CFTR-related disorder (6)
- ○ CF diagnosis not resolved - needs further testing (3)
- ○ CF carrier (7)
- ○ None of the above (8)

Q3.3 In your opinion this individual should receive:

- ○ Follow up outside of a multi-disciplinary CF Clinic (1)
- ○ Modified multi-disciplinary CF Clinic follow up (reduced frequency/monitoring/shared-care family doctor or respirologist where possible) (2)
- ○ Full standard of care multi-disciplinary CF Clinic follow-up (quarterly review, sputum, spirometry) (3)

Q38 How easy did you find classifying this case?

	Very difficult (1)	Fairly difficult (2)	Average (3)	Fairly easy (4)	Very easy (5)
Click to write Choice 1 (1)	○	○	○	○	○

End of Block: Case 1

Start of Block: Case 2

Q4.1
CASE 2

A 58-year-old Caucasian female is referred for assessment following two successive sweat chloride measurements of 67 & 61 mmol/L.

The **indication for CF testing** was a history of ongoing GI bloating, a remote history of nasal polyposis and her child being known to have CF (phe508del homozygous). Genetic analysis (139 variants) revealed a single phe508del mutation in this patient.

Respiratory: No antibiotic requirements and no relevant lower respiratory issues until age 55, when exposure to a bleach spill at work resulted in symptoms consistent with reactive airways dysfunction syndrome. FEV1 at baseline assessment was 106% predicted on low dose ICS/LABA inhaler. Sputum culture revealed MSSA and *Mycobacterium avium* complex (MAC). CT chest demonstrated no abnormality and specifically no bronchiectasis.

ENT: Previous nasal polyposis, current IgE 112ug/L (assay ULN 515). No peripheral eosinophilia. No active symptoms or issues.

GI: > 10 years of mild-moderate abdominal bloating and cramping. GERD controlled by PPI, in the setting of a known hiatus hernia. No constipation. Fecal elastase measured 363 µg/gram (assay defines "insufficiency" as <200 µg/gram). A single pancreatic cyst was identified on CT, otherwise morphologically normal pancreatic appearance. No liver disease. No history of bowel obstruction.

Other: No history of diabetes. HbA1c 5.4% (no OGTT performed), 25-OH Vit D normal, Vit A/E normal. No fertility issues.

Neonatal/infantile history: No failure to thrive, no childhood asthma or respiratory issues. Nasal polyposis.

Q4.2 Based on the available information I believe the most appropriate diagnosis is:

- ○ CF (1)
- ○ CFTR-related disorder (3)
- ○ CF diagnosis not resolved - needs further testing (6)
- ○ CF carrier (7)
- ○ None of the above (8)

Q4.3 In your opinion this individual should receive:

- ○ Follow up outside of a multi-disciplinary CF Clinic (1)
- ○ Modified multi-disciplinary CF Clinic follow up (reduced frequency/monitoring/shared-care family doctor or respirologist where possible) (2)
- ○ Full standard of care multi-disciplinary CF Clinic follow-up (quarterly review, sputum, spirometry) (3)

Q43 How easy did you find classifying this case?

	Very difficult (1)	Fairly difficult (2)	Average (3)	Fairly easy (4)	Very easy (5)
Click to write Choice 1 (1)	○	○	○	○	○

End of Block: Case 2

Start of Block: Case 3

Q5.1
CASE 3

A 44-year-old Caucasian male is referred for assessment on the basis of three abnormal sweat chloride tests at 50, 69 and 70 mmol/L respectively.

The **indication for testing** was a 20-year history of daily severe coughing paroxysms driven by difficult to expectorate mucus plugs and post-nasal nasal discharge. CF genetics (whole gene sequencing with MLPA del/dup and intronic variant analysis) revealed a single phe508del mutation. No known family history of CF.

Respiratory: No respiratory symptoms until his early 20s, following nasal surgery to correct a sports-related defect. Subsequently, the patient developed the sensation of mucus balls/plugs dropping from his nasopharynx to his throat and great difficult clearing them. Over the subsequent ten years these symptoms increased from once weekly to 6 times daily. Now daily production of thick green plugs. No wheeze, no annual antibiotic use or exercise limitation. No hospitalizations. CT chest shows no bronchiectasis. FEV1 is 110% predicted. Sputum (and sinus) microbiology recurrently grows only normal flora.

ENT: Previous corrective septoplasty in early 20s. CT sinuses demonstrates bilateral mucus retention cysts but no features of rhino-sinusitis and normal sinus structure. No polyposis radiologically or at direct examination. The patient reports post-nasal mucus as previously described, not visualized at endoscopy.

GI: Mild esophageal dysmotility and mild GERD confirmed both symptomatically and radiologically. Occasional bloating. No constipation or history of bowel obstruction. Fecal elastase >500 µg/gram (assay defines "insufficiency" as <200). Normal pancreatic and liver morphology on abdominal ultrasound and CT.

Other: HbA1c 5.7%, normal OGTT, Vit A/D/E all normal. Bone density normal for age. Ultrasound scrotum normal (no CBAVD). Declined semen analysis. No family history. Sputum negative for eosinophilia. IgE 105 µg/L (assay normal <405 µg/L).

Neonatal/infantile history: No failure to thrive, no childhood asthma or respiratory issues.

Q5.2 Based on the available information I believe the most appropriate diagnosis is:

- ○ CF (1)
- ○ CFTR-related disorder (6)
- ○ CF diagnosis not resolved - needs further testing (3)
- ○ CF carrier (7)
- ○ None of the above (8)

Q5.3 In your opinion this individual should receive:

- ○ Follow up outside of a multi-disciplinary CF Clinic (1)
- ○ Modified multi-disciplinary CF Clinic follow up (reduced frequency/monitoring/shared-care family doctor or respirologist where possible) (2)
- ○ Full standard of care multi-disciplinary CF Clinic follow-up (quarterly review, sputum, spirometry) (3)

Q42 How easy did you find classifying this case?

	Very difficult (1)	Fairly difficult (2)	Average (3)	Fairly easy (4)	Very easy (5)
Click to write Choice 1 (1)	○	○	○	○	○

End of Block: Case 3

Start of Block: Case 4

Q6.1
CASE 4

A 56-year-old Caucasian male isreferred due to sweat chloride levels <30, 43 and 43 mmol/L

sequentially. The **indication for testing** was a diagnosis of diffuse bronchiectasis, made in the preceding 5 years. Subsequent CF genetic screening identified heterozygous phe508del/D1152H mutations (for reference from cftr2.org - "*This variant combination has varying consequences*"). No known family history of CF.

Respiratory: Mild/subtle diffuse bronchiectasis. All respiratory symptoms (cough, daily purulent sputum) came on after 50 years of age. Sputum culture identified *Psudomonas aeruginosa* (PA) and MSSA. Typically, no annual requirement for antibiotics. Spirometry demonstrates an FEV1 of 134% predicted. No symptoms of wheeze/asthma. Normal IgE.

ENT: Post nasal drip, physician-diagnosed chronic rhino-sinusitis. CT sinuses demonstrates septal deviation, opacification of the right maxillary sinus, no soft tissue abnormality. No polyposis.

GI: Pancreatic exocrine insufficiency with fecal elastase 46 µg/gram (assay defines "insufficiency" as <200 µg/gram), but no symptoms of steatorrhea. Mild GERD reported, no bloating, pain or constipation. No history of bowel obstruction. No liver disease.

Other: HbA1c 5.9%, OGTT shows impaired fasting glycaemia. Bone density normal for age. Vit D low, Vit A/E normal.

Fertility: Confirmed congenital absence of the vas deferens (CBAVD).

Neonatal/infantile history: No failure to thrive, no childhood asthma or respiratory issues.

Q6.2 Based on the available information I believe the most appropriate diagnosis is:

- ○ CF (1)
- ○ CFTR-related disorder (6)
- ○ CF diagnosis not resolved - needs further testing (3)
- ○ CF carrier (7)
- ○ None of the above (8)

Q6.3 In your opinion this individual should receive:

- ○ Follow up outside of a multi-disciplinary CF Clinic (1)
- ○ Modified multi-disciplinary CF Clinic follow up (reduced frequency/monitoring/shared-care family doctor or respirologist where possible) (2)
- ○ Full standard of care multi-disciplinary CF Clinic follow-up (quarterly review, sputum, spirometry) (3)

Q41 How easy did you find classifying this case?

	Very difficult (1)	Fairly difficult (2)	Average (3)	Fairly easy (4)	Very easy (5)
Click to write Choice 1 (1)	○	○	○	○	○

End of Block: Case 4

Start of Block: Case 5

Q7.1
CASE 5

A 61-year-old Caucasian female was referred for assessment due to sweat chloride measurements of 29 and 31 mmol/L and CF genetics (139 variants) identifying a phe508/5T allele (TG tract not provided) genotype (for reference from cftr2.org - " *This variant combination has varying consequences"*). No known family history of CF. The **indication for testing** was a known history of bronchiectasis with PA and MAC chronic infection.

Respiratory: Symptoms include daily cough and purulent sputum production with a history of frequent antibiotic requirements. CT chest demonstrates diffuse bronchiectasis, with no cavitary disease. Sputum culture is positive for PA and MAC. Baseline FEV1 is 75% predicted.

ENT: Symptoms include post-nasal drip. No polyposis, with normal CT sinus findings. Normal IgE.

GI: Symptoms are limited to mild post-prandial bloating. No history of pancreatitis. Fecal elastase >500 µg/gram (assay defines "insufficiency" as <200 µg/gram). No history of bowel obstruction. Morphologically normal liver and pancreas.

Other: HbA1c 5.3%, OGTT normal, Vit A/D/E all normal, low bone density for age. No fertility issues.

Neonatal/infantile history: No failure to thrive, no childhood asthma or respiratory issues.

Q7.2 Based on the available information I believe the most appropriate diagnosis is:

- ○ CF (1)
- ○ CFTR-related disorder (6)
- ○ CF diagnosis not resolved - needs further testing (3)
- ○ CF carrier (7)
- ○ None of the above (8)

Q7.3 In your opinion this individual should receive:

- ○ Follow up outside of a multi-disciplinary CF Clinic (1)
- ○ Modified multi-disciplinary CF Clinic follow up (reduced frequency/monitoring/shared-care family doctor or respirologist where possible) (2)
- ○ Full standard of care multi-disciplinary CF Clinic follow-up (quarterly review, sputum, spirometry) (3)

Q40 How easy did you find classifying this case?

	Very difficult (1)	Fairly difficult (2)	Average (3)	Fairly easy (4)	Very easy (5)
Click to write Choice 1 (1)	○	○	○	○	○

Page Break

Q42 Would the availability of information regarding the 5T TG tract (11 vs 12 vs 13) influence your final decision regarding diagnosis in the previous case?

- ○ Not at all (1)
- ○ Possibly (2)
- ○ Yes (3)

End of Block: Case 5

Start of Block: Case 6

Q8.1
CASE 6

An 18-year-old mixed heritage (Asian/Caucasian) patient is referred with a series of sweat chloride tests of 58, 42, 62 and 62 mmol/L. The **indication for testing** was a known history of nasal polyposis and chronic rhino-sinusitis. Genetic testing including whole gene sequencing and subsequent epithelial sodium channel (eNaC) and Carbonic Anhydrase mutation analysis reveals no CFTR/other variants. There is no family history of CF.

Respiratory: Physician-diagnosed pneumonia aged 9. Occasional throaty cough and occasional clear sputum. No recent/recurrent antibiotic requirements for lungs. Sputum culture demonstrated MSSA. CT chest reveals no bronchiectasis or other anomalies. FEV1 is 114% predicted. She reports no wheeze and no asthma symptoms. IgE (172µg/L) and Eosinophils are normal.

ENT: Symptoms include frequent episodic frontal sinus pain and congestion. Frequent "head colds" and perennial post-nasal drip. Known polyposis in childhood, medically managed with nasal corticosteroid.

No polypectomy. CT sinuses shows moderate to severe mucosal thickening throughout and stenosis of the ostiomeatal complexes. No residual polyposis.

GI: No symptoms. No constipation and no history of bowel obstruction. Fecal elastase >500 µg/gram (assay defines "insufficiency" as <200 µg/gram). Morphologically normal pancreas and liver. no liver disease. BMI 21.

Other: HbA1c 5.5%, normal OGTT. Vit D low, Vit A/E normal. Bone density low for age. No attempts to get pregnancy thus no overt fertility issues.

Neonatal/infantile history: No failure to thrive/GI issues. Nasal polyposis as stated.

Q8.2 Based on the available information I believe the most appropriate diagnosis is:

- ○ CF (1)
- ○ CFTR-related disorder (6)
- ○ CF diagnosis not resolved - needs further testing (3)
- ○ CF carrier (7)
- ○ None of the above (8)

Q8.3 In your opinion this individual should receive:

- ○ Follow up outside of a multi-disciplinary CF Clinic (1)
- ○ Modified multi-disciplinary CF Clinic follow up (reduced frequency/monitoring/shared-care family doctor or respirologist where possible) (2)
- ○ Full standard of care multi-disciplinary CF Clinic follow-up (quarterly review, sputum, spirometry) (3)

Q39 How easy did you find classifying this case?

	Very difficult (1)	Fairly difficult (2)	Average (3)	Fairly easy (4)	Very easy (5)
Click to write Choice 1 (1)	○	○	○	○	○

End of Block: Case 6

Start of Block: Case 7

Q9.1
CASE 7

A 41-year-old Caucasian female is referred having undergone sweat chloride tests demonstrating levels of 20 mmol/L and subsequently 25 mmol/L. She has a child with known homozygous phe508del CF. The **indication for testing** is a known family history of CF (in her child), along with a personal history of poorly controlled asthma.
Genetic analysis reveals heterozygous phe508del (pathogenic) / R347C (mutation of variable clinical significance) / M348K (mutation of unknown clinical significance).

Respiratory: Episodic asthma and wheeze for many years. Minimal cough between episodes. Frequent infections requiring antibiotics and the addition of prednisone. Sputum identification of MAC and MSSA. FEV1 121% predicted. CT chest reveals no bronchiectasis, and minimal tree-in-bud changes. Peripheral eosinophil count and serum IgE are normal.

ENT: The patient endorses symptoms of post-nasal drip and congestion. CT sinuses demonstrates normal morphology and normal mucosa. No polyposis.

GI: No symptoms. No GERD. No constipation or history of bowel obstruction. Fecal elastase is >500 µg/gram (assay defines "insufficiency" as <200 µg/gram). The pancreas is morphologically normal on ultrasound. There is no evidence of liver disease.

Other: HbA1c is 5.5%, OGTT is normal. Vit D is low, and Vit A/E are normal. Bone density is normal for age. There is no history of infertility or difficulty conceiving.

Q9.2 Based on the available information I believe the most appropriate diagnosis is:

- ○ CF (1)
- ○ CFTR-related disorder (6)
- ○ CF diagnosis not resolved - needs further testing (3)
- ○ CF carrier (7)
- ○ None of the above (8)

Q9.3 In your opinion this individual should receive:

- ○ Follow up outside of a multi-disciplinary CF Clinic (1)
- ○ Modified multi-disciplinary CF Clinic follow up (reduced frequency/monitoring/shared-care family doctor or respirologist where possible) (2)
- ○ Full standard of care multi-disciplinary CF Clinic follow-up (quarterly review, sputum, spirometry) (3)

Q38 How easy was this case to classify?

	Very difficult (1)	Fairly difficult (2)	Average (3)	Fairly easy (4)	Very easy (5)
Click to write Choice 1 (1)	○	○	○	○	○

End of Block: Case 7

Start of Block: Guidelines

Q10.1 The current CFF guidelines suggest that the first step in the diagnostic workup should be the presence of a "Clinical Presentation of CF"

Q10.2 In your opinion, how easy is it to define a "Clinical Presentation of CF", independently of sweat chloride result or CFTR genetics in patients presenting as adults?

- ○ Extremely difficult (1)
- ○ Relatively difficult (2)
- ○ Neither easy nor difficult (3)
- ○ Relatively easy (4)
- ○ Extremely easy (5)

Page Break

Q10.3 Please rate your opinion on the contribution each of the following has in supporting a "clinical presentation of CF" in patients presenting as adults

	Not individually supportive (1)	Somewhat supportive (2)	Strongly supportive (3)
Bronchiectasis - diffuse (1)	○	○	○
Bronchiectasis - asymmetrical (2)	○	○	○
Obstructive spirometry (3)	○	○	○
Radiographic rhinosinusitis (4)	○	○	○
Nasal polyposis (5)	○	○	○
Radiographic evidence of pancreatic fibrosis/fibrocystic change (6)	○	○	○
Constipation (7)	○	○	○
Vit D deficiency (8)	○	○	○
Vit A/E deficiency (9)	○	○	○
Osteoporosis/Osteopenia (10)	○	○	○
Infertility/Congenital Bilateral Absence of the Vas Deferens (11)	○	○	○
Aquagenic wrinkling (12)	○	○	○
ABPA diagnosis (13)	○	○	○
Liver disease/steatosis/cirrhosis (14)	○	○	○

Pancreatic insufficiency (15)	○	○	○
Daily sputum production (16)	○	○	○
Frequent need for antibiotics for chest (17)	○	○	○

Page Break

Q10.4 Please rate your opinion on the contribution each of the following airway pathogens has in supporting a "clinical presentation of CF"

	Not supportive (1)	Somewhat supportive (2)	Strongly supportive (3)
MSSA (1)	○	○	○
Pseudomonas aeruginosa (2)	○	○	○
MRSA (3)	○	○	○
Burkholderia cepacia complex organisms (6)	○	○	○
Stenotrophomonas maltophilia (7)	○	○	○
Achromobacter species (8)	○	○	○
Mycobacterium avium complex (9)	○	○	○
Mycobacterium abscessus sp. (11)	○	○	○
Streptococcus pneumoniae (13)	○	○	○
Aspergillus fumigatus sp (14)	○	○	○

End of Block: Guidelines

Start of Block: Follow up care

Q11.1 Regarding individuals meeting a diagnosis of CFTR-related disorder: Please rate the following in terms of their effect on your opinion on the need for follow up in a CF-MDT centre

	Would not contribute to decision (1)	Contributes somewhat (2)	Major determinant (3)
Younger age at presentation (1)	○	○	○
Worse lung function at presentation (2)	○	○	○
Lung function relative to age at presentation (3)	○	○	○
Frequent pulmonary exacerbations (4)	○	○	○
Nutritional status/BMI (5)	○	○	○
Pseudomonas sputum positive (6)	○	○	○
MRSA sputum positive (7)	○	○	○
Burkholderia Cenocepacia Complex sputum positive (8)	○	○	○
NTM sputum positive (9)	○	○	○
Other bacterial sputum positivity (Stenotrophomonas, Achromobacter, MSSA) (10)	○	○	○
Diagnosis of ABPA (11)	○	○	○
Confirmed diagnosis of diabetes (12)	○	○	○
Already attending a pulmonary specialist (13)	○	○	○

Recurrent pancreatitis (14)	○	○	○
Confirmed exocrine pancreatic insufficiency (15)	○	○	○

End of Block: Follow up care

Start of Block: Please rate your agreement with the following statements:

Q12.1 Accurate distinction between CF and CFTR-rd has become significantly more pertinent with the advent of highly effective CFTR-modulators.

- ○ Strongly disagree (1)
- ○ Somewhat disagree (2)
- ○ Neither agree nor disagree (3)
- ○ Somewhat agree (4)
- ○ Strongly agree (5)

Q12.2 Since the approval of Elexacaftor/Tezacaftor/Ivacaftor I feel more compelled to arrange Whole Gene Sequencing in individuals with clinical features of CF, sweats > 60mmol/L and a single phe508del allele.

- ○ Strongly disagree (1)
- ○ Somewhat disagree (2)
- ○ Neither agree nor disagree (3)
- ○ Somewhat agree (4)
- ○ Strongly agree (5)

Q12.3 Increased CFTR-rd identification has the potential for significant resource utilisation implications for CF centres.

- Strongly disagree (1)
- Somewhat disagree (2)
- Neither agree nor disagree (3)
- Somewhat agree (4)
- Strongly agree (5)

Q12.4 The current guidelines for CF/CFTR-rd diagnosis provide a good framework for high inter-clinician agreement regarding final diagnosis and classification.

- Strongly disagree (1)
- Somewhat disagree (2)
- Neither agree nor disagree (3)
- Somewhat agree (4)
- Strongly agree (5)

End of Block: Please rate your agreement with the following statements: