

ONLINE SUPPLEMENTARY MATERIAL

COMPREHENSIVE METHODS

Study design

A three-round, iterative Delphi survey process was used to systematically develop consensus among key expert groups regarding ExACT in CF (Figure 1). A maximum of three rounds in this study was decided *a priori*, as there is little known benefit, in terms of greater movement towards consensus, after three rounds and this can prevent participant fatigue and minimise attrition [1]. Three survey rounds also allowed free-text responses from Round 1 to be incorporated as new statements in Round 2 and re-evaluated in light of the group consensus in Round 3 (Figure 1). This was a UK multicentre study (Figure 1). Ethical approval was granted by the University of Portsmouth Faculty of Science and Health Ethics Committee (SHFEC 2021-047). Participants provided informed consent as part of the online survey and all data was handled in accordance with UK data protection regulations.

Contributors and expert panel recruitment

We recruited four key expert groups (1) pwCF; 2) caregivers (parents/partners) of pwCF; 3) doctors (CF specialists); and 4) CF specialist physiotherapists (Table 1). We invited participation from members of the Association of Chartered Physiotherapists in CF (ACPCF), whose membership draws from the 25 adult and 29 paediatric specialist CF centres in the UK; clinicians from the UK CF Medical Association and British Paediatric Respiratory Society; pwCF or their parents/guardians/partners (approached via the UK CF Trust Patient Involvement Group and CF Warriors Charity). Participants had to register interest in the study and be eligible to receive the survey link. Those eligible were required to be ≥ 18 years, have internet access, be fluent in English, able to understand and cooperate with study requirements, and be a member of one of the identified four expert groups. All 83 participants who registered interest completed Round 1.

Survey development and distribution

The study team (1 researcher/clinical exercise physiologist (ZS), 2 physiotherapists (LM, EM), 2 CF specialist clinicians (DU, SC), and 1 pwCF (SR)) was formed to express opinions and formulate statements, based on knowledge and experience of the physiotherapy management of pwCF. Round 1 statements, developed by this multidisciplinary study team, were iteratively tested and refined by members of the ACPCF, selected health care professionals and pwCF through the UK CF Trust Involvement team. This helped ensure that the methods and language used in the survey were comprehensible to all expert panel members.

To meet the study objectives, the initial survey was divided into three sections: 1) exercise as ACT, 2) exercise type and duration for ExACT, and 3) exercise intensity for ExACT. Furthermore, responses would be requested in relation to a person having 'stable' or 'unstable' CF, to understand different responses and inform trial design, particularly around the role of tACT during periods of respiratory instability. An iterative process of feedback was undertaken to improve the structure and readability of statements and determine whether any additional statements were needed.

All surveys were administered using the onlinesurveys.ac.uk interface (JISC, Bristol, UK), with survey links distributed with notification via email. In all three rounds, agreement with each statement was ranked on a scale of 0–9, with 0 being total disagreement and 9 total agreement. Scores between 7–9 represented good agreement. When >70% of participants scored 7–9 on any statement, this was regarded as an acceptable level of consensus. For duration of exercise, we sought the modal average from the 10 time epochs provided: 0–10, 11–20, 21–30, 31–40, 41–50, 51–60, 61–70, 71–80, 81–90 and >90-minutes; with an option to select '*would never consider this*'. Following each round, participants were provided their individual responses and summary results from the group as a whole (summary charts showing the responses to each statement). In addition to new statements, those not reaching consensus in a prior round were re-presented. Participants were asked to reconsider the prior statements, considering the feedback of results from the previous round, and re-rate their level of agreement with each statement. They were advised that they did not have to change their response.

Respondents were assigned a unique code to access the online survey, to permit monitoring of survey completion and attrition. Panellists were sent up to three email reminders of deadlines to maximise completion. e-Delphi principles of expert anonymity (where possible), iterative questionnaire surveys, and individual feedback [1] were adhered to. Participants responding to each survey were invited to respond to the subsequent survey.

E-Delphi

Round 1

Eight statements across the '*exercise as airway clearance*' and '*exercise intensity*' domains were presented in Round 1. For the '*exercise type and duration*' domain, participants were asked to rank their agreement with 21 pre-defined types of exercise proposed as ExACT candidates (one being '*other*'), and for each to select a duration considered equivalent to a session of tACT. If respondents agreed with '*other*', they were asked to also provide free-text detail proposing additional types of exercise for consideration in future rounds. A free-text option was available within each survey statement, providing the opportunity to elaborate/explain responses, add statements and/or suggest modifications to original statements. At the end of Round 1, the modified responses were summarised and the degree of consensus evaluated. For statements achieving an acceptable degree of consensus (>70% scoring 7-9 for agreement), the process ceased. Any statements with a consensus level of <70% were further explored in Rounds 2 and 3. In Round 1, demographics were also captured for all expert panellists, including: gender, year of birth, closest city, which sub-group they represented and, for physiotherapists and doctors, years working in the field of CF (Table 1).

Round 2

Fifteen statements were provided in Round 2 for the '*exercise as airway clearance*' and '*exercise intensity*' domains, including 4 statements from Round 1 that did not reach consensus and 11 new statements derived from the Round 1 free-text responses. Amended *exercise type* and *exercise duration* statements were also presented to include 9 additional exercise types from Round 1 and with wording amended based on panel feedback from '*At times of stable cystic fibrosis, I would consider the following types of exercise to be*

equivalent to airway clearance for people with cystic fibrosis to *'At times of stable cystic fibrosis, I would consider the following types of exercise to be equivalent to airway clearance for people with cystic fibrosis only if undertaken at an intensity that means the person is out of breath (deep breathing)'*. In Round 2 free-text responses were restricted to statements regarding whether coughs or huffs are useful before, during or after exercise, to expand on free-text comments and feedback in Round 1, and to refine new statements.

Round 3

Respondents who completed Round 2 were invited to Round 3. Seventeen statements were provided in Round 3, including 8 statements from Round 2 that did not reach consensus and 9 new statements derived from Round 2 free-text responses. There was no option for free-text responses, however we did ask respondents to provide any further comments regarding the what they believe an ExACT session for pwCF who are stable should look like, particularly for a future clinical trial.

Data analysis

The quantitative data from each round was exported from JISC into Microsoft Excel[®] (Microsoft Corporation. 2019) and SPSS Version 27 (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp.). To identify which statements had reached consensus in Rounds 1 or 2, percentage agreement and median response were calculated. Descriptive statistics (counts and percentages) were used to describe participants' demographic characteristics and group responses to each statement, with missing responses removed from percentage calculations. Specifically, the median, and proportion of scores ranked 7-9 (good agreement - consensus) overall and for each of the 4 expert sub-panels were calculated. Consensus was defined a priori as >70% agreeing/strongly agreeing or disagreeing/strongly disagreeing with a statement in Round 3. Differences in rankings between the sub-panels were evaluated using 1-way ANOVA testing with Bonferroni post-hoc (where equal variances were assumed) or Tamhane's T2 test (unequal variances). $P < 0.05$ was considered statistically significant. Free-text comments were imported into a Microsoft Word document.

COMPREHENSIVE RESULTS

In Round 1, the total expert panel consisted of 83 participants; 29 physiotherapists (35%), 17 (21%) doctors, 23 (28%) pwCF, and 14 (17%) parents/partners of pwCF. All physiotherapists and doctors reported CF experience (Table 1), with doctors averaging a greater duration of experience. Respondents represented well the different areas of the UK. In Round 2, 67 participants (27 physiotherapists [40%], 13 [19%] doctors, 16 [24%] pwCF, and 11 [16%] parents/partners of pwCF) completed the survey. At the end of all three rounds the retention rate was 72%, leaving a final e-Delphi panel of 60 participants (24 physiotherapists [40%], 11 [18%] doctors, 15 [25%] pwCF, and 10 [17%] parents/partners of pwCF).

The use of exercise as a form of ACT in pwCF

Consensus was reached that the right kind of exercise could act as a form of ACT in pwCF (Statement 1, 75%) and that, if evidence were supportive, it would be adopted into clinical practice (Statement 8, 89%). A majority of respondents also agreed with the question '*if you had the opportunity to take part in a research study looking at exercise as an alternative for airway clearance would you do so?*', 88% ($n = 53/60$).

The use of exercise was qualified by disease stability and intensity prior to final consensus on type and duration. Consensus was reached (Statement 12, 73%) that ExACT should only apply in stable CF. Consensus could not be achieved on exercise replacing chest physiotherapy during chest exacerbations, even if evidence were supportive (Table S3), but a combination of tACT and ExACT exercise were considered important during chest exacerbations (Table 2). Further consensus was reached that intensity is key for ExACT as a tACT substitute (Statement 14, 85%), exemplified by deep breathing (Statement 15, 90%) or ability to talk in short sentences but not whistle or sing (Statement 17, 77%). Assessment breaths, coughs and huffs can be used before exercise to see if secretions are there (Statement 7, 72%). Coughs and huffs are needed to remove loose secretions during or after exercise (Statement 2, 80%; Statement 4, 72%; Statement 5, 82%), and must be included to be an effective ACT (Statement 3, 80%) to ensure secretions are effectively mobilised and cleared.

Types of exercise that could be considered for ExACT in pwCF

Types of exercise considered as options for ExACT during times of stable CF, performed at a moderate-high intensity that makes the person breathe deeply and with assessment breaths, coughs and huffs, are presented in Table 3. Of the list of exercises developed during Rounds 1 and 2, 14 exercise types did not reach consensus after three rounds and were removed (Table 3). Of these, gymnastics (69%), martial arts (67%), tennis / badminton (67%) were just below the level of consensus agreement.

Consensus regarding durations of approved exercises that could be considered for ExACT in pwCF

For the types of exercise reaching consensus agreement as options for ExACT, the panel provided duration recommendations in Round 3 (Table S2). For the majority of exercise types, the duration category with the highest proportion panel agreement was 21-30-minutes.

Differences between expert sub-groups

Median scores for the expert groups and any between group differences are shown in Table S1. Two statements differed significantly in ranking between the expert panel subgroups. Firstly, '*Coughs and huffs are needed to remove loose secretions in the airway, especially during or after exercise*' differed significantly in ranking, with the CF physiotherapist subgroup ranking this with significantly higher (agreement) than pwCF ($p=0.001$, mean difference: 2.3), CF doctors ($p=0.002$, mean difference: 2.0) and parents/partners of pwCF ($p=0.01$, mean difference: 1.3). Secondly, '*Coughs and huffs must be included in exercise for it to be effective as a form of airway clearance*' differed significantly in ranking, with the CF physiotherapist subgroup ranking this with significantly higher (agreement) than pwCF ($p=0.003$, mean difference: 2.2), CF doctors ($p=0.01$, mean difference: 2.1) and parents/partners of pwCF ($p=0.04$, mean difference: 3.0). Importantly, the different expert groups, representing the CF community, were comparable in their agreement ranking for all other statements.

ONLINE SUPPLEMENT - FIGURES AND TABLES

Figure S1. Summary of the stages of the e-Delphi surveys.

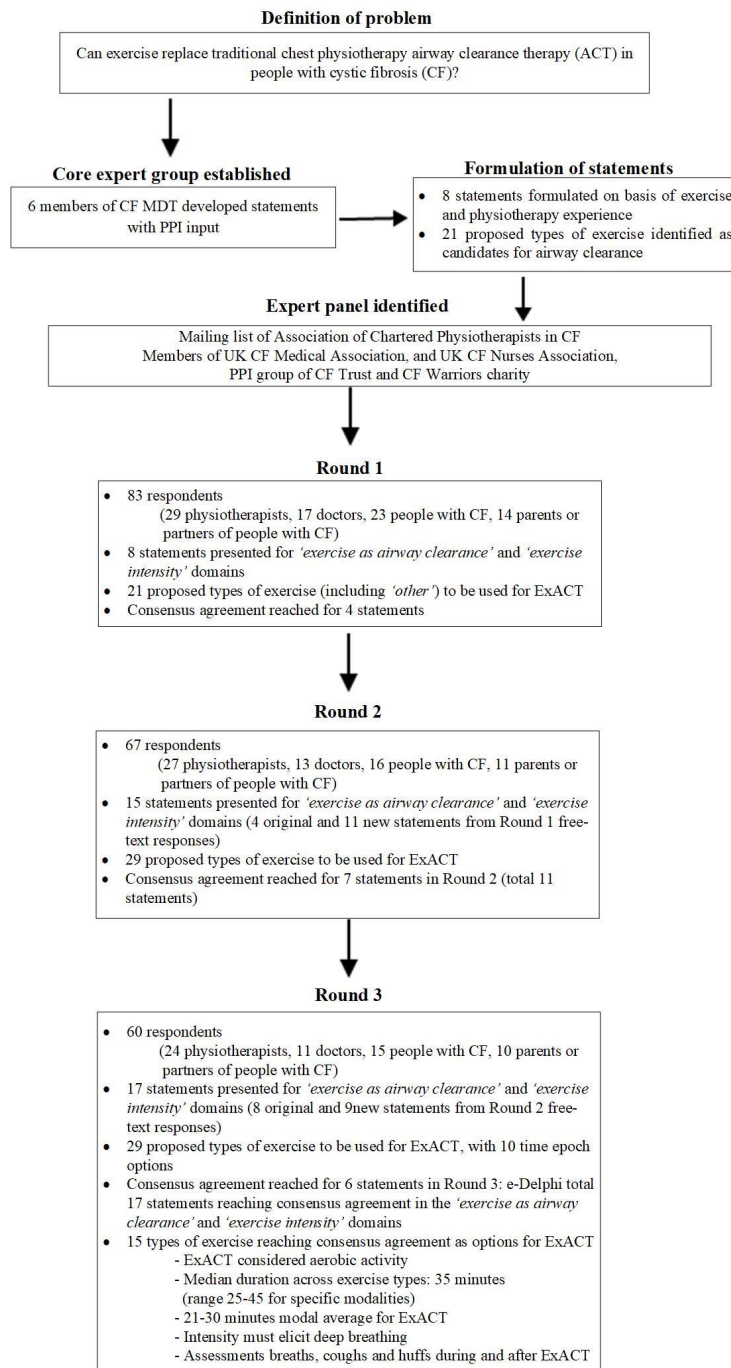


Table S1. Statements relating to exercise airway clearance therapy in cystic fibrosis from the 'exercise as airway clearance' and 'exercise intensity' domains, which reached panel consensus agreement, split by expert group

Statement	People with CF (n=15)		Physiotherapists (n=24)		Doctors (n=11)		Parents/partners (n=10)		p-value
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	
1 The right kind of exercise can loosen and move secretions in a similar way to chest physiotherapy in people with cystic fibrosis	9	7–9	7	6–8.5	7	6.5–8	8.5	6.75–9	0.27
2 Coughs and huffs are needed to remove loose secretions in the airway, especially during or after exercise	7	5–9	9	8–9	7	5–8	8	7–8	< 0.01*
3 Coughs and huffs must be included in exercise for it to be effective as a form of airway clearance	7	6–8	9	9–9	7	6–7	7	3.5–7.25	< 0.01*
4 Coughs and huffs should also be used regularly during exercise to ensure that any secretions mobilised are effectively cleared	7	5–8	8	7–9	7	6–8	7.5	5.5–8	0.08
5 Coughs and huffs should also be used in the recovery period after an exercise session, to ensure that any secretions mobilised are effectively cleared	8	6–9	9	8–9	8	7–8	8	6.25–9	0.13
6 Assessment breaths and huffs can be used in people with cystic fibrosis to help see if secretions are there	8	7–9	9	8–9	7	7–8	7.5	5.75–9	0.10
7 Assessment breaths, coughs and huffs can be used in people with cystic fibrosis before exercise to help see if secretions are there	8	7–9	7	5.25–9	7	6–8	7	6–8.25	0.89
8 If evidence were supportive, I would be happy for exercise to replace chest physiotherapy for airway clearance during stable cystic fibrosis periods	9	8–9	8	7–9	8	8–9	9	8.75–9	0.59
9 How often airway clearance should be undertaken depends on the individual (e.g. whether they are productive, lung function)	9	7–9	9	8–9	8	7–8.5	8	8–9	0.61
10 It is important for people with cystic fibrosis to keep their chest as clear as possible. Regular clearance will help this	9	7.25–9	9	8–9	9	8–9	9	8–9	0.35
11 People with cystic fibrosis should try to do something at least once a day that helps clear their airways	8	7–9	8	7–9	9	8–9	9	8–9	0.10
12 A combination of exercise and traditional chest physiotherapy methods are important during a cystic fibrosis chest exacerbation	8	5–9	8	7–9	8	7–9	6.5	4.75–8.25	0.16
13 People with cystic fibrosis should try to do something at least once a day that helps clear their airways, if they have chest symptoms and feel as though mucus needs moving	9	8.25–9	9	9–9	9	9–9	9	9–9	0.20
14 For exercise to be used for airway clearance, exercise intensity is key	8	7–9	8	8–9	7	6.5–8	8	7–9	0.64
15 For exercise to be used for airway clearance, the intensity must be such that the person is deep breathing during exercise	8	7–9	9	8–9	8	7–8.5	8	7–9	0.27
16 Whatever type of exercise is used for airway clearance, it needs to be at a moderate-intensity depending on the individual's fitness and health	8.5	7–9	8	7–9	8	6–8	8	7–9	0.38
17 Exercise should be undertaken at a level that means, although able to talk in short sentences, the person could not whistle or sing	7	5–9	8	7–9	8	7–8	8	5.5–9	0.05

Note: Median is scored on a scale of 0 to 9, where 0 represents total disagreement and 9 represents total agreement. Scores between 7 and 9 were considered to represent good agreement. Consensus was achieved when > 70% of participants scored between 7 and 9 on any statement. IQR = interquartile range. * indicates significant at the $p < 0.05$ level.

Table S2. Durations of different types of exercise (agreed through consensus – see Table 3) considered as options for exercise airway clearance therapy during times of stable cystic fibrosis.

Exercise type	Proportion of panel (%)										Would never consider this
	0-10 minutes	11-20 minutes	21-30 minutes	31-40 minutes	41-50 minutes	51-60 minutes	61-70 minutes	71-80 minutes	81-90 minutes	>90 minutes	
Aerobics	-	8.8	38.6¹	19.3	12.3	15.8	-	1.8	-	1.8	1.8
Basketball / netball / volleyball	-	1.8	33.3¹	26.3	14.0	19.3	1.8	-	1.8	-	1.8
Body combat	-	5.3	42.1¹	22.8	10.5	15.8	-	-	-	-	3.5
Boxing	-	14.0	40.4¹	19.3	7.0	19.3	-	-	-	-	-
Circuit training / CrossFit	-	7.0	43.9¹	19.3	8.8	21.1	-	-	-	-	-
Cycling	-	5.3	29.8¹	15.8	17.5	22.8	1.8	5.3	-	1.8	-
Dance	-	5.3	29.8	15.8	10.5	31.6¹	3.5	1.8	-	-	1.8
Football / hockey (field, roller, ice) / rugby	-	3.5	26.3	17.5	15.8	29.8¹	3.5	1.8	-	-	1.8
High-intensity interval training (HIIT)	3.5	17.5	36.8¹	21.1	3.5	15.8	1.8	-	-	-	-
Rowing	-	8.8	36.8¹	10.5	14.0	22.8	3.5	1.8	1.8	-	-
Running / jogging / orienteering	1.8	7.0	40.4¹	26.3	5.3	17.5	1.8	-	-	-	-
Skipping	3.5	15.8	38.6¹	21.1	7.0	12.3	1.8	-	-	-	-
Squash	1.8	5.3	35.1¹	19.3	17.5	15.8	3.5	1.8	-	-	-
Swimming	1.8	5.3	24.6¹	22.8	14.0	22.8	3.5	3.5	1.8	-	-
Trampolining	1.8	5.3	40.4¹	19.3	10.5	19.3	1.8	1.8	-	-	-

Note: **Bold text¹** denotes highest proportion exercise duration rating for each exercise type; - represents 0%. Modes were selected based on being performed at a moderate-high intensity that makes the person breathe deeply and with assessment breaths, coughs and coughs.

Table S3. Statements relating to exercise airway clearance therapy in cystic fibrosis from the ‘*exercise as airway clearance*’ and ‘*exercise intensity*’ domains that did not reach consensus agreement.

	Statement	Median*	IQR	Proportion of scores ranked 7-9
Exercise as airway clearance	- People with cystic fibrosis who feel well and like no mucus needs shifting may need to do airway clearance less than once daily	6	4 – 8	48.4
	- If evidence were supportive, I would be happy for exercise to replace chest physiotherapy for airway clearance during a cystic fibrosis chest exacerbation	7	3.8 – 8	56.7
	- I would not be happy for exercise to replace chest physiotherapy for airway clearance during a cystic fibrosis chest exacerbation	6	3 – 8	40.0
	- During a cystic fibrosis chest exacerbation, exercise would be too difficult to undertake so chest physiotherapy for airway clearance would be recommended	6	5 – 8	39.9
	- Blowing the nose before exercise can help clear sputum in people with cystic fibrosis	4.5	2 – 6	21.7
	- Assessment breaths can help determine the need to airway clearance in people with cystic fibrosis	7	6 – 8	58.3
	- Assessment breaths and huffs can be used in people with cystic fibrosis before exercise to help see if secretions are there	7	6- 9	68.4
Exercise intensity	- Exercise should be undertaken using heart rate targets and wearable technology to achieve this	5	3.8 – 7	30.0
	- For exercise to be used for airway clearance, intensity is more important than the type of exercise and should be the priority	7	5.8 – 8	66.6
	- For exercise to be used for airway clearance, both the intensity and the type of exercise are important	6	5 – 8	48.3
	- Exercise should be undertaken at a level that makes the person sweaty enough to need a shower afterwards	6.5	5.8 – 8	49.9

Note: * Scored on a scale of 0 to 9, where 0 represents total disagreement and 9 represents total agreement. Scores between 7 and 9 were considered to represent good agreement. Consensus was achieved when > 70% of participants scored between 7 and 9 on any statement. IQR = interquartile range.

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