

## **CAN EXERCISE REPLACE AIRWAY CLEARANCE TECHNIQUES IN CYSTIC FIBROSIS? A SURVEY OF PATIENTS AND HEALTHCARE PROFESSIONALS.**

**AUTHORS** N.J. Rowbotham\*<sup>1</sup>, S.J. Smith<sup>1</sup>, G. Davies<sup>2</sup>, T. Daniels<sup>3</sup>, Z.C. Elliott<sup>4</sup>, K. Gathercole<sup>5,6</sup>, O.C. Rayner<sup>7</sup>, A.R. Smyth<sup>1</sup>

\*Corresponding author

Dr Nicola J Rowbotham,

Address: Evidence Based Child Health Group, Division of Child Health, Obstetrics & Gynaecology, E Floor East Block, Queens Medical Centre, Nottingham NG7 2UH.

Email: nicola.rowbotham@nottingham.ac.uk

Telephone: (+44) 01158230079

### **AFFILIATIONS**

<sup>1</sup>University of Nottingham, Evidence Based Child Health Group, Nottingham, United Kingdom, <sup>2</sup>UCL Great Ormond Street Institute of Child Health, London, United Kingdom, <sup>3</sup>York Hull Adult Cystic Fibrosis Centre, York Teaching Hospital NHS Foundation Trust, York, United Kingdom, <sup>4</sup>Parent of Children with CF, Nottingham, United Kingdom, <sup>5</sup>University of Leeds, Leeds, United Kingdom, <sup>6</sup>Person with CF, Leeds, United Kingdom, <sup>7</sup>Person with CF, Plymouth, United Kingdom,

**Word count:** 1308, abstract 150

### **Abbreviations:**

ACT: Airway Clearance Technique

HCP: Healthcare Professionals

JLA: James Lind Alliance

NIHR: National Institute for Health Research

pwCF: people with CF

PSP: Priority Setting Partnership

## **ABSTRACT**

Airway clearance techniques (ACTs) are recommended in cystic fibrosis (CF) to prevent accumulation of secretions and lung infection. “Can exercise replace chest physiotherapy for people with CF?” is one of the CF community’s top 10 research questions. We conducted an online survey of the CF community to gather data on current ACT use, recommendations, reported adherence levels and exercise strategies used. There were 488 respondents: 194 (40%) people with CF (pwCF), 141 (29%) family and 153 (31%) healthcare professionals (HCPs) (mostly physiotherapists). Only 10/285 (4%) of pwCF do no exercise at present and 163/303 (54%) already incorporate exercise into ACTs. ACTs were omitted by 128/267 (48%) of pwCF when they exercised. Nearly all (110/129, 93%) of HCPs currently recommend exercise to support ACTs. A trial replacing some or all ACTs with exercise, was supported by 80/110 (73%) of HCPs, with an additional 9/110 (8%) willing to consider in selected patients.

## **KEYWORDS**

Exercise. Airway clearance techniques. Cystic fibrosis. Clinical trial. Co-production. Priority setting.

## INTRODUCTION

Cystic fibrosis (CF) is characterised by a failure of mucociliary clearance and accumulation of viscid secretions in the airway, leading to recurrent infection. To mitigate this process, CF treatment guidelines recommend the regular use of an airway clearance technique (ACT), with exercise as an adjunct(1). In people with CF (pwCF), exercise such as running or cycling, increases ease of sputum expectoration, minute ventilation and respiratory flow(2). A comparison of one ACT with treadmill exercise showed that these approaches performed similarly over a single session(3). These studies suggest that exercise might be a replacement rather than an adjunct to some or all of a patient's ACT programme.

In a recent patient engagement exercise, the James Lind Alliance (JLA) Priority Setting Partnership (PSP) in CF, the patient and clinical community jointly identified the top 10 questions for clinical research in CF(4). "Can exercise replace chest physiotherapy for people with CF?" was one of these research priorities. Exercise also featured as a topic of importance in the US CF Foundation's Insight CF project(5). We conducted an online survey in order to understand further how the CF community currently uses exercise to supplement or replace ACT, and to assess the acceptability to patients and healthcare professionals (HCPs) of a clinical trial to investigate replacing ACT with exercise.

## METHODS

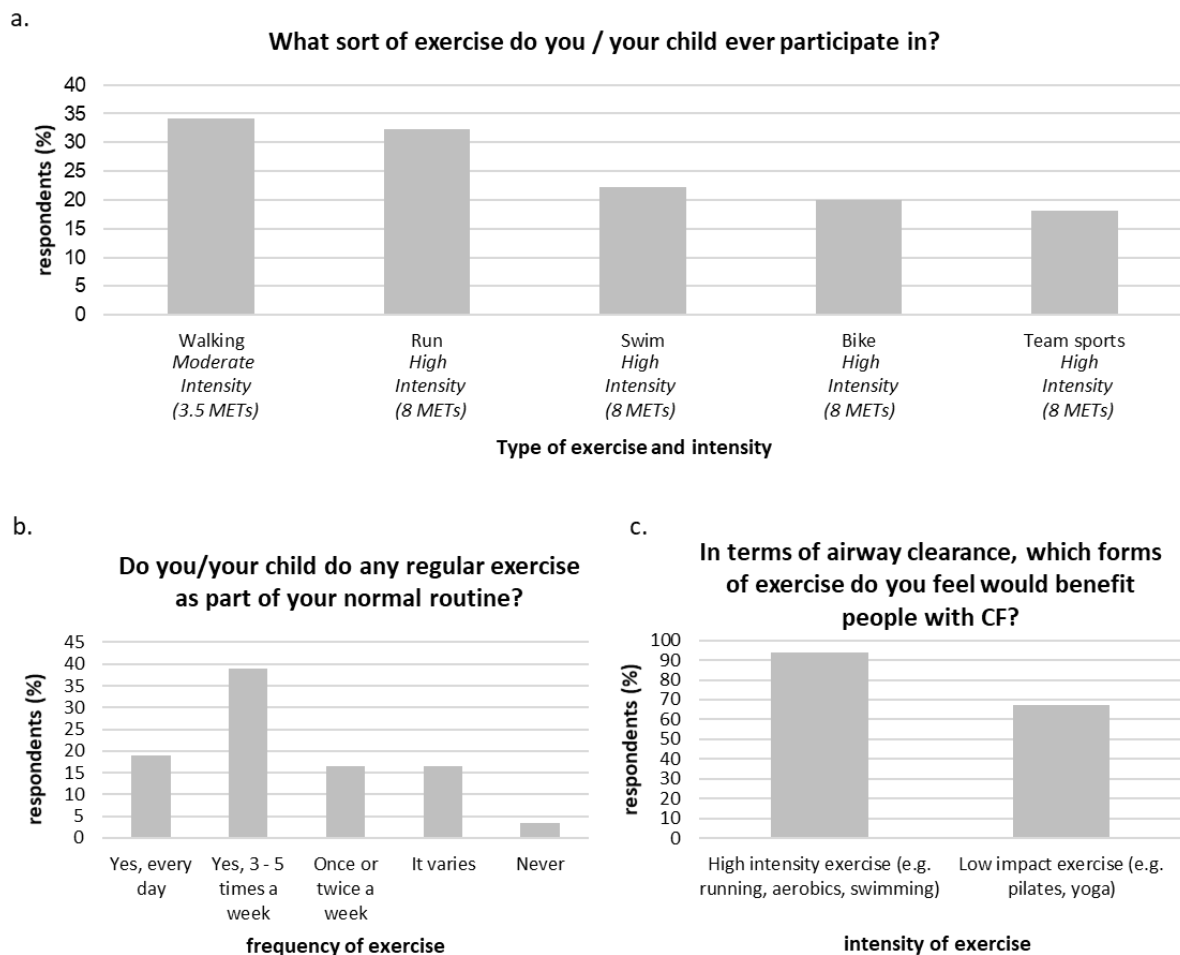
This work was led by a steering group representative of the CF community (lay and professional) and supported by the UK National Institute for Health Research (NIHR) under the title "James Lind CF2". An online questionnaire was co-produced using SurveyMonkey™ to help us understand which ACTs are currently undertaken by people with CF and recommended by HCPs, current levels of reported adherence and exercise strategies used (See online supplement 1). The survey was designed to be inclusive, with no minimum age or restrictions on location, and was open over 5 weeks in December 2018-January 2019. There were separate streams for lay and professional respondents to complete. It was promoted via our Twitter™ account (@questionCF), professional networks, UK CF Trust, US CF Foundation Community Voice group and the NIHR. The survey data were downloaded to Excel for quantitative analysis (closed questions) and NVivo for thematic analysis (free text comments) in order to generate topics which represented recurring themes.

## RESULTS

There were 488 respondents, with 335 (69%) from the lay community. Of these 194 (58%) were people with CF and 141 (42%) family of people with CF. Of the HCPs, 63% were physiotherapists. The greatest number of respondents were from the UK (n = 220, 45%) followed by North America (n=134, 28%). Median age of respondents with CF was 33 years (range 14-74 years) and median age of those whose parents or family answered on their behalf was 8 years (range 1 – 33 years). Survey respondent characteristics are summarised in appendix table 1. Not all respondents answered every question so denominators will vary (supplement 2).

Figure 1a shows the type of exercise most popularly undertaken by people with CF and grading of intensity using metabolic equivalent of tasks (METs)(6), with walking (moderate intensity) and running (high intensity) the most popular. The majority of people with CF exercise 3-5 times a week with only 10/285 (4%) of lay respondents reporting no exercise (figure 1b). Almost all (110/129, 93%) HCPs currently recommend exercise as a way of supporting ACTs and recommend all intensities of exercise (figure 1c). A full list of the top 20 exercises with METs are in appendix table 2.

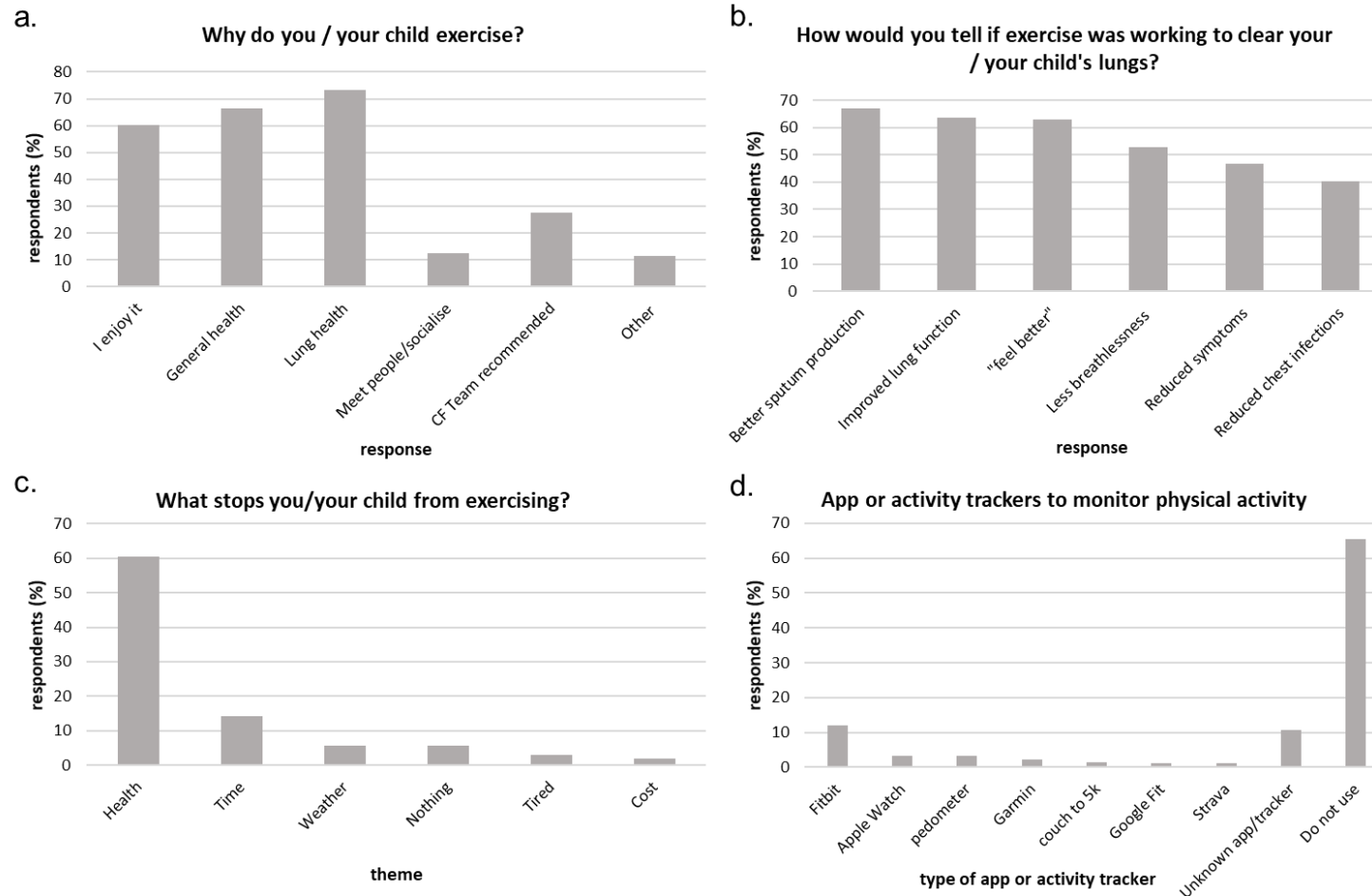
**Figure 1. Current exercise habits and intensity in CF. a)** The top five types of exercise currently undertaken by people with CF as indicated by the survey respondents (n=266). Coded from free text answers where respondents could give more than one exercise type. Corresponding exercise intensity with metabolic equivalence values (METs) (6) shown for each type of exercise. Cut offs for exercise intensity (in METs) were as follows: light = <3, moderate = 3-5.9, high = >6(6). **b)** Frequency of exercise undertaken at present by survey respondents (n=285). Single response allowed per respondent. **c)** Intensity of exercise believed to be beneficial by HCPs (n=110). Multiple responses allowed per respondent.



People with CF do exercise for many reasons (figure 2a), with the most popular being for lung health (204/279, 73%) followed by general health (185/279, 66%) and enjoyment (168/279, 60%). Only two of 277 respondents felt that exercise does not help clear their lungs. Better sputum production (184/275, 67%), better lung function (175/275, 64%) and “feeling better” (173/275, 63%) were the top three ways that people with CF believe exercise is working to clear their lungs (figure 2b). Poor health (161/266, 61%), time (38/266, 14%) and weather (15/266, 6%) were the top three factors that stopped people with CF from exercising. Six percent (15/266) replied that nothing ever gets in the way of exercise (figure 2c).

Only 35% of respondents with CF (98/284) reported using an App or tracker to monitor physical activity and 68 reported the type of device used. Wearable devices were used by 85% of those who told us what they used (58/68) and Apps by 15% (10/68). Of the wearable devices, Fitbit™ was the most popular (figure 2d).

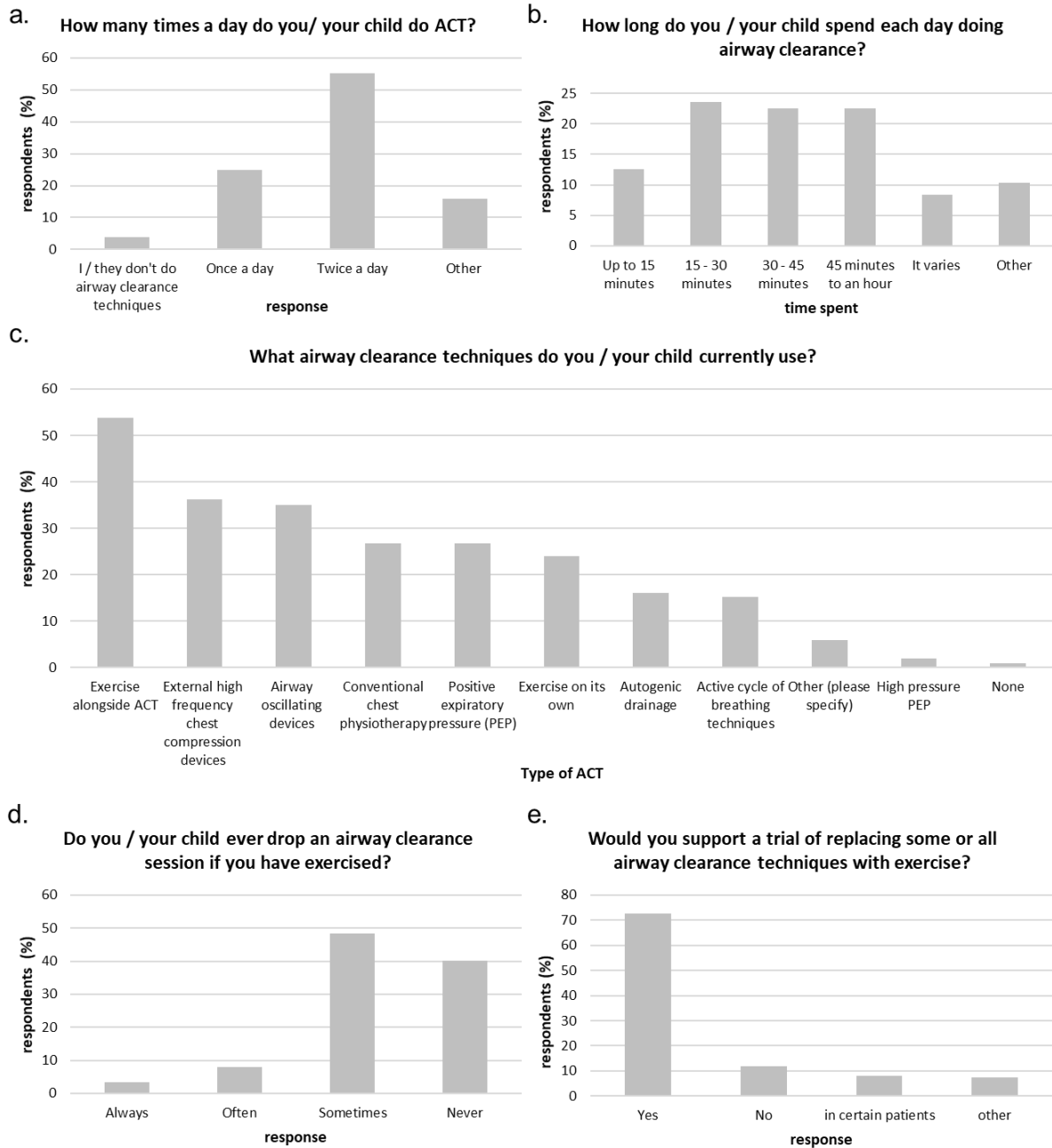
**Figure 2. Drivers behind exercise.** **a)** Reasons why people with CF exercise (n=279). Multiple responses allowed per respondent. **b)** Effects of exercise (n=275). Multiple responses allowed per respondent **c)** Factors that stop people with CF from exercising (n=266). ). Coded from free text answers where respondents could give more than one reason. **d)** Current app/technology use to aid exercise in people with CF (n=284). Single response allowed per respondent.



Time spent on ACTs varied among respondents, with, on average, people with CF spending 30mins-one hour a day over two sessions (figure 3a and 3b) (range 0-3 hours a day over 0-5 sessions a day). Over half of people with CF (163/303, 54%) already incorporate exercise into their ACTs and almost a quarter (73/303, 24%) already do exercise alone for their ACT (figure 3c). Almost 60% (180/302) of respondents admit to skipping their ACTs, with “life”, “how I feel” and “time” being the main explanatory themes given for this.

Almost half (128/267, 48%) of all respondents may drop their prescribed ACT if they have exercised (figure 3d) (including 49% (80/163) of those who incorporate exercise into their ACT). Nearly three quarters (80/110 , 73%) of HCPs would support a trial of replacing some or all airway clearance techniques with exercise, with an additional 8% (9/110) willing to consider supporting a trial in selected patients (figure 3d). Online supplement 3 shows trial suggestions collected from the CF community.

**Figure 3. Current ACT practice and views on future trials.** **a)** Average number of sessions spent daily on ACT (n=302). Single response allowed per respondent. **b)** Average time spent daily on ACT (n=301). Single response allowed per respondent. **c)** The use of exercise, ACT and combinations of the two in survey respondents (n=303). Multiple responses allowed per respondent **d)** Numbers reporting dropping an ACT session when they have exercised (n=267). Single response allowed per respondent. **e)** Support for a trial of replacing ACT with exercise (n=110). Single response allowed per respondent.



## **DISCUSSION**

Here we have explored current exercise use in people with CF and the influence it has on their ACT regimens. Most people with CF already incorporate exercise into their lives. Activity levels are higher than the general population. Around 20% of the UK population are classed as “inactive”(7) whereas only 4% of our CF population claimed to do no exercise. Almost half of people with CF regularly omit their prescribed ACT if they have exercised. This level of adherence is consistent with previous studies that have estimated adherence levels with CF physiotherapy to be 40-50%(8, 9) .

We found that most HCPs would support a trial replacing ACT with exercise. A recent Cochrane review looking at exercise for CF found 15 studies assessing the effect of exercise on people with CF but all included control groups who were not exercising rather than omitting any ACT (10). A systematic review comparing current clinical trials with the JLA top 10 did find two trials that loosely matched with “Can exercise replace physiotherapy?”(11). One is a feasibility study evaluating whether those who adhere to an exercise programme can then drop their ACT(12). The other is a crossover study looking at the effect of mucus clearance from exercise, ACT or sitting still(13). These studies aim to enrol small numbers (17 and 25 patients respectively) and results are, as yet, unpublished. A larger, adequately powered, multicentre trial is needed.

As with all anonymous online surveys, there are limitations. What people self-report and what they actually do can be quite different. However, an advantage of anonymity is that it allows respondents to be more honest without worry of repercussions. People with CF may be more conscious of things they can do to improve their health or it may be that the subsection of the CF population taking part in our survey are more interested in exercise, leading to response bias.

Many people with CF omit ACT if they have exercised. There is support amongst professionals for a trial of replacing current ACT with exercise. The data presented here will allow us to design clinical studies which will begin to answer the question of whether exercise can replace some ACT. Although most of our respondents were from the UK and US over a quarter were from elsewhere in the world. It is therefore reasonable to conclude that the themes and trends noted are applicable to the global CF population.

## **Acknowledgements**

We would like to thank all the people with CF and their families, and the multi-disciplinary CF health care professionals for taking part in this survey. Members of the James Lind Alliance CF2 steering group include: Brownlee K, Collins S, Daniels T, Davies G, Duff AJA, Elliot ZC, Gathercole K, Hurley MN, Leighton PA, Rayner OC, Rowbotham NJ, Smith SJ, Chandran S, Nash EF, Smyth AR (Chair), Wilson P.



## **Declarations**

### **Conflict of Interests Statement**

NJR has given lectures at meetings sponsored by TEVA. AS has provided consultancy for Vertex and holds a current unrestricted research grant from Vertex. He has taken part in clinical trials sponsored by Vertex, Raptor and Insmmed. He has given lectures at meetings sponsored by Teva and Vertex. GD has given lectures at meetings sponsored by Chiesi.

### **Funding**

This work was supported by the UK CF Trust. NJR is an NIHR Academic Clinical Fellow at University of Nottingham. GD is an NIHR Clinical Trials Fellow and was previously supported by a NIHR Clinical Lectureship at UCL.

### **Authors' contributions**

All authors were involved in the study design process and contributed in preparation of the manuscript.

**Appendix Table 1. Survey participant characteristics**

<b>Characteristic</b>	<b>n</b>	<b>%</b>
Total survey participants	488	-
<b><i>Category of Respondent</i></b>		
Lay persons	335	69%
Person with CF	194	(58%)
A parent of a child or children with CF	130	(39%)
Spouse or partner of a person with CF	2	(1%)
Other relative or friend of a person with CF	9	(3%)
Professionals	153	31%
Physiotherapist	93	61%
Dietitian	22	14%
Respiratory Paediatrician	11	7%
Nurse	9	6%
Researcher	5	3%
Respiratory Physician	5	3%
Pharmacist	2	1%
Exercise therapist	2	1%
Junior Doctor	1	1%
Psychologist	1	1%
Physiologist	1	1%
Healthcare professional occupation unknown	1	1%
<b><i>Geographical location</i></b>		
UK	220	45%
North America	134	27%
Europe (non UK)	19	4%
Australia and New Zealand	7	1%
South America	1	-
Asia	1	-
Africa	1	-
Participant location unknown	105	22%

<b>Age of survey participants</b>	
Median age (all participants), years (range)	37 (14-74)
Median age of respondents with CF or those answering on their behalf, years (range)	15.5 (1-74)
Median age of respondents with CF (range)	33 (14-74)
Median age of people with CF whose parents or family answered on their behalf, years (range)	8 (1-33)

**Appendix Table 2. Top 20 most popular exercise activities for people with CF**

<b>Activity</b>	<b>number of respondents</b>	<b>% of total respondents</b>	<b>Mets</b>
Walking	91	34%	3.5
Run	86	32%	8
Swim	59	22%	8
Bike	53	20%	8
Team sports	48	18.%	8
Strength training	46	17%	8
Gym	40	15%	5.5
Trampolining	33	12%	4.5
Dance	31	12%	6.5
Yoga	26	10%	2.5
Gymnastics	19	7%	4
Martial Art	10	4%	10
HIIT	9	3%	8
Cross Fit	8	3%	8
Exercise Class	8	3%	6.5
Pilates	8	3%	3.5
Climbing	5	2%	11
Horse riding	4	2%	4
Rowing	4	2%	7
Skiing	4	2%	7

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## Supplement 2

Table to show number of responses to each question (see blank version of survey in supplement 1 for questions).

Question	Total no. responses	Applies to Lay (L) / Professional (P)/ All (A)
1	488	A
2	303	L
3	302	L
4	301	L
5	301	L
6	285	L
7	266	L
8	279	L
9	265	L
10	266	L
11	233	L
12	284	L
13	267	L
14	277	L
15	251	L
16	275	L
17	152	P
18	129	P

Question	Total no. responses	Applies to Lay (L) / Professional (P)/ All (A)
19	111	P
20	120	P
21	115	P
22	113	P
23	105	P
24	98	P
25	94	P
26	110	P
27	89	P
28	110	P
29	380	A
30	198	L
31	383	A
32	379	A
33	377	A
34	290	A
35	66	A

### Supplement 3. RAW TRIAL SUGGESTIONS

The responses have not been edited, aside from for anonymity purposes.

We asked

**“If you would like to suggest an idea for a research trial to look into how exercise could replace airway clearance techniques, please feel free to write your suggestion here”**

- Correlation of functional capacity/ physical activity per week and airway clearance issues in different age group CF patients.
- analysis of variety of exercise that include Anaerobic, aerobic and body weight training in children. Does this improve FEV1, does this variety help prevent exacerbations, does it improve immune system?
- CFers skip conventional airway clearance sessions and instead participate in aerobic exercise (measured by either breaths per minute or heart rate), and measure outcomes:)
- Child on play physio trial at the moment under \*\*\*\*
- Clinical trials seeing which is more proficient at air way clearance , the vest takes too long and my child doesn't even cough , he coughs and moves phlegm with being active .... we need the best not time consuming mediocre clearance , it is time for the best for our cf ers , all the older cf ers say exercise and manual is the best , why don't our cf ers get physical therapy for manual as a resource ...airway is number one correct ?!
- Could you do a FEV - FEV1 test daily. Every morning carry out airway clearance as normal, every after noon / evening swap between exercise and airway clearance to test the values immediately afterwards?
- CrossFit trial - it took our \*\*\* 3 months to see marked improvement doing CrissFit twice a week.
- crossover trial comparing standard airway clearance, aerobic exercise and controlled breathing (yoga)
- Develop an exercise plan best suited for mucus clearance for various levels of lung health and ability.
- Differentiate on the severity of the CF mutation and focus on CF population sample of those who are 20 to 30 and their exercise practices and those over 50 and their exercise practices. The aim is to see if there is a correlation between exercise and longevity in CF with the 20-30 year-olds as your baseline reference group. I would also like to thank you for all that you do in terms of CF research to make the lives of those of us with the condition better and eventually find a cure or control.
- Exercise should be about teaching people with cf to set short and medium term goals calibrated to their abilities, which require adherence to care to achieve. This is about maximizing health, ability, and quality of life. It also happens to be great for the lungs.
- Get a group who use just a acapella etc and get a group to do exercise for a few weeks. Test lung functions at beginning and end.
- Given that 1 in 88 kids have autism, and that it severely impacts the ability to care for the child's CF, maybe some research into this area. Ways to encourage exercise in a CF/Autism patient. My \*\*\*\* has CF and autism) and can't really understand or follow the rules of organized sporting activities at school or in the community.
- Herbal medication, yoga, arm bike, resistance stretch bands
- High intensity interval training
- High Intensity Interval Training v Extended Cardio v traditional therapies
- HITT training for "well CF" clients.
- I am curious the amount of exercise that would need to be done, daily vs 3x/wk to replace daily AC. What type of exercise is needed and the duration?
- I don't think any exercise could replace or trump hand cpt.
- I don't think exercise can replace airway clearance techniques, because the latter ones work specifically on the lungs. In my opinion we need to include exercise in the basic scheme of therapies and activities to improve patient's wellbeing and lifespan, because it educates the patient to follow a program and organize daily time. Perhaps we can implement a research trial to look into how exercise could be accepted by patients as part of their daily maintenance program (read Cox NS, Cochrane Review, 2013).

- I have a feeling I've read something about this before, but better understanding of exercise with an impact involved (e.g running) over similar efforts without an impact (e.g exercise bike)
- I know it won't go but somehow create a buddy system to working out. It works when others push you along or some level of competitiveness??
- I think a research trial just measuring running vs. airway clearance would be very interesting.
- I think before this study starts we need some outcome measure that works for airway clearance. Otherwise it is hard to prove with no gold standard outcome measure.
- I think regularly doing something like parkruns definitely has an impact on my children's fitness, maybe something in line with that??
- I think that pre / post exercise spirometry both demonstrates the effect of exercise and more precisely identifies trends over time as more data points leads to better averaging. I also think that HRV is an interesting, non-invasive tracing tool that helps understand the effect on our immune / inflammation response to exercise.
- I think the trial would have to be quite long term and include people with a variety of ages, lung functions, and infection status. It's also hard to measure exertion/effort relating to both exercise and airway clearance. To interpret any trial results you'd really need to know how hard people were trying relative to their ability.
- I think this kind of question may best be addressed with longitudinal observational studies and big data analysis.
- I would be very interested to see the flip side of this questionnaire and see why people don't do exercise and airway clearance (is it lack of understanding the importance of it, is it other factors?)
- I would never recommend replacing exercise with a vest treatment. I think both are very important. Ps I'm absolutely LOVING my new \*\*\* vest! I haven't noticed a wheeze or chest tightness like I normally do before treatment times with my regular air vest
- I would suggest maybe trying to just replace a few airway clearance sessions a week with a specific kind of exercise and see if patients do as well as a group that is doing all their airway clearance sessions.
- I'm uncertain about a "replace with" trial - I don't feel we'd be comfortable with the risks of dropping airway clearance for exercise on an experimental basis. Would it be ethical? Anyway, putting that aside... The Swedes do very interesting work with rebounders and sophisticated trampoline routines tailored to CF. An interesting trial might: -- take 100 paediatric patients with similar baseline stats for age/weight/infections/FEV etc. -- give 50 of them a proper rebounder (high-spec, weight-appropriate, covered-springs) like this model [https://www.sport-thieme.co.uk/Therapy-psychomotricity/Physiotherapy/Therapy\\_trampoline/art=1279203](https://www.sport-thieme.co.uk/Therapy-psychomotricity/Physiotherapy/Therapy_trampoline/art=1279203) -- have their team physio give them a routine tailored to CF clearance, based on Swedish models, for them to do twice a day immediately after (or during -- split the trial arm?) clearance. -- monitor compliance -- crunch the data after a year. Did children who added 2x 15 minute daily CF-tailored rebounder routines have fewer infections? Feel better? Better sustained FEV etc.? Total cost in equipment would be <£10K. I bet CF centre physios would be interested and supportive
- If the trial compares twice daily airway clearance with once daily exercise for a specified time and once daily airway clearance, that could aim to demonstrate equivalence
- Investigating sputum collection over time (day, week, month), with each individual doing normal controlled physio, and then combined with low intensity steady state cardio or physio combined with High intensity interval training. Even if the same nebulisers were used but not any of the other physiotherapy devices.
- It would be great to have exercise video
- Let me think about it but yes would have some ideas.
- Long term effects of antibiotics on mental health Citalopram beneficial effects on CFTR salt transfer resulting in decrease in productivity of sputum
- Maybe an online video class where other CFers can join in via video link. Since they can't be within 6ft of each other this is a way to be "with" each other and exercise as well. The more support they have from fellow CFers the better.
- Measure lung function before and after an exercise session, then compare the reading with those taken before and after a physiotherapy session

- Monitor patients partaking in exercise of different sorts from walking to hit and see the fev % improvements over time
- More detailed exercise trackers rather than just step counters to see the type of exercise that benefits.
- My experience is that exercise cannot replace a physio, as a physio carried out a few hours after exercise tends to be extremely effective for airway clearance. However, I feel that my requirement for a physio 24 hours after an exercise session is reduced as this physio tends to be less productive than a normal physio. This is possibly because I have cleared my chest very effectively during the physios shortly after exercise and the following morning.
- Need a way to monitor and track. Maybe with a respiratory incentive device, tracking O2 sats, a way to measure lung volume etc...
- Not directly connected but relevant I think: I would like to see an audit between areas doing percussion & PD with newborns VS areas doing gym ball bouncing with parents and see the difference in infection rates. I strongly believe that influencing/encouraging active physio and exercise from birth is a positive thing and would be interested to see if gym ball bouncing could replace percussion as a standard treatment
- Note: Exercise shouldn't be the only form of chest clearance I feel - techniques such as AD/ acapella reach areas of the lung that are often not reached with exercise alone. AD is targeted to specific areas and is very effective at reaching different levels and depths. I feel the most effective form is a combination of both exercise and standard chest physiotherapy.
- Parkrun + airway clearance techniques Vs airway clearance techniques alone. Effects of a 12 week trial of 1 X 5k run a week (Parkrun) Vs conventional chest treatment
- Perhaps, you could compare FEV1 for patients before starting an exercise regime and after completing an exercise regime after a certain amount of time has passed (e.g, six weeks or two months).
- Phone app, with added section for chest clearance, fit bit to track daily exercise. Two monthly appointments to track lung functions and general health. Over a year.
- Please do a research trial in \*\*\*\*! I'd love to take part in this
- Singing including breathing techniques like a professional singer - stretches lungs/breathing to music so to speak
- So, interestingly enough, this Christmas I slept on an air mattress and my kids jumped and every time someone stepped on air mattress, I had major sputum production. It was very helpful
- Start a new hobby vs airway clearance
- Starting lung function for participants to be similar - variety of sports - trampolining, swimming, self defence, running, cycling and 're measure every month for three months, against airway clearance only and acapella devices
- starting point with patients who have minimal resp symptoms and doing study comparing exs v ACT
- Thank you for researching this issue!
- The best outcome measure that is ideal for studying the effect of various types of exercise on airway clearance is clearance of inhaled radiolabeled isotopes. While this technique is expensive and limited in locations, it is truly THE measure of all forms of airway clearance. I would highly support a smaller trial using this outcome measure to a larger one that looks at less precise/specific outcomes (sputum weight, PFTs, patient report).
- There has been some work at the University of Sydney looking at impact of exercise (treadmill) vs PEP for airway clearance, this used radio-isotopes I believe. They found that exercise moved secretions more centrally but unlike cycles of PEP, no huff or cough was regularly encouraged so no sputum was cleared. There was a theory that the addition of regular huffs and coughs to exercise could be shown to be as effective as ACT alone. Maybe work in conjunction with this group could be of use. Its pretty difficult to find a reliable outcome measure for comparing methods of ACT, so maybe the other option could be to use a similar system to McIlwaine when they compared VEST and PEP and use exacerbations etc as an outcome measure.
- There is so much research on child activity levels and drop out rates from physical activity and school PE etc, body image comes up a lot. We could use existing generic factors of low participation in children and socioeconomic factors that affect children's participation to identify high risk children and put intervention in to make them active individuals. Historically prescribed exercise for various reasons has high drop out



rates we need to make sure CF children enjoy being active because it's fun, or a hobby or makes them feel good, not because it good for their lungs as that will become a factor in teen drop out and rebellion

- Types of exercise
- We recently purchased a mobile spirometer. This would be an ideal way to measure lung function when comparing the 2 groups in the research trial. I can provide additional information if necessary.
- With Orkambi and other similar drugs on the market, will we be able to replace the airway clearance devices with excer
- Would like to be able to quantify the impact of exercise compared with airway clearance techniques. ie: how much of which exercise equates to 30 mins of AC?
- You should only include validated outcomes related to airway clearance
- You would need a way of monitoring adherence to ACT in ACT group, as well as activity monitors for exercise group