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A Randomised Crossover Trial Evaluating the Short-Term Effects of Non-Invasive Ventilation as an Adjunct to Airway Clearance Techniques in Adults with Cystic Fibrosis.

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TITLE PAGE

ARTICLE TITLE

A Randomised Crossover Trial Evaluating the Short-Term Effects of Non-Invasive Ventilation as an Adjunct to Airway Clearance Techniques in Adults with Cystic Fibrosis.

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KEYWORDS

- Non-invasive ventilation
- Airway clearance
- Cystic fibrosis
- Physiotherapy

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KEY MESSAGES

WHAT IS THE KEY QUESTION?

Does the addition of positive pressure support via the use of non-invasive ventilation (NIV) during chest physiotherapy improve sputum clearance for adults with cystic fibrosis (CF) compared to their usual airway clearance technique?

WHAT IS THE BOTTOM LINE?

This research concludes that while NIV has not been shown to be superior to usual ACT, we cannot rule out that it has no clinical benefit especially for patients with lower lung function or who are acutely unwell ~~neither is it inferior,~~ and so it is an important tool to be considered when assessing a person's ACT needs.

WHY READ ON?

This work discusses the outcomes of a randomised controlled cross-over trial investigating the use of NIV with ACT in adults with CF who were inpatients at our CF unitt ~~the trial~~, and the difficulties of conducting research in this patient group; alongside the issues that investigators of ACT face due to the lack of accepted robust outcome measures available at present time.

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A Randomised Crossover Trial Evaluating the Short-Term Effects of Non-Invasive Ventilation as an Adjunct to Airway Clearance Techniques in Adults with Cystic Fibrosis.

ABSTRACT

Introduction – Non-invasive ventilation (NIV) is used in CF to support airway clearance techniques (ACT) by augmenting tidal volumes and reducing patient effort. However, the evidence-base for this is limited. We hypothesised NIV in addition to usual ACT would increase sputum clearance. In addition, we investigated ease of sputum clearance (EoC), work of breathing (WoB) and NIV tolerability.

Methods - CF adults (16+ years) at the end of hospitalisation for a pulmonary exacerbation were randomised to a crossover trial of NIV-supported ACT or ACT alone on two consecutive days. No other changes to standard care were made. The primary outcome was total 24hr expectorated sputum wet weight after the intervention. Spirometry was completed pre and post treatments. Oxygen saturations were measured pre, during and post treatments. EoC and WoB were assessed using visual analogue scales.

Results - 14 subjects completed the study (7 male, mean age 35 (SD 17) years, mean FEV_1 49 (20) %predicted. The difference between treatment regimens was -0.98 (95% confidence interval -11.5 to 9.6; p=0.84) g sputum over 24 hours. During treatment oxygen saturations were significantly higher with NIV-supported ACT (MD 2.01~~1.75~~ (95% CI 0.9~~86~~ to 2.6~~4~~) p=0.0004). No other significant differences were found in post-treatment FEV_1, EoC, WoB, oxygen saturations or subject preference.

Conclusions - There was no difference in treatment effect between NIV-supported ACT and ACT alone, although the study was underpowered. Oxygen saturations were significantly higher during NIV-supported ACT, but with no effect on post-treatment saturations. NIV was well tolerated.

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BACKGROUND

Cystic Fibrosis (CF) is a genetic disorder affecting over 10,000 people in the UK[1]. CF is characterised by the production of thickened bodily secretions, affecting the function of organs such as the pancreas and the lungs due to altered ion transport across cell membranes. Within the lungs, dehydration of the airway surface liquid alters normal mucocillary clearance mechanisms, resulting in airway obstruction, mucus plugging and infections[2]. Recurrent infections and subsequent inflammation are thought to be the major mechanism towards lung tissue damage and the occurrence of fibrosis[3, 4], which decreases lung function, lowers tissue oxygenation and eventually leads to respiratory failure and death. Traditional CF management includes prevention of these complications by optimising removal of airway secretions. Combinations of mucolytic or hydrator therapy to make the secretions less viscous, and chest physiotherapy to mobilise secretions and improve airway clearance are prescribed on an individual basis[5].

There are a range of airway clearance techniques (ACT) available for patients with CF, including breathing methods such as the Active Cycle of Breathing Techniques (ACBT) or Autogenic Drainage (AD), and adjuncts such as Positive Expiratory Pressure (PEP), and oscillatory devices such as the Flutter or Acapella. Selection of the optimal ACT is driven mostly by patient preference and thorough assessment and teaching by a trained physiotherapist[6], as current research indicates no differences in effectiveness of techniques[7], as long as they are performed correctly and regularly. During a pulmonary exacerbation or in end-stage severe disease, breathlessness, fatigue, or excessive secretions can inhibit effective airway clearance. The addition of positive pressure via non-invasive ventilation (NIV) to ACTs has been shown to decrease patient fatigue[8, 9, 10, 11] and respiratory rate during clearance[8, 9, 10]. Improvements in oxygenation[8], respiratory muscle strength[8], lung clearance index[12] and forced expiratory volume in 1 second (FEV_1)[11] have also been reported.

To date, no research has reported an increase in sputum expectorated with the addition of positive pressure; however the ability to augment greater tidal volumes through positive pressure is thought to be a mechanism which could improve sputum clearance. We have previously reported the subjective viewpoints of patients using NIV to support ACT, in which they felt their sputum clearance had increased[13]. The aim of the present study was to investigate this observation objectively by assessing sputum cleared in 24 hours in a randomised cross-over trial of usual ACT versus NIV-supported ACT.

We hypothesised that the inclusion of NIV in addition to a patient's normal airway clearance technique would objectively increase sputum clearance. In addition, we hypothesised that NIV would improve ease of sputum clearance, work of breathing and be well tolerated.

METHODS

Recruitment

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Subjects were recruited from the Adult CF Centre at Royal Brompton Hospital, London. They were eligible to participate in the trial if they had a diagnosis of CF confirmed by standard criteria[14]; were ≥ 16 years old; had been hospitalised for a pulmonary exacerbation which was resolving (by clinician's assessment); had been an inpatient for ≥7 days; and had an established ACT regime. Exclusion criteria included haemoptysis; pneumothorax; dependency on positive pressure support for ACT; history of spontaneous rib fracture; pregnancy; inability to give consent for participation; inclusion in another research study and subjects requiring more than two supervised ACT sessions a day. Discontinuation criteria included voluntary withdrawal from the study, discharge from hospital prior to completion of study or evidence of clinical deterioration during the study that required a change in medical treatment as determined by the CF medical team.

Written informed consent was gained prior to randomisation. Subjects were recruited between July 2013 and May 2017. Ethical approval was granted by the London - Chelsea Research Ethics Committee (reference number 13/LO/0565) and registered on clinicaltrials.gov (reference number NCT01885650).

Treatment

The trial was a randomised cross-over design over two days, with subjects completing one day of their usual ACT regime, and one day of NIV-supported ACT utilising the Breas I-Sleep 25 (Breas Medical AB, Sweden). Randomisation was completed via a computerised programme created by the trial statistician. Subjects were familiarised with NIV-supported ACT prior to randomisation. NIV settings were individually determined by a specialist physiotherapist based upon patient comfort and augmented thoracic expansion for each subject. NIV was administered via a mouthpiece with a Portex® Thermovent® heat and moisture exchange filter (Smiths Medical, UK) within the circuit. During the NIV session subjects completed 10 supported NIV breaths followed by up to four repetitions of the forced expiration technique and coughing as required. During usual ACT subjects completed similar routines of forced expirations and coughs. Subjects received two 30 minute sessions of supervised ACT a day from an adult CF specialist physiotherapist trained in NIV (GS). The same physiotherapist completed 93% of all trial treatment sessions and NIV familiarisation. No other changes to usual clinical care occurred during the trial period. No adverse events occurred during either treatment arm during the trial period.

Outcome Measures

The primary outcome measure was the 24 hour total sputum wet weight expectorated timed from initiation of the first ACT session of a research day to the same time the following day. Secondary outcome measures were qualitative assessment of ease of clearance (EoC), work of breathing (WoB) during clearance and treatment satisfaction using a 10 centimetre Visual Analogue Scale (VAS) (see supplementary material), sputum expectorated during ACT sessions, forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), forced expiratory flow at 25% of FVC (FEF_{25}), forced expiratory flow at 75% of FVC (FEF_{75}), oxygen saturations during and post- ACT. Blinded independent observers completed all the outcome measurements pre-, immediately post and 30 minutes post treatment, and weighed the 24 hour sputum. Oxygen saturations were recorded during the session and downloaded afterwards by the research team. At the end of the study, subjects completed a questionnaire asking their preferences on the different treatment regimes (see

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supplementary material). Spirometry was completed according to the American Thoracic Society/European Respiratory Society guidelines[15] using the Microloop hand held spirometer (CareFusion UK 306 Ltd, Basingstoke, UK. Supplier: Williams Medical Supplies, Rhymney, UK); oxygen saturations were recorded using a Pulsox®-3i oximeter (Konica Minolta, Japan. Supplier: Stowood Scientific Instruments Ltd, Stowood, UK).

Statistical Analysis

A sample size calculation was completed (powered at 80% with 5% significance level) based on assuming a standard deviation (SD) of 7.38g for expectorated sputum, ~~, and a correlation of 0.6~~ which required 28 participants to detect an absolute difference of 4g of sputum. The sample size was calculated using results from a previous RCT on treatment effects[16]. Data was described using mean (SD) or median (range) if non-parametric. Pre- and post-treatment effect was reported using mean differences (MD) and 95% confidence intervals (CI), with paired t-tests completed to analyse significance levels. A p-value of <0.05 was considered significant. An unplanned interim analysis was approved for completion by the London - Chelsea Research Ethics Committee and carried out at the halfway point of recruitment due to slow recruitment and for the determining the feasibility of study completion.

The interim analysis showed that the difference between the two treatment arms was -0.98 (95% confidence interval -11.5 to 9.6; p=0.84) g sputum over 24 hours, with NIV-supported ACT clearing less than usual ACT. Analysis by the trial statistician indicated that based on the true difference in the mean response of the matched pairs of the data collected, the trial would require over 6000 pairs of subjects to be able to reject the null hypothesis that the response difference was zero with probability (power) of 0.8. There was a high (0.05) probability of a type I error associated with this test of the null hypothesis. Due to these results the decision was made to terminate the study early.

RESULTS

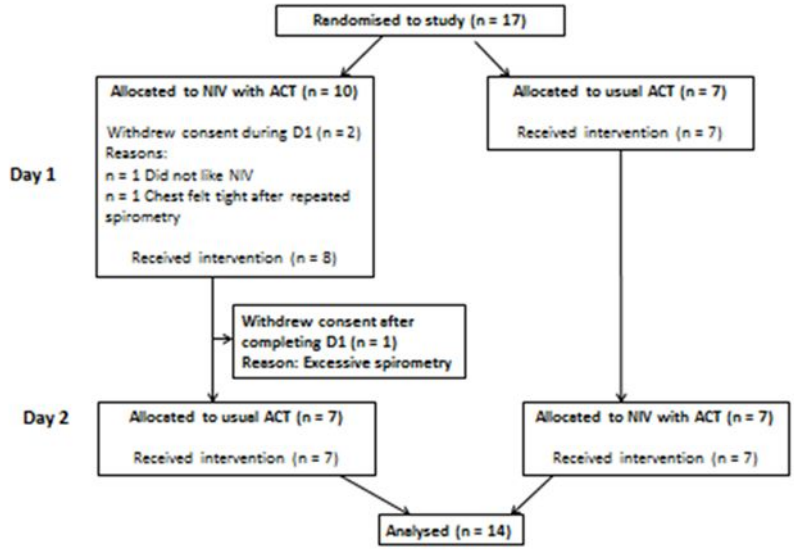
Participant Demographics

14 subjects completed the study, 7 males, mean (SD) age 35.3 (17.1) years with a mean FEV_1 of 48.9 (20) % predicted. Figure 1 illustrates the flow of recruitment and table 1 shows the details of the subject baseline characteristics.

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~~Figure 1: Consort diagram for study~~

T



~~T~~able 1: Participant baseline characteristics

Baseline Characteristics	**n = 14**
Mean age (SD) years	35.5 (17.1)
Sex – female/male	7:7
Mean FEV_1 litres (SD)	1.75 (0.90)
Mean FEV_1 % predicted (SD)	48.9 (20.1)
Mean FVC litres (SD)	2.88 (1.15)
Mean FVC % predicted (SD)	68.4 (18.4)
Genotype; n (%) Homozygous F508del F508del + another mutation 2 other mutations	 7 (50%) 6 (43%) 1 (7%)
Main usual airway clearance technique; n (%) Positive expiratory pressure (PEP) Autogenic Drainage (AD) Oscillatory Device (Flutter®/Acapella®) Active Cycle of Breathing Techniques (ACBT)	 6 (43) 5 (36) 2 (14) 1 (7)
Mucoactive agents; n (%) * DNase	 13 (93)

Hypertonic Saline	4 (29)
Mannitol	4 (29)

FEV_1 – forced expiratory volume in 1 second; FVC – forced vital capacity.
* Some participants were taking more than one mucoactive agent

Treatment details

The median NIV settings were an inspiratory positive airway pressure (IPAP) of 25 cmH_20 (IQR 25-75 24.6-25) and an expiratory positive airway pressure (EPAP) of 5.8 cmH_2O (IQR 25-75 5-6).

A variety of usual ACTs were included, with AD completed by five subjects (36%), PEP by six subjects (43%), an oscillatory device by two subjects (14%) and ACBT by one subject (7%).

Before and after treatment results

No significant differences in sputum (table 2), spirometry, or pre- to post treatment oxygen saturations were found (see supplementary material)

Table 2: Sputum pre-, post- and 30 minutes post-treatment

	Usual ACT Mean (SD)	NIV-Supported ACT Mean (SD)	MD (95% CI)	P-value
Sputum cleared after AM ACT session (g)	12.0 (5.0)	13.0 (6.18)	1.0 (-1.4 to 3.3)	0.41
Sputum total 30 mins after AM ACT session (g)	14.7 (20.6)	14.5 (7.2)	-0.2 (-2.7 to 2.3)	0.86
Sputum total after PM ACT session (g)	35.0 (20.6)	30.6 (15.2)	-4.4 (-12.2 to 3.3)	0.24
Sputum total 30 mins after PM ACT session (g)	36.7 (21.4)	32.6 (15.5)	-4.1 (-12.1 to 4.0)	0.29
Total sputum cleared in 24 hours (g)	49.0 (29.4)	48.1 (30.8)	-1.0 (-11.5 to 9.6)	0.84

Comparisons between regimens

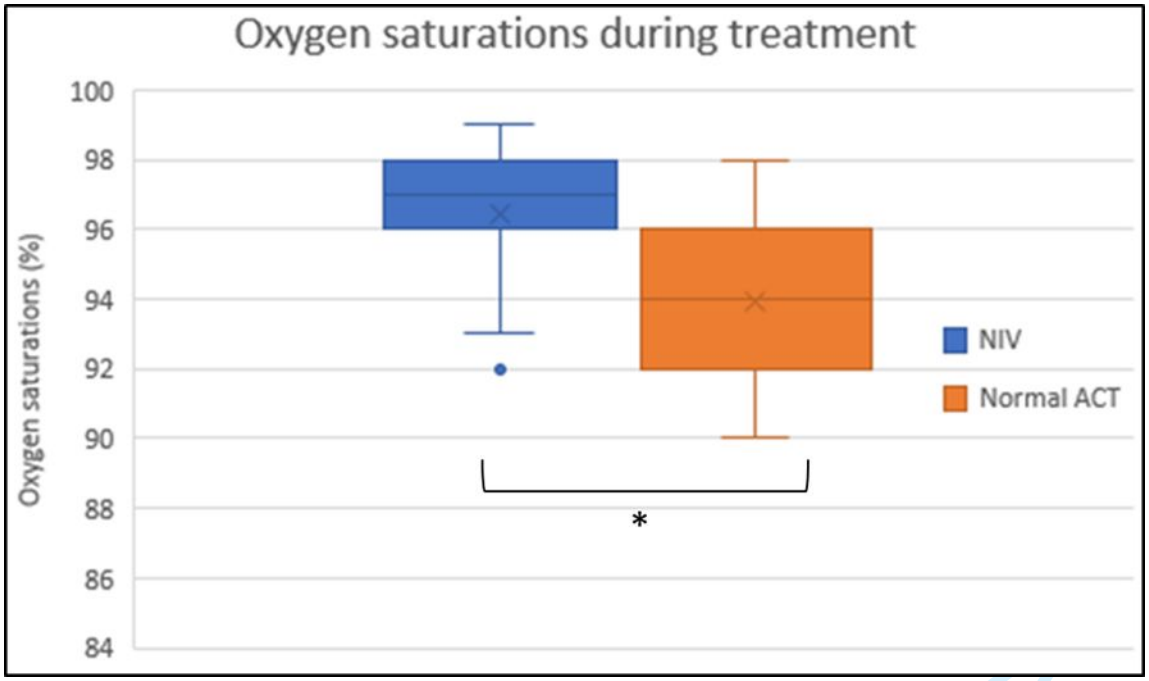
MD between treatment regimens indicated that NIV-supported ACT cleared 1g less sputum over 24 hours (95% CI -11.5 to 9.6) than usual ACT (p=0.84) (table 2). During treatment mean oxygen saturations were significantly higher during NIV-supported ACT (95.7%, SD

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2.3) compared to usual ACT (94%, SD 2.5), MD 2.0~~1.8~~ (0.9 to 2.6 95% CI) (p = 0.004) (fig 2). Post-treatment values for FEV_1 (p = 0.16), FVC (p = 0.97), MEF 25 (p = 0.70) and MEF 75 (p = 0.19) did not differ significantly between the two regimens (see supplementary material). No significant differences in patient reported outcome measures, which included ease of clearance and work of breathing, were found (table 3).

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~~**Figure 2: Oxygen saturations during treatment**~~
~~*p=0.000T4~~



~~T~~**able 3: Participant ease of clearance questionnaire**

Question	Mean (SD) answers		Mean Difference (95% CI)	P value
	NIV-supported ACT	ACT alone		
How easy was it to clear your chest using this technique? (0 most easy, 10 most difficult)	4.0 (2.6)	3.7 (2.2)	-0.3 (-0.9 - 1.5)	0.61

How breathless did you feel during your session using this technique? (0 least breathless, 10 most breathless)	2.7 (2.0)	3.9 (2.0)	1.1 (-2.4 - 0.1)	0.08
How tired did you feel during your physiotherapy session? (0 least tired, 10 most tired)	3.6 (1.8)	4.9 (2.1)	1.4 (-2.9 - 0.2)	0.07
How comfortable did you find this technique? (0 least comfortable, 10 most comfortable)	6.1 (2.2)	6.9 (1.8)	0.71 (-2.4 - 0.9)	0.36
What difference do you think this technique had to your sputum clearance? (0 no difference, 10 most difference)	4.6 (3.0)	4.5 (2.7)	-0.1 (-1.3 - 1.4)	0.91
How would you score this technique overall? (0 worst score, 10 best score)	6.6 (1.4)	6.7 (1.9)	0.1 (-1.5 - 1.4)	0.92

Results of the questionnaire asking subject's opinions of the two techniques were analysed for themes. 8 (57%) subjects had a preference for usual ACT, and 6 (47%) for NIV-supported ACT. The main reasons for preferring usual ACT were that the person was used to it (n = 4) and that the techniques were more portable (n = 3); reasons for preferring NIV-supported ACT included feeling it would be easier when feeling unwell (n = 4), feeling like they got a deeper breath (n = 5) and that deeper deposits of sputum were cleared (n = 3).

DISCUSSION

Airway clearance, especially in severe CF is a complex process and physiotherapists and patients strive to find techniques which are effective, while being easy to perform and low in effort. In this study we tested the hypothesis that the addition of NIV to usual ACT would be more effective in clearing sputum than usual ACT alone.

This study found no significant difference in the primary outcome measure (the amount of sputum cleared in 24 hours) between usual ACT and NIV-supported ACT which is comparable to the results of other studies investigating NIV and ACT[8, 9], and agrees with findings of the recent Cochrane review on NIV for CF[176]. However, the study was significantly underpowered. Additional explanations for concluding no treatment difference include the short-term duration of the intervention and possibly due to NIV-supported ACT being comparable in effect to usual ACTs.

Significant differences were determined in oxygen saturations of the participants during the ACT session, with subjects having higher saturations when using NIV, although it can be argued that a 2% difference in oxygen levels is not a clinically relevant difference. We~~, however, we~~ also did not demonstrate a carry-over of these improvements after the session unlike Holland et al[8]. During ACT sessions oxygen saturations are an important clinical consideration when completing ACT, especially with more acutely unwell patients or those

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with advanced lung disease and it may be that this is an area where NIV-supported ACT has a role.

Airway clearance research has been debated within the physiotherapy, CF and wider research community as lacking in a robust outcome measure which appropriately measures the effect of ACT. Sputum weight has been criticised as being a subjective measure, based on the will of the subject to expectorate and at risk of contamination with saliva which would alter results[6, 18~~7~~]. FEV_1 is thought to be difficult to use as a short-term outcome due to its effort dependency and lack of sensitivity to small changes[6, 7, 18~~7~~, 19~~8~~]. This may explain why we found no significant differences in FEV_1 and other spirometric measures during this study. There was a slight trend for an increase in FVC after NIV supported ACT, especially in the morning session, and although this did not reach statistical significance it may make NIV support a viable consideration in patients with loss of lung volume.

An alternative outcome measure which has been suggested is the lung clearance index (LCI) which is derived from multiple breath washout. One recent study comparing NIV-supported ACT with PEP used the lung clearance index as an outcome measure, and reported a significant reduction (improvement) in LCI when subjects used NIV compared to PEP[12]. Their study provides support for this outcome measure, although other published research investigating ACTs with LCI as an outcome have reported variable LCI results[20~~19~~].

A key aspect of ACT is the patient's own perspective, as fundamentally it is the patient who will be required to complete the technique daily. Using our self-designed questionnaires subjects reported that NIV-supported ACT did not differ significantly from their usual ACT in terms of ease of clearance, breathlessness, comfort or fatigue. There were trends for lower reported levels of breathlessness and fatigue with the use of NIV, but these did not reach significance. This differs from our previously reported results where subjects did subjectively rate NIV-supported ACT significantly higher for ease of clearance and reduced effort[13], however those results were from a more severe patient group (median FEV_1 26%) over a 1-year period. Several of the participants of the current study commented that they felt NIV would be useful for them if they were more unwell, breathless or unable to expectorate, as they felt it would be more supportive at that time which may then provide more comparable data. This suggestion has been supported by Moran et al[16] in their recent Cochrane review and may be where NIV supported ACT has a role. A consideration for future ACT studies is the timing of the intervention for maximal effect, as our subjects were nearing the end of admission with many of them feeling very well which may have reduced the effect of ACT. However, it is noted that studying more unwell patients would have its own difficulties in terms of need for treatment changes and ethical considerations.

This study has several limitations, firstly the low participant numbers which resulted in early termination of the study. Recruitment, even on a busy CF unit, was difficult due to tight inclusion criteria, especially the need to be stable and at the end of a hospital admission. Clinical practice and patient preference for early discharge meant that often these patients were sent home to complete their intravenous antibiotics, rendering them unable to complete the study. These difficulties, led to a long recruitment time for the study which was not ideal. Recently O'Neill et al[21 ~~20~~] reported similar difficulties with recruitment and participant inclusion in their work looking at timing of hypertonic saline and ACT, again

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resulting in early termination of the study. In our clinical practice NIV is considered to support ACT in CF patients advanced lung disease who are struggling with their usual ACT. In order to replicate this practice in this study we would have needed to only include patients with a low FEV_1, however due to recruitment we included all FEV_1 ranges, which may explain why differences with NIV were not identified, as patients with good lung function probably do not require the assistance of NIV to aid them taking deep breaths. Another limitation, particularly in the subjects with higher lung function, was the limit of positive pressure support the Breas I-Sleep 25 could offer, often these participants were asking for more pressure for a deeper breath which the NIV was unable to provide. We included all ACT techniques to compare against NIV-supported ACT - this decision was taken to ensure familiarity of technique to the patient – but in doing so we accept this introduced more variability in the control arm. It may be that NIV-supported ACT is more effective than some usual ACTs, for example PEP as described by Rodriguez Hortal et al[12], but due to our low numbers it was not possible to analyse techniques separately.

Although the study was underpowered, we believe it provides important insights into the role of NIV-supported ACT. A recent review of the UK's national data registry has shown that NIV use is increasing with beneficial effects on lung function decline[22] and so research investigating the optimal use of NIV for our patients remains essential. From this study w~~W~~e cannot provide definitive conclusions about efficacy, but NIV was well tolerated and improved oxygenation during the intervention. NIV – for select patients – is likely to be where it fits but further studies are required. With careful clinical consideration, we suggest it should be included in the specialist CF physiotherapist's airway clearance 'toolbox,' as concluded by Moran et al[176]. Low participant numbers and insensitive outcome measures are well recognised problems of ACT trials[7, 187, 198, 210, 231]. Our work provides important context for future ACT trial design as more robust outcome measures need to be developed. Further work needs to be done with these more robust outcome measures to optimise power so that we can better understand who will benefit from this intervention and when it should be introduced.

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Conflicts of interest – Gemma Stanford, Diana Bilton, Winston Banya, Helen Parrott and Penny Agent have no conflicts of interest to report. ~~Winston Banya and~~ Nicholas Simmonds has consulted for Vertex Pharmaceuticals, Chiesi, Roche, Pulmocide, PTC Therapeutics and Gilead~~....~~.

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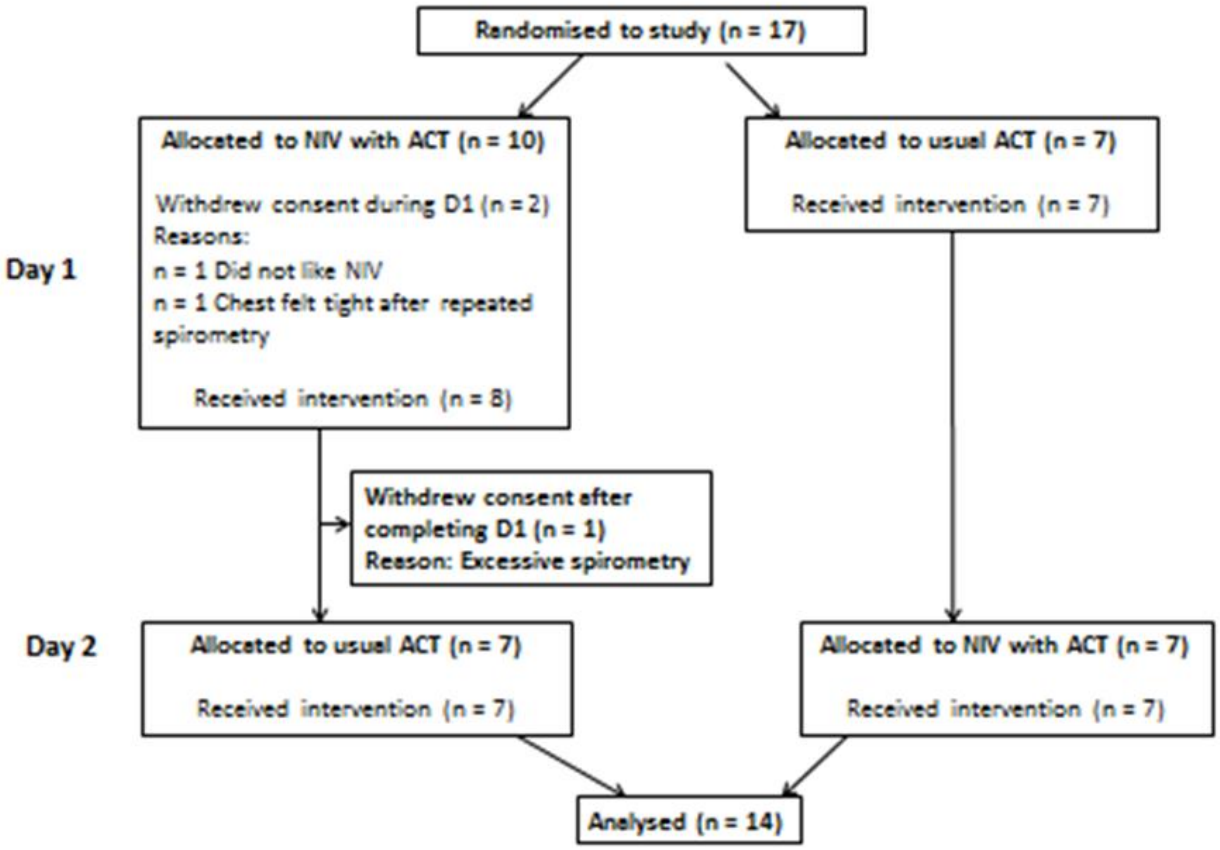
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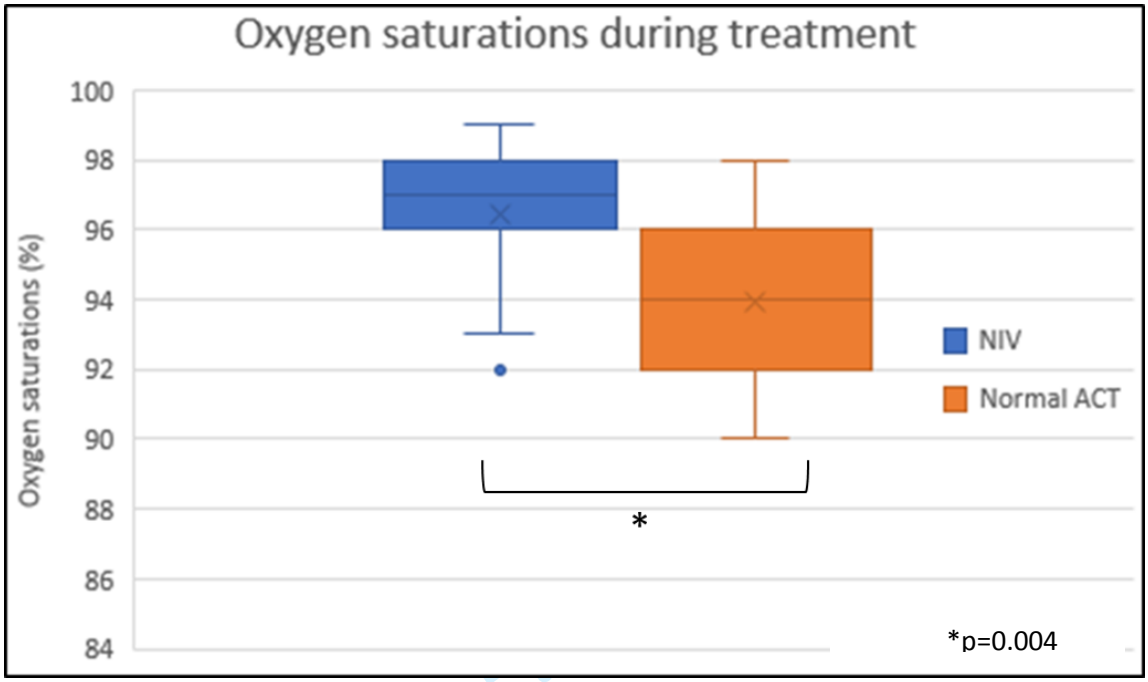
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SUPPLEMENTARY MATERIAL 1

Table: Spirometry and oxygen saturations before and after morning and afternoon treatments

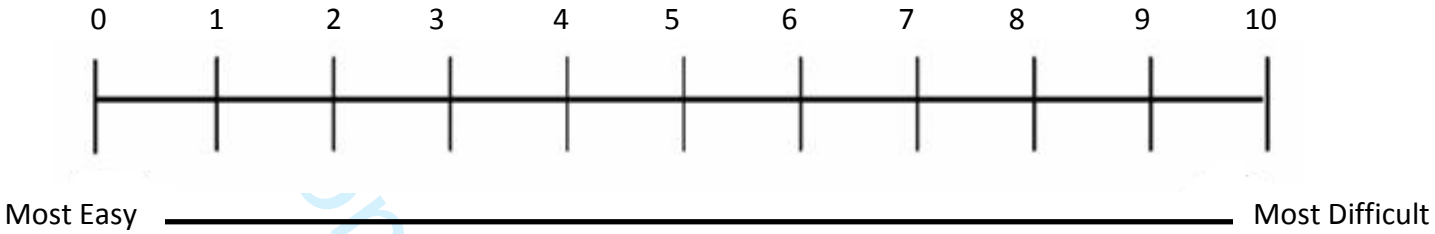
	NIV Supported ACT (n=14)				Usual ACT (n=14)			
	Baseline	**Post**	**MD (95% CI)**	**P value**	**Baseline**	**Post**	**MD (95% CI)**	**P value**
Morning Results								
Mean (SD) FEV_1% pred (%)	49.0 (19.9)	49.2 (18.8)	0.2 (-1.9 to 1.4)	0.78	48.9(20.0)	48.4 (19.4)	-0.5 (-1.1 to 2.1)	0.5
Mean (SD) FVC% pred (%)	68.1 (18.7)	71.9 (16.7)	3.8 (-7.7 to 0.1)	0.06	68.9 (18.77)	70.3 (15.5)	1.4 (-4.3 to 1.5)	0.31
Mean (SD) MEF 25% pred (%)	34.3 (20.9)	33.1 (20.5)	-1.1 (-1.4 to 3.7)	0.35	31.9 (21.7)	33.6 (21.2)	-0.6 (-1.4 to 2.7)	0.51
Mean (SD) MEF 75% pred (%)	17.3 (10.3)	16.1 (9.2)	-1.2 (-0.9 to 3.3)	0.24	15.4 (8.9)	15.9 (10.1)	0.5 (-2.0 to 1.0)	0.47
Mean (SD) oxygen saturations (%)	94.9 (2.7)	93.3 (2.3)	-0.5 (-0.9 to 1.9)	0.45	93.9 (2.8)	94.4 (2.5)	0.5 (-1.4 to 0.4)	0.26
Afternoon Results								
Mean (SD) FEV_1% pred (%)	49.6 (18.9)	50.8 (19.1)	1.1 (-3.7 to 1.4)	0.35	48.9 (19.2)	48.9 (18.0)	0.0 (-1.34 to 1.34)	1
Mean (SD) FVC %pred (%)	69.6 (16.9)	70.4 (16.5)	0.9 (-3.0 to 1.3)	0.40	71.1 (17.6)	72.1 (16.9)	1.1 (-4.0 to 1.8)	0.44
Mean (SD) MEF 25 %pred (%)	34.1 (22.8)	34.4 (23.3)	0.3 (-2.9 to 2.4)	0.82	34.4 (19.9)	33.1 (20.2)	-1.3 (-0.3 to 2.8)	0.10
Mean (SD) MEF 75 %pred (%)	15.9 (10.2)	16.1 (9.4)	0.2 (-2.8 to 2.4)	0.86	16.1 (9.6)	14.5 (7.2)	-1.6 (-0.6 to 3.9)	0.13
Mean (SD) oxygen saturations (%)	94.9 (2.7)	94.5 (2.7)	-0.4 (-0.3 to 1.1)	0.29	94.3 (2.4)	94.0 (3.0)	-0.3 (-0.7 to 1.3)	0.56

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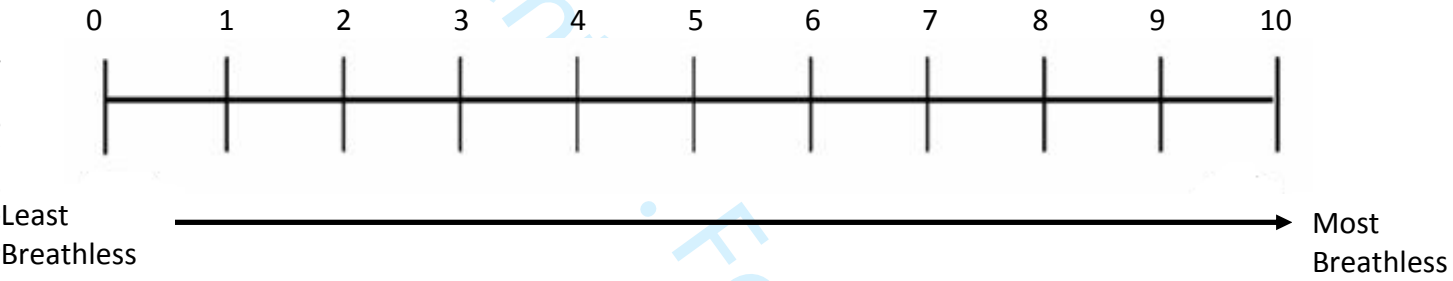
ARTICLE TITLE – A Randomised Crossover Trial Evaluating the Short-Term Effects of Non-Invasive Ventilation as an Adjunct to Airway Clearance Techniques in Adults with Cystic Fibrosis

Supplementary Material 2 - Patient Satisfaction Questionnaire

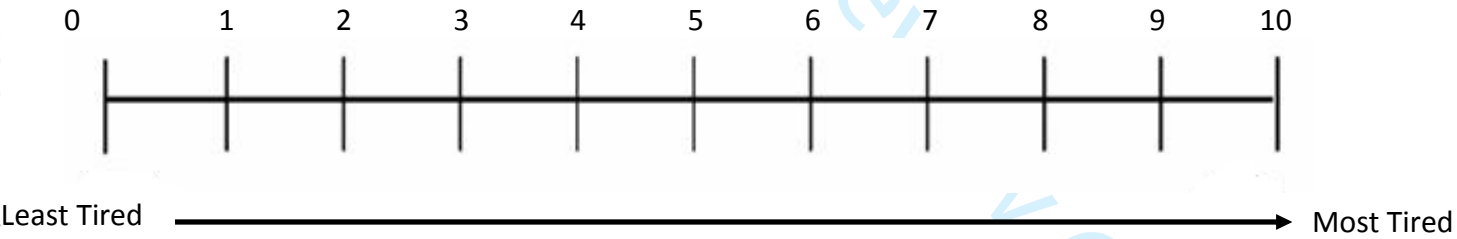
How easy was it to clear your chest using this technique?



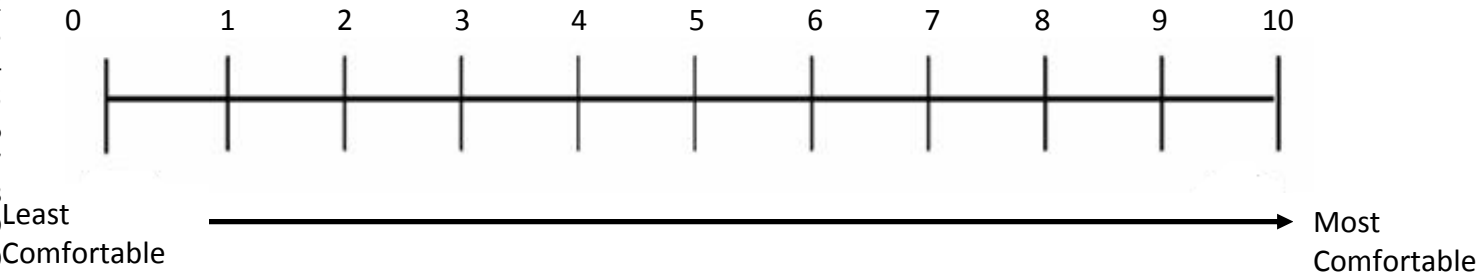
How breathless did you feel during your session using this technique?



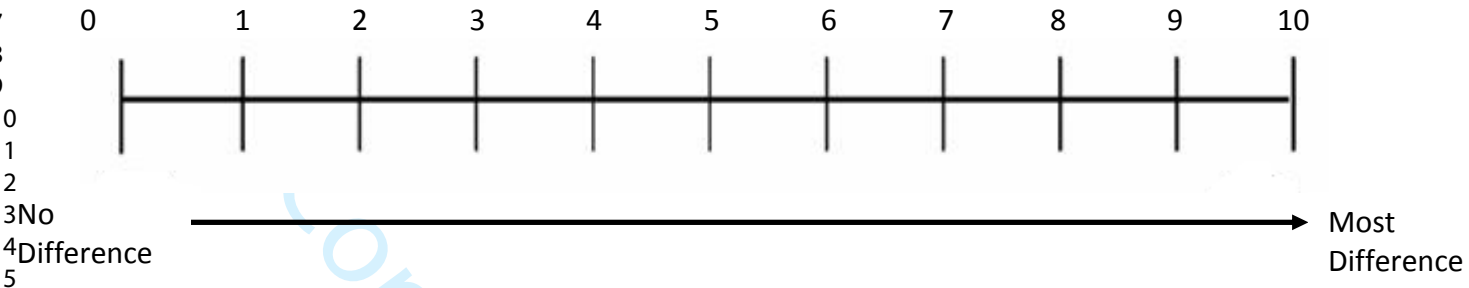
How tired did you feel during your physiotherapy session?



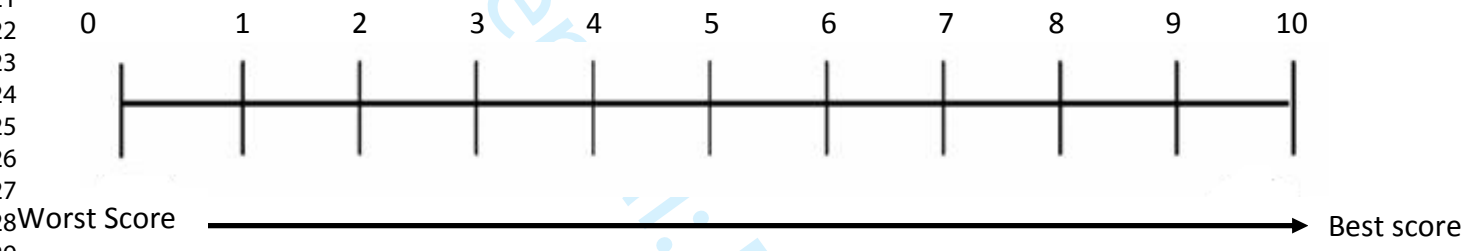
How Comfortable did you find this technique?



What difference do you think this technique had to your sputum clearance?



How would you score this technique overall?



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ARTICLE TITLE – A Randomised Crossover Trial Evaluating the Short-Term Effects of Non-Invasive Ventilation as an Adjunct to Airway Clearance Techniques in Adults with Cystic Fibrosis

Supplementary Material 3 – Patient Preference Questionnaire

1. a) What was your preferred physiotherapy technique (Usual physiotherapy or using NIV?)

b) Why was this your preferred physiotherapy technique?

2. If you prefer using NIV to your usual physiotherapy technique, what do you think this adds to your current physiotherapy regime?

3. If you prefer your current regime to using NIV with physiotherapy, why is this?

4. a) Which technique (using NIV or your usual physiotherapy) do you think cleared the most sputum?

b) Why do you think it cleared the most sputum?

5. Any other comments?

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