Web-based physical activity promotion in young people with CF: a randomised controlled trial

Dr Narelle S Cox[1,2]	narelle.cox@monash.edu
Dr Beverley Eldridge[3,4]	bev.eldridge@outlook.com
Sarah Rawlings[1,5]	Sarah.Rawlings@monashhealth.org
Julianna Dreger[1]	jdreger@ucalgary.ca
Jennifer Corda[6]	jen.corda@rch.org.au
Jennifer Hauser[7]	jenny.hauser@ths.tas.gov.au
Dr Brenda Button[8,9,10]	b.button@alfred.org.au
Jennifer Bishop[11]	Jennifer.Bishop@health.nsw.gov.au
Amanda Nichols[5]	amanda.nichols@monashhealth.org
Dr Anna Middleton[12]	anna.middleton@health.nsw.gov.au
Dr Nathan Ward[13]	Nathan.Ward2@sa.gov.au
Dr Tiffany J Dwyer[14]	tiffany.dwyer@sydney.edu.au
Dr Ruth Dentice[15]	ruth.dentice@health.nsw.gov.au
Raynuka Lazarus[11]	Raynuka.Lazarus@health.nsw.gov.au
Dr Paul O'Halloran[3]	p.ohalloran@latrobe.edu.au
Joanna YT Lee[1]	joanna.lee2@monash.edu
Christie Mellerick[1]	christie.mellerick@monash.edu
Dr Kelly A Mackintosh[16]	k.mackintosh@swansea.ac.uk
Dr Melita A McNarry[16]	m.mcnarry@swansea.ac.uk
Prof Craig Williams[17]	c.a.williams@exeter.ac.uk
Prof Anne E Holland[1,2,8]	anne.holland@monash.edu

On behalf of Youth Activity Unlimited – A Strategic Research Centre of the UK Cystic Fibrosis Trust award #008. The funders had no involvement in the research.

1. Respiratory Research@Alfred, Monash University, Melbourne Australia

2. Institute for Breathing and Sleep, Melbourne Australia

3. College of Science, Health and Engineering, La Trobe University, Melbourne Australia

4. Children's Medical Research Institute, Melbourne Australia

5. Monash Health, Melbourne Australia

6. Physiotherapy, Royal Children's Hospital, Melbourne Australia

7. Tasmanian Adult CF Service, Royal Hobart Hospital, Hobart Australia

8. Physiotherapy, Alfred Health, Melbourne Australia

9. Allergy, Immunology and Respiratory Medicine, Alfred Health, Melbourne Australia

10. Faculty of Medicine, Monash University, Melbourne Australia

11. Respiratory Medicine, Westmead Hospital, Sydney Australia

12. Physiotherapy, Sydney Children's Hospital Network– Westmead, Sydney Australia

13. Physiotherapy, Royal Adelaide Hospital, Adelaide Australia

14. Discipline of Physiotherapy, Sydney School of Health Sciences, Faculty of Medicine and Health, University of Sydney, Sydney Australia; Respiratory Medicine, Royal Prince Alfred Hospital, Sydney, Australia

15. Physiotherapy, Royal Prince Alfred Hospital, Sydney Australia

16. Applied Sports, Technology, Exercise and Medicine Research Centre, Swansea University, Swansea Wales

17. Children's Health & Exercise Research Centre, University of Exeter, Exeter UK

**Corresponding author:

Dr Narelle S Cox

Monash University & Institute for Breathing and Sleep

Level 6 The Alfred Centre, 99 Commercial Road

Melbourne Victoria 3004 Australia

Email: narelle.cox@monash.edu

Phone: + 61 3 9903 0134

Fax: +61 3 9903 0556

Author contributions:

Procured funding: CAW, AEH, KAM, MAM, NSC, PO'H

Conceptualisation and design: NSC, AEH, PO'H

Data acquisition: NSC, JD, BE, SR, JC, AN, BB, JH, JB, RL, RD, TJD, AM, NW, JYTL, CM

Data analysis: NSC, AEH, KAM, MAM

Drafting manuscript: NSC, AEH

Critical review of manuscript: JD, BE, SR, JC, AN, BB, JH, JB, RL, RD, TJD, AM, NW, P'OH, JYTL, CM, KAM, MAM, CAW

Funding:

Funding for this trial was from a competitive UK Cystic Fibrosis Trust Strategic Research Centre (SRC) grant award #008.

Data sharing statement:

Will individual participant data be available (including data dictionaries)? Yes

What data in particular will be shared? Individual participant data can be shared after de-identification and once approval has been obtained from the relevant Human Research Ethics Committee.

What other documents will be available? Study protocol

When will data be available (start and end dates)? Data will be available indefinitely on a case by case basis, at the discretion of the co-ordinating principal investigator and relevant Human Research Ethics Committee.

With whom? Data will be available on a case by case basis, at the discretion of the co-ordinating principal investigator and relevant Human Research Ethics Committee.

For what types of analyses? Type of analysis data will be available for will be at the discretion of the relevant Human Research Ethics Committee.

By what mechanism will data be made available? Data requests should, in the first instance, be addressed to Professor Anne Holland (anne.holland@monash.edu). Access to data will be subject to approval by the co-ordinating principal investigator and relevant Human Research Ethics Committee.

Abstract

Background: Physical activity levels are known to decline following hospitalisation for people with cystic fibrosis (pwCF). However, optimal physical activity promotion strategies are unclear. This study investigated the effect of a web-based application (ActivOnline) in promoting physical activity in young pwCF.

Methods: Multi-centre RCT with assessor blinding and qualitative evaluation. People with CF (12-35 years) admitted to hospital for a respiratory cause were eligible and randomised to the 12-week ActivOnline intervention (AO) or usual care (UC). The primary outcome was change in device-based time spent in moderate-to-vigorous physical activity (MVPA) from baseline to post-intervention. Follow-up was at six-months from hospital discharge when qualitative evaluation was undertaken.

Results: 107 participants were randomised to AO (n=52) or UC (n=55). Sixty-three participants (59%) contributed to the intention to treat analysis. Mean (SD) age was 21(6) years (n=46 <18years). At baseline physical activity levels were high in both groups (AO 102(52) versus UC 127(73) mins·day^{-1}). There was no statistically significant difference in MVPA between groups at either time-point (post-intervention mean difference (MD)(95%CI) -14 mins(-45 to 16)). Uptake of the intervention was low with only 40% (n=21) of participants accessing the web-application.

Conclusion: A web-based application, including individualised goal-setting, real-time feedback, and motivation for behaviour change, was no better than usual care at promoting physical activity in young pwCF following hospital discharge. High levels of baseline physical activity levels in both groups, and limited engagement with the intervention, suggest alternative strategies may be necessary to identify and support young pwCF who would benefit from enhanced physical activity.

Abstract word count: 246 of 250 words

Key message:

What is already known on the topic?

Greater physical activity participation is associated with improved health outcomes for people with CF; however, many people with CF do not meet physical activity guideline recommendations, and physical activity participation is known to decline after respiratory exacerbation.

What this study adds?

A web-based application, including individualised goal-setting, real-time feedback, and motivation for behaviour change, was no better than usual care at promoting physical activity in young people with CF following hospital discharge.

How this study might affect research, practice or policy?

This is the first RCT to describe a technology-based strategy to promote physical activity in young people with CF; the negative findings described highlight important therapeutic considerations for clinicians in light of increasing use of remotely delivered interventions in response to restrictions associated with COVID-19.

Manuscript word count: 3041

Reference list: 35 out of 40

Keywords

Paediatric

Telehealth

Adults

Exercise

Internet

Rehabilitation

Manuscript

INTRODUCTION

Physical activity and exercise participation confers benefits for people with Cystic Fibrosis (CF), including improved cardiovascular and bone health, enhanced blood glucose control, clearance of pulmonary secretions and relief of breathlessness.[1] International treatment guidelines for CF recommend regular physical activity and exercise participation[2] as higher levels of activity and aerobic fitness have been related to reduced hospitalisation,[3] slower rate of lung function decline,[4, 5] and increased life expectancy.[6] Despite the favourable health outcomes for people with CF associated with physical activity participation, adherence to activity recommendations is often poor with commonly cited barriers including a lack of interest, energy or time.[7]

In CF, higher physical activity levels have been associated with reduced need for hospitalisation,[3] and decreased systemic inflammation post-exacerbation.[8] However, in the period immediately following hospitalisation, physical activity levels have been shown to decline by over 50%.[3] Despite clear associations between low physical activity levels and adverse clinical outcomes, few interventions promoting physical activity have been tested in randomised controlled trials,[9] and none have targeted the period following hospitalisation for a respiratory exacerbation. Small cohort studies of relatively short duration, provide limited evidence that interventions to promote exercise and/or physical activity using technology are feasible and acceptable to both children[10] and adults[11, 12] with CF. In an 8-week pilot study in 10 young adults with CF, a technology-based intervention to promote physical activity participation, that incorporated behaviour change strategies, was feasible and acceptable to participants, with the majority (70%) identifying the ideal time to use such a program as during or immediately after hospital admission for a respiratory exacerbation.[12] As a result of the intervention, there was some improvement in daily activity (step count) (mean difference 2050 steps (95%CI -1230 to 5330) but this was not statistically significant and limited by the small sample size.[12] Whether a technology-based intervention to promote physical activity can improve activity levels in people with CF following a respiratory exacerbation is unclear.

The aim of this study was to investigate the effect of a web-based application (ActivOnline) in promoting physical activity in young people with CF. We also sought to evaluate the effect

of such a technology-based intervention, undertaken in the period immediately following hospitalisation, on key clinical outcomes, including: health-related quality of life (HRQoL); psychological wellbeing; lung function; sleep quality; exercise capacity and healthcare utilisation. Additionally, we wished to understand participant attitudes toward physical activity and their experience of the intervention.

METHODS

Study design & participants

This multi-site randomised controlled trial, with assessor blinding and embedded qualitative evaluation, was undertaken at eight CF centres in Australia (see Supplementary Material). The Alfred Health Human Research Ethics Committee approved the study for all sites, with governance approvals obtained from participating sites. The trial was registered prospectively (ACTRN12617001009303, July 13 2017) and the trial protocol published.[13] Participants were recruited during a hospital admission for a respiratory cause. Full details of eligibility requirements, and inclusion and exclusion criteria have been published previously[13] and are described in the online supplement. Initially, only adolescents with CF (12 to 24 years)[14] were included in the trial, however, due to slower than anticipated recruitment over the first 12 months and following approval of a protocol amendment in October 2018, recruitment was opened to individuals up to age 35 years. Therefore, the study findings will also be applicable to young adults,[15] with both adolescence and young adulthood corresponding to key life stages where changes in physical activity behaviour are known to occur.[16] All participants and/or their carer provided written informed consent.

Randomisation and masking

Participants were randomised 1:1, to the usual care control group or to the technology-based intervention 'ActivOnline', using a computer-generated block scheme with stratification for recruitment site and school enrolment status (fulltime primary or secondary school enrolment versus not in fulltime schooling). The randomisation sequence was generated by an individual independent of the study. Participants were advised of their group allocation by a researcher independent of their clinical care team. All outcome assessments were completed by an assessor blind to group allocation.

Study procedures

Participants were recruited during their inpatient stay and completed baseline questionnaires and collection of demographic information prior to hospital discharge. Baseline physical activity monitoring was undertaken during the first week following hospital discharge, prior to randomisation. Follow-up assessments were completed post the 12-week intervention period, and at 6-months from hospital discharge. Post-intervention and 6-month follow-up assessments were completed in-person at the site of recruitment in conjunction with a scheduled clinic appointment, or remotely via post where assessment did not coincide with a clinic visit, to ease participant burden.

All participants received usual care and were provided with information, via a web-link, on age-appropriate recommendations for being physically active. In addition, participants randomised to the intervention (ActivOnline) group were provided with individualised access (username and password) to a secure web platform (www.activonline.com.au). Details of the previously piloted intervention have been published elsewhere,[12, 13] with additional details available in the Online Supplementary Material. In brief, the web-platform was used to record and monitor physical activity, and set goals, for the 12-week intervention period. Data entered were updated in real-time and feedback presented in graphical display (Online supplement Figure S1). ActivOnline could be accessed from any internet-enabled device. Participants were free to choose the frequency with which they logged their activity, but received an email reminder notification after three days of no-activity.

Outcomes

The primary outcome, as recommended for the assessment of physical activity in people with CF,[17] was change in device-based average daily moderate-to-vigorous physical activity (MVPA) from baseline to the end of the 12-week intervention period (ActiGraph Link, ActiGraphcorp LLC, Pensacola FL, USA). Secondary outcomes (see Online Supplement) included measures of physical activity (self-reported), self-determination for exercise, health-related quality of life (HRQoL), psychological well-being, exercise capacity (modified shuttle test) and lung function. All participants were offered the opportunity to participate in a semi-structured qualitative interview, in order to examine attitudes to physical activity and experiences of the intervention (Online Supplement and Table S1). Interviews were undertaken by the blinded assessor following the 6-month follow-up assessment, either in-person or over the telephone. Healthcare utilisation (hospital admissions and hospital days)

were assessed from the medical record at 12 months following completion of the intervention period.

Analysis

Sample size calculations indicated that 56 participants (28 in each group) were required. This was based on a between-group difference of 20 mins·day^{-1} MVPA, with a standard deviation of 26, to achieve 80% power, with alpha set at 0.05.[3] Whilst it was planned to randomise 75 participants, allowing for 25% drop-out, recruitment was extended beyond this initial target due to poorer than anticipated rate of return of activity monitoring devices used for assessment of the primary outcome measure over the first 18 months of the trial.[13]

Statistical analyses were conducted using IBM SPSS statistics (Version 26.0; IBM Corp. Armonk, NY). All data were analysed by intention-to-treat (ITT). A post hoc per protocol analysis was also undertaken to assess whether there were effects in those who received the intervention. Differences between groups for change over time were analysed with linear mixed models, accounting for recruitment site. Models included treatment group, time, group×time interaction and a random effect for participants. The baseline value of the outcome variable was included as a covariate. A per protocol analysis of participants who did versus did not achieve age-recommended daily physical activity levels was intended, but there were insufficient numbers of participants who did not achieve these targets.

Qualitative interviews were audio-recorded and transcribed verbatim. Two authors (NSC, JYTL) undertook independent line-by-line iterative thematic analysis of de-identified interview transcripts[18] Data analysis was in accordance with the six steps for ensuring trustworthiness of qualitative data identified by Nowell and colleagues[19]: data familiarization; initial code generation; searching for themes; reviewing themes; defining themes; and describing findings. Initial stages of data analysis, including development of codes and themes, was undertaken independently. Development of overarching themes was determined by discussion, with consideration of predominant themes and subthemes, until a consensus was achieved. A third author (AEH) was available for arbitration if necessary.[20] See also Online Supplement.

RESULTS:

Between September 2017 and February 2020, 109 participants, from 549 potentially eligible hospital admissions, were recruited (20%). In total, 107 participants were randomised (Figure 1). Two participants changed their mind about study participation between consenting and undertaking the baseline assessment. At the conclusion of the trial, data were available for 63 participants (59%) for the primary outcome (intervention: n=29 (56%); control: n=34 (62%)). There were no intervention-related adverse events reported by any participants. There was one instance of server failure, resulting in participants being unable to access the web-portal, which was resolved inside 24 hours.

Participant characteristics are presented in Table 1. The mean (standard deviation (SD)) age of participants was 21(6) years with 46 participants (43%) aged younger than 18 years. At baseline, percent predicted forced expiratory volume in one second (FEV_1) was higher in the control group (control group: 72(20) %predicted; intervention group: 63(24) %predicted. Thirty-four participants (32%) were prescribed modulator therapy, 55 (51%) were homozygous for ΔF508.

Table 1. Participant characteristics at baseline

	ActivOnline Intervention n=52	**Usual care control n=55**
Age, years	21 (7)	20 (6)
Age <18 years, n (%)	22 (42%)	24 (44%)
Male/female, n	24 / 28	23 / 32
FEV_1, L	2.2 (1.0)	2.5 (0.9)
FEV_1, %predicted	63 (24)	72(20)
FVC, L	3.3 (1.3)	3.5 (1.1)
FVC, %predicted	78.4 (20.4)	86.7 (17.1)
Height, cm	166 (13)	164 (10)
Weight, kg	57 (15)	56 (12)
BMI, $kg \cdot m^{-2}$	21 (3)	21 (3)
CFRD, n (%)	21 (40%)	18 (33%)
Genotype, n (%)		
- ΔF508 homozygous	33 (63%)	32 (58%)
- ΔF508 heterozygous	17 (33%)	19 (35%)
- other	2 (4%)	3 (5%)
- unknown	0	1 (2%)
Modulator therapy, n(%)	22 (42%)	12 (22%)

Full Time school attender, n (%)	18 (35%)	26 (47%)
MVPA, mins·day^{-1}	102 (52)	127 (73)
HAES		
Weekday hrs active	3 (3)	3 (3)
Weekend hrs active	3 (4)	2 (3)
CFQ-R		
Respiratory domain	53 (25)	56 (22)
Physical	55 (29)	59 (28)
Treatment	50 (23)	49 (21)
Vitality	45 (20)	42 (19)
HADS anxiety	6 (4)	7 (5)
Case*, n (%)	9 (17)	13 (24)
HADS depression	4 (3)	4 (4)
Case*, n(%)	3(6)	6(12)
CES-D	17 (11)	16 (11)
Case¥, n(%)	20 (38)	25 (45)
PSQI	7 (4)	7 (4)
No case, n(%)	32	21
Case§, n(%)	18	29
BREQ-2		
Amotivation	0.5 (0.8)	0.4 (0.7)
External regulation	1.0 (1.0)	0.8 (0.8)
Introjected regulation	1.1 (1.1)	1.3 (1.2)
Identified regulation	2.4 (1.0)	2.7 (1.0)
Intrinsic regulation	2.3 (1.3)	2.2 (1.2)

LEGEND: Data are Mean (SD) unless indicated
n, number; hrs, hours; CF, cystic fibrosis; FEV_1, forced expiratory volume in one second; L, litres; %predicted, percentage of predicted normal; FVC, forced vital capacity; BMI, body mass index; CFRD, cystic fibrosis related diabetes; MVPA, moderate-to-vigorous physical activity; HAES, habitual activity estimation scale; CFQ-R, cystic fibrosis questionnaire – revised; HADS, hospital anxiety and depression scale; CES-D, centre for epidemiological studies depression scale; PSQI, Pittsburgh sleep quality index; BREQ-2, behavioural regulations in exercise questionnaire.
*HADS case definition score ≥11; ¥CES-D case definition score ≥16; §PSQI case definition score >5

Use of the online intervention (ActivOnline) was variable. Of the 52 participants allocated to the intervention group, only 21 (40%) logged on to the web-application (Table S5 and Table S6). Participants logged a total of 633 entries to the ActivOnline platform (range 1 to 179 entries per participant), however individualised goal-setting was rarely completed.

The ITT analysis found no significant difference between groups for time spent in MVPA from baseline to either post-intervention, or at the 6-month follow-up (Table 2). There were no within-group differences in MVPA from baseline to either time-point (Figure 2). Similar findings were seen in the per protocol analysis (Table S7).

Post-intervention there were no between-group differences for HRQoL (CFQ-R), psychological well-being (CES-D, HADS), self-reported physical activity (HAES), sleep quality (PSQI) or lung function (Table 2). Post-intervention, better external motivation for exercise favoured the intervention group (mean difference (MD) 0.6 points, 95% confidence interval (CI) 0.1 to 1.1); however intrinsic motivation for exercise was poorer in the intervention group (MD -0.8 points (95%CI -1.2 to -0.3; Table 3). At the 6-month follow-up, change scores on the role function domain of the CFQ-R (MD -22.6 points (95%CI -34.1 to -11.1)) and self-reported weekday active hours (MD -1.9 hours (95%CI -3.2 to -0.5)) favoured the control group. For all other outcomes there were no differences between the intervention group and control group at 6-month follow-up. There were similar findings in the per protocol analysis with the exception that participants in the control group self-reported more weekday active hours (MD -1.6 hours (95% CI-3.2 to -0.1)) at 6-months follow-up.

In post-hoc analyses there was no difference in time spent in MVPA according to age (Table S4) or use of modulator therapy (Table S9).

Table 2. Clinical outcomes – Intention to treat analysis

		Within group differences from baseline (95% CI)				Between group differences	
		ActivOnline n= 29		Usual care control n= 34		ActivOnline – Control (95% CI)	
		Post intervention	6 months	Post intervention	6 months	Post intervention	6 months
Primary outcome	MVPA, mins·day^{-1}	1 (-25 to 23)	-12 (-34 to 9)	-5 (-36 to 26)	-33 (-71 to 6)	-14 (-45 to 16)	-4 (-37 to 29)
Secondary outcomes	FEV_1L	0.1 (-0.1 to 0.2)	0.1 (-0.03 to 0.2)	-0.1 (-0.3 to 0.1)	0.0 (-0.1 to 0.1)	0.1 (-0.3 to 0.1)	0.1 (-0.1 to 0.3)
	FEV_1 %predicted	0.5 (-4.0 to 5.0)	-0.4 (-4.1 to 3.3)	-3.9 (-7.8 to 0.05)	-1.2 (-4.9 to 2.4)	0.3 (-3.7 to 6.2)	-0.3 (-5.2 to 4.6)
	FVC, L	0.1 (-0.1 to 0.3)*	0.2 (0.03 to 0.3)*	-0.2 (-0.3 to 0.04)	0.4 (-0.4 to 1.1)	0.2 (-0.2 to 0.6)	-0.1 (-0.5 to 0.3)
	FVC, %predicted	1.7 (-3.8 to 7.1)	1.2 (-2.9 to 5.2)	-3.5 (-7.3 to 0.3)	-3.3 (-9.1 to 2.4)	1.2 (-4.3 to 6.7)	1.1 (-4.4 to 6.6)
	CFQR-						
	Physical	15.5 (3.8 to 27.3)*	8.2 (-1.9 to 18.3)	11.3 (2.1 to 20.5)*	15.7 (4.9 to 26.4)*	0.9 (-11.4 to 13.2)	-10.1 (-22.7 to 2.5)
	Vitality	7.6 (-3.4 to 18.5)	2.6 (-6.6 to 11.8)	16.0 (6.1 to 25.8)	12.9 (2.6 to 23.2)	-5.3 (-18.3 to 7.7)	-8.3 (-21.3 to 4.5)
	Treatment	4.0 (-2.0 to 10.1)	1.4 (-7.1 to 9.9)	6.9 (0.1 to 13.7)*	11.1 (-1.5 to 20.7)	-2.3 (-11.3 to 6.7)	-7.3 (-16.5 to 1.9)
	Respiratory	4.4 (-3.1 to 12.0)	4.0 (-3.5 to 11.4)	7.5 (0.2 to 14.9)*	10.2 (-1.3 to 21.7)	-2.6 (-13.3 to 8.1)	-4.8 (-15.8 to 6.3)
	HAES-						
	Weekday somewhat active, hrs	-0.0 (-0.8 to 0.8)	0.4 (-0.8 to 1.6)	0.3 (-1.0 to 1.6)	-0.2 (-1.5 to 1.1)	-0.2 (-1.6 to 1.2)	0.8 (-0.6 to 2.1)
	Weekday active, hrs	0.5 (-0.6 to 1.6)	-0.1 (-1.1 to 0.8)	1.1 (0.0 to 2.2)*	1.6 (0.6 to 2.7)*	-0.7 (-2.0 to 0.6)	-1.9 (-3.2 to -0.5)*
	Weekday total activity, hrs	0.5 (-0.5 to 1.5)	0.3 (-1.2 to 1.7)	1.5 (-0.2 to 3.1)	1.4 (0.1 to 2.8)*	-0.8 (-2.6 to 0.9)	-1.3 (-3.1 to 0.5)
	Weekend somewhat active, hrs	-0.6 (-2.1 to 0.9)	0.4 (-1.3 to 2.1)	-1.2 (-2.5 to 0.1)	-0.2 (-1.2 to 0.8)	0.3 (-1.3 to 1.9)	0.3 (-1.3 to 1.8)
	Weekend active, hrs	0.3 (-0.6 to 1.2)	0.5 (-0.6 to 1.6)	1.3 (-0.3 to 2.8)	0.8 (-0.1 to 1.7)	-0.6 (-2.0 to 0.9)	-0.6 (-2.0 to 0.8)
	Weekend total activity, hrs	-0.3 (-2.0 to 1.4)	0.9 (-1.1 to 2.8)	0.2 (-1.7 to 2.1)	0.5 (-0.8 to 1.9)	-0.2 (-2.3 to 2.0)	-0.3 (-2.4 to 1.8)

BREQ-2-						
Amotivation	0.1 (-0.3 to 0.5)	0.04 (-0.4 to 0.5)	0.02 (-0.2 to 0.2)	-0.1 (-0.2 to 0.1)	0.2 (-0.2 to 0.6)	0.2 (-0.2 to 0.6)
External	0.5 (0.04 to 0.9)*	0.1 (-0.3 to 0.5)	-0.1 (-0.4 to 0.2)	-0.2 (-0.5 to 0.1)	0.6 (0.1 to 1.1)*	0.5 (-0.01 to 1.0)
Introjected	0.2 (-0.1 to 0.5)	-0.02 (-0.3 to 0.2)	-0.01 (-0.3 to 0.3)	-0.01 (-0.5 to 0.5)	0.1 (-0.3 to 0.6)	-0.05 (-0.5 to 0.4)
Identified	0.01 (-0.3 to 0.4)	0.1 (-0.2 to 0.4)	-0.1 (-0.4 to 0.2)	-0.3 (-0.6 to 0.1)	-0.2 (-0.6 to 0.3)	-0.03 (-0.5 to 0.4)
Intrinsic	-0.5 (-1.2 to 0.3)	-0.2 (-0.9 to 0.6)	0.5 (-0.2 to 1.2)	0.4 (-0.3 to 1.1)	-0.8 (-1.2 to -0.3)*	-0.2 (-0.7 to 0.2)
CES-D	-1.0 (-4.1 to 2.1)	-0.3 (-4.8 to 4.1)	-0.2 (-5.5 to 0.8)	-3.0 (-8.1 to 2.1)	1.2 (-3.8 to 6.3)	3.1 (-2.1 to 8.3)
HADS -A	0.4 (-0.8 to 1.6)	0.0 (-1.9 to 1.9)	-0.6 (-2.1 to 0.9)	-0.7 (-2.4 to 0.9)	0.8 (-1.4 to 3.0)	0.7 (-1.5 to 2.9)
HADS -D	-0.6 (-1.7 to 0.5)	-0.9 (-2.2 to 0.4)	-0.4 (-1.8 to 1.1)	-0.3 (-2.2 to 1.5)	0.2 (-1.6 to 2.1)	0.2 (-1.7 to 2.1)
PSQI	-0.9 (-2.0 to 0.3)	-0.3 (-1.3 to 0.6)	-0.4 (-1.8 to 0.9)	-1.0 (-2.2 to 0.2)	-0.1 (-1.8 to 1.6)	0.9 (-0.9 to 2.7)

LEGEND:
Data are mean difference and 95% CIs adjusted for baseline values.
*p<0.05

MVPA, moderate-to-vigorous physical activity; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; CFQ-R, Cystic Fibrosis Questionnaire – revised version; HAES, Habitual Activity Estimation Scale; hrs, hours; BREQ-2, exercise regulation questionnaire; CES-D, Centre for Epidemiological Studies – Depression scale; HADS-A, Hospital Anxiety and Depression Scale – Anxiety; HADS-D, Hospital Anxiety and Depression Scale – Depression; PSQI, Pittsburgh Sleep Quality Index

Fewer than half of all participants (47%) completed assessment of exercise capacity (modified shuttle test – 25 levels) at baseline, with only 25% completing this outcome post-intervention. Failure to assess exercise capacity was primarily due to participants declining to undertake the test and/or completing their evaluation remotely. As such, a between group comparison for exercise capacity was unable to be meaningfully analysed (Online Supplement Table S3).

Qualitative interviews

Forty-four participants (control n=24; intervention n=20) completed a qualitative interview. (Table S10). Mean (SD) interview duration was 14.6 (4.4) minutes (range7.5 to 24.5 minutes). Five over-arching, but inter-linked, themes were identified in relation to physical activity, exercise, and, for those allocated to the intervention group, the use of the intervention (Table 3 and Online Supplement Table S11).

Table 3. Qualitative themes and descriptors

Theme	Descriptor
Using the app	Participants were not averse to using mobile applications or technology to support their physical activity, but the perceived key components of any such application or technology varied across individuals. While some participants desired a bespoke application, ideally with additional remote-monitoring capabilities, such as distance tracking, others would like forced-choice options for data entry to streamline use
The 'watch' as a physical reminder	Participants described the accelerometer ('the watch') as a reminder and motivation to exercise/be active, but they would have preferred a device that was more aesthetically pleasing, and which ideally provided feedback or reminders for activity.
The impact of symptoms	Fatigue, a lack of energy, and coughing were regularly reported barriers to physical activity. Conversely, some participants described how being active made them feel good, and had a positive impact on their respiratory symptoms, making physical activity something they felt they were more likely to do
Motivation for physical activity and exercise	Getting enjoyment out of physical activity, and having the support or company of friends or family whilst being active, were important for motivation

Time	Competing demands, such as from school, work or family commitments, and a feeling of being time poor meant that activity was often not prioritised.

Healthcare utilisation

During 12 months of follow-up 19 participants in the intervention group and 25 in the control group had at least one all-cause hospital admission (relative risk 0.8 (95%CI 0.51 to 1.27) (n=18 and n=24 at least one respiratory admission, respectively). There was no statistically significant difference between groups for median [IQR] number of all-cause hospitalisations per participant (intervention 1 [0 to 3] vs control 1 [0 to 2], *Z*=-0.04, p=1.0) or respiratory hospitalisations (1 [0 to 3] vs 1 [0 to 2], *Z*=-0.5, p=0.6), nor for time to first admission (all-cause or respiratory)(Online Supplement Fig S2 and S3) or hospital days (all cause: 29 [13 to 64] vs 18 [14 to 45]; respiratory related: 29 [12 to 62] vs 15 [13 to 43], p=0.3).

DISCUSSION:

The web-based application, ActivOnline, comprising individualised goal-setting, feedback, and motivation for behaviour change, was no better than usual care at promoting physical activity in younger people with CF following hospital discharge. For the primary outcome of change from baseline in device-based MVPA, there was no difference between groups either post the 12-week intervention or at 6-month follow-up. Although participants were open to using technology to support being active, including activity tracking, engagement with the online intervention was low. There were no intervention-related adverse events.

The rapid growth of the digital health sector has created the opportunity to reduce therapeutic burden and promote treatment adherence in people with CF.[21] Upwards of 80% of young adults access the internet regularly,[22] and the use of digital technology to support symptom-monitoring and CF care delivery is acceptable to patients.[23] However, non-compliance with data-entry procedures for technology-based interventions has been reported to exceed 50%.[23] Limited engagement with the online intervention, and study procedures, was noted in the present study, with 60% of participants allocated to the intervention failing to access the web-based platform and 40% of participants not completing scheduled study assessments. This is not dissimilar to a large RCT with a multicomponent physical activity intervention where adherence was just over 50%;[24] but is in contrast with two recent small studies in CF that reported intervention adherence of

70%-85%, in children and adults with CF.[10] However, both of these interventions made use of video-conferencing to directly interact with participants and support an exercise training program. Despite favourable feedback for the ActivOnline web-application on earlier pilot testing with a group of young people with CF,[12] it is possible that adherence to the intervention was affected by failure of the web-application to keep pace with technological advances. Adoption of consumer fitness tracking technology has increased almost four-fold since 2015[25] with end-users having greater experience and higher expectations in terms of design, connectivity, and interactivity.[26] This was confirmed by qualitative data with some participants indicating a preference for applications that offered rewards, incentives and interactive features. Whether young people with CF would demonstrate greater engagement with a technology-based intervention by using a high-specification, consumer device remains to be investigated. Additionally, participants were provided with group allocation and intervention information by a researcher independent of their clinical care. Recent evidence highlights the importance of the CF care team, as perceived by patients and their families, in providing support and assistance to adhere to therapeutic interventions.[27] Whether targeted input from the CF care team regarding use of the web-application, and/or an add-on intervention such as an in-person motivational interviewing session would enhance adherence warrants investigation.

The physical activity levels found in the present study are high in comparison to other device-based activity assessment in CF.[3, 28] Device-based assessment methods are recommended when assessing physical activity in people with CF,[17] and can overcome typical issues of over-reporting seen with self-report measures of physical activity.[17] A wrist-worn accelerometer was chosen to support wear compliance and acceptability,[29] as preferred by young people with CF.[30]. However, wrist-worn devices can lead to mis-classification of activity intensity such that light intensity activity associated with vigorous wrist movement may be classified as more intense activity.[31] In addition, recent evidence suggests that population specific cut-points for categorising physical activity intensity may be required to delineate activity levels in clinical populations.[32] That participants in the current study self-reported activity levels nearly four times less than the device-based assessment suggests further investigation of activity classification in this group is warranted.

Beyond data processing variables, the high activity levels in our participants may reflect increased activity in response to monitoring or incidental recruitment of individuals who are

more interested in being physically active. Although a non-significant difference in MVPA time was detected between groups, given that both groups achieved daily MVPA above guideline recommended levels at all time points it is unlikely that this difference in MVPA performance (14 minutes) is clinically relevant. Further, a notable theme identified from participant qualitative interviews was the 'reminder' and 'motivation' to be active inferred from wearing the accelerometer ('the watch'). Whether the relatively high levels of physical activity reported in the present study are a function of consenting participants being those who are more active already, reflect awareness of the act of physical activity monitoring as indicated by qualitative data, or relate to the application of non-CF specific data cut-points for analysis is not clear, and has implications for the generalisability of our findings. It is possible monitoring activity over a longer-period might have diminished any unintended Hawthorne effect, but longer monitoring periods also come with the risk of reduced wear compliance.

Strengths of this study include participants from diverse geographical locations, an intervention underpinned by behaviour change theory and device-based assessment of physical activity. Recruiting from multiple sites around Australia, all of which had similar underlying CF management strategies, enhanced the potential generalisability of our findings. However, recommendations for physical activity in the Australian context may not be the same as found in CF centres in other countries, with possible differences relating to cultural, economic and meteorological factors. A key limitation of this work is the lack of engagement with the intervention by participants in the ActivOnline group, as well as collection of the primary outcome in only 61% of participants at the end of the intervention. While our intervention included key components associated with physical activity promotion strategies, namely capacity for self-monitoring, real-time feedback and goal-setting, it may have failed to address factors associated with adherence to internet-based interventions. Theoretical models suggest adherence to internet-based interventions is determined by end-user characteristics, environmental factors and website/application (intervention) factors.[33] While there are presently no consistent features attributed to those who do or do not engage with web-based programs,[33] sustained engagement is believed to be a product of user perception of the usability, relevance, interactivity, motivational and persuasive features of the intervention.[33] Usability, together with motivation and interactive features of ActivOnline were reported to be positive, or adapted in response to feedback, during pilot testing of the program.[12] However, the mean age of participants in

the current study were younger than those in the pilot, and it is possible that the intervention did not address the needs of this younger group. In addition, the intervention was designed to be 'light touch' in an effort to minimise participant burden. This may have had the confounding effect of failing to provide participants with sufficient motivation or persuasion to regularly engage. Recent meta-analyses suggest that greater physical activity behaviour change success is achieved when interventions include more than once-weekly contact.[34]

Although we conducted an ITT analysis with inclusion of all participants regardless of exposure to the intervention, the nature of the primary outcome (device-measured physical activity) meant that we did not have available data on those who did not wear or return the device. This meant that a reduced number of participants could be included in the ITT analysis. We chose not to impute the missing data because of the proportion of data unavailable was large (nearly 40%) increasing the risk that confirmative findings may be erroneously generated with multiple imputation.[35] Failure to complete physical activity monitoring at the end of the intervention, was predominantly a result of participants failing to wear or return or losing the activity monitoring device. Although this was unexpected, a recent systematic review of adherence to activity monitor device wear in adults with cardiac disease reports average monitoring device adherence of 59% at final follow-up;[36] while in adolescents adherence to activity monitoring device wear decreased from 75% at baseline to 56% at follow-up 10-weeks later, despite a gift voucher reward for device return.[37] Future studies employing device based activity assessment may need to account for higher than anticipated attrition rates.

Future research considerations

Our minimal burden intervention, including individualised goal setting, is in keeping with suggestions from recent publications supporting a 'low pressure' approach to motivating people with CF to be physically active.[24] Despite this, we had low uptake of the intervention, and poor compliance with study procedures. Future studies may need to consider intervention designs that more explicitly target physiological, psychological and practical factors associated with achieving long-term behaviour change with respect to physical activity.[38] This might include study designs that allow participants their choice of intervention. Choice-based interventions have been shown improve participant retention, adherence, satisfaction and behaviour change.[39] Of individuals assessed for eligibility 61%

declined to participate. The underlying reasons for declining participation in this trial are unable to be elucidated, however in other respiratory populations undertaking exercise/activity related studies, a preference for receiving a specific treatment arm is commonly cited.[40] Further, interventions with greater co-design elements, that have the capacity to replace or substitute for an existing treatment rather than in addition to usual treatments, may more effectively address research priority areas identified by people with CF and their carers and reduce participant burden.[41]

Conclusions

A web-based application, including individualised goal-setting, feedback, and motivation for behaviour change, was no better than usual care at promoting physical activity in adolescents and young adults with CF following hospital discharge. Low engagement with the intervention, as well as high baseline physical activity levels - irrespective of group- likely limited any intervention effect and may not make these results generalisable to all adolescents and young adults with CF. For people with CF who need support to increase their physical activity levels, the best way to facilitate this remains to be determined.

ACKNOWLEDGEMENTS:

The authors wish to acknowledge Associate Professor Graham Hepworth for providing statistical consultation.

FUNDING:

Funding for this trial was from a competitive UK Cystic Fibrosis Trust Strategic Research Centre (SRC) grant award #008.

CONFLICT OF INTEREST STATEMENT:

NSC, AEH, KAM, MAM, PO'H and CAW were all named investigators on the grant which provided funding for this study. For all other authors nil to declare.

REFERENCES:

[1] Radtke T, Nevitt SJ, Hebestreit H, Kriemler S. Physical exercise training for cystic fibrosis. *Cochrane Database Syst Rev*. 2017:CD002768.

[2] Castellani C, Duff AJA, Bell SC, et al. ECFS best practice guidelines: the 2018 revision. *J Cyst Fibros*. 2018;17:153-78.

[3] Cox NS, Alison JA, Button BM, et al. Physical activity participation by adults with cystic fibrosis: An observational study. *Respirology*. 2016;21:511-8.

[4] Schneiderman JE, Wilkes DL, Atenafu EG, et al. Longitudinal relationship between physical activity and lung health in patients with cystic fibrosis. *Euro Respir J*. 2014;43:817-23.

[5] Collaco JM, Blackman SM, Raraigh KS, et al. Self-reported exercise and longitudinal outcomes in cystic fibrosis: a retrospective cohort study. *BMC Pulm Med*. 2014;14:159.

[6] Hebestreit H, Hulzebos EHJ, Schneiderman JE, et al. Cardiopulmonary Exercise Testing Provides Additional Prognostic Information in Cystic Fibrosis. *Am J Respir Crit Care Med*. 2019;199:987-95.

[7] Burnett DM, Barry AN, Mermis JD. Physical Activity Level and Perception of Exercise in Cystic Fibrosis. *Respir Care*. 2020;65:500-6.

[8] Burton K, Morris NR, Reid D, et al. Increased physical activity post-exacerbation is associated with decreased systemic inflammation in cystic fibrosis - An observational study. *Physiother Theory Pract*. 2020;36:1457-65.

[9] Cox N, Alison JA, Holland AE. Interventions for promoting physical activity in people with cystic fibrosis. *Cochrane Database Syst Rev.* 2013:CD009448.

[10] Chen JJ, Cooper DM, Haddad F, et al. Tele-Exercise as a Promising Tool to Promote Exercise in Children With Cystic Fibrosis. *Front Pub Health*. 2018;6:1-5.

[11] Tomlinson OW, Shelley J, Trott J, et al. The feasibility of online video calling to engage patients with cystic fibrosis in exercise training. *J Telemed Telecare*. 2019;26:356-64.

[12] Cox NS, Alison JA, Button BM, et al. Feasibility and acceptability of an internet based program to promote physical activity in adults with Cystic Fibrosis. *Respir Care*. 2015;60:422-9.

[13] Cox NS, Eldridge B, Rawlings S, et al. A web-based intervention to promote physical activity in adolescents and young adults with cystic fibrosis: protocol for a randomized controlled trial. *BMC Pulm Med*. 2019; 19:253**.**

[14] Paraskeva MA, Edwards LB, Levvey B, et al. Outcomes of adolescent recipients after lung transplantation: An analysis of the International Society for Heart and Lung Transplantation Registry. *J Heart Lung Transplant*. 2018;37:323-31.

[15] Corrado D, Basso C, Rizzoli G, et al. Does sports activity enhance the risk of sudden death in adolescents and young adults? *J Am Coll Cardiol.* 2003;42:1959-63.

[16] Bray SR, Born HA. Transition to university and vigorous physical activity: implications for health and psychological well-being. *J Am Coll Health*. 2004;52:181-8.

[17] Bradley J, O'Neill B, Kent L, et al. Physical activity assessment in cystic fibrosis: A position statement. *J Cyst Fibros*. 2015;14:e25-32.

[18] Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol*. 2006;3:77-101.

[19] Nowell LS, Norris JM, White DE, et al. Thematic Analysis: Striving to Meet the Trustworthiness Criteria. *Int J Qual Methods.* 2017;16:1609406917733847.

[20] Liamputtong P, Ezzy D. Qualitative Research Methods. 2nd ed. Victoria, Australia: Oxford University Press; 2005.

[21] Calthorpe R, Smith S, Gathercole K, et al. Using digital technology for home monitoring, adherence and self-management in cystic fibrosis: a state-of-the-art review. *Thorax.* 2020;75:72-7.

[22] Pink B. Australian Bureau of Statistics: Household use of information technology. Canberra, Australia.: Australian Bureau of Statistics; 2009.

[23] Cox NS, Alison JA, Rasekaba T, et al. Telehealth in cystic fibrosis: a systematic review. *J Telemed Telecare*. 2012;18:72-8.

[24] Hebestreit H, Kriemler S, Schindler C, et al. Effects of a Partially Supervised Conditioning Program in Cystic Fibrosis: An International Multicenter Randomized Controlled Trial (ACTIVATE-CF). *Am J Respir Crit Care Med.* 2021; doi: 10.1164/rccm.202106-1419OC. Online ahead of print.

[25] Dehghani M, Joon Kim K, Dangelicoa R. Will smartwatches last? Factors contributing to intention to keep using smart wearable technology. *Telemat Inform*. 2018;35:480-90.

[26] Dehghani M, Abubakar AM, Pashna M. Market-driven management of start-ups: The case of wearable technology. *Appl Comput Inform*. 2020; Epub ahead of print. doi.org/10.1016/j.aci.2018.11.002

[27] Nicolais C, Bernstein R, Saez-Flores E, McLean K, Riekert KA, Quittner AL. Identifying Factors that Facilitate Treatment Adherence in Cystic Fibrosis: Qualitative Analyses of Interviews with Parents and Adolescents. *J Clin Psych Med Settings*. 2019;26:530-40.

[28] McNarry MA, Stevens D, Stone M, et al. Physical activity, sedentary time and sleep in cystic fibrosis youth: A bidirectional relationship? *Pediatr Pulmonol*. 2021;56:450-6.

[29] Fairclough S, Noonan R, Rowlands A, et al. Wear Compliance and Activity in Children Wearing Wrist- and Hip-Mounted Accelerometers. *Med Sci Sports Exerc.* 2016;48:245-53.

[30] Shelley J, Fairclough S, Knowles Z, et al. A formative study exploring perceptions of physical activity and physical activity monitoring among children and young people with cystic fiboris and health care professionals. *BMC Pediatr*. 2018;18:335.

[31] Van Loo C, Okely A, Batterham M, et al. Wrist Acceleration Cut Points for Moderate-to-Vigorous Physical Activity in Youth. *Med Sci Sports Exerc.* 2018;50:609-16.

[32] Bianchim M, McNarry MA, Larun L, et al. Calibration and validation of accelerometry to measure physical activity in adult clinical groups: A systematic review. *Prev Med Rep*. 2019;16:101001.

[33] Ryan C, Bergin M, Wells JSG. Theoretical Perspectives of Adherence to Web-Based Interventions: a Scoping Review. *Int J Behav Med*. 2018;25:17-29.

[34] Sharp P, Spence JC, Bottorff J, et al. One small step for man, one giant leap for men's health: a meta-analysis of behaviour change interventions to increase men's physical activity. *Br J Sports Med*.. 2020;54:1208-16.

[35] Jakobsen J, Gluud C, Wetterslev J, et al. When and how should multiple imputation be used for handling missing data in randomised clinical trials – a practical guide with flowcharts. *BMC Med Res Methodol*. 2017;17.

[36] Marin TS, Kourbelis C, Foote J, et al. Examining adherence to activity monitoring devices to improve physical activity in adults with cardiovascular disease: A systematic review. *Eur J Prev Cardiol*. 2018;26:382-97.

[37] Audrey S, Bell S, Hughes R, et al. Adolescent perspectives on wearing accelerometers to measure physical activity in population-based trials. *Eur J Pub Health.* 2013;23:475-80.

[38] Gruet M, Saynor ZL, Urquhart DS, et al. Rethinking physical exercise training in the modern era of cystic fibrosis: A step towards optimising short-term efficacy and long-term engagement. *J Cyst Fibros*. 2022;21:e83-e98.

[39] Carlisle S, Ayling K, Jia R, et al. The effect of choice interventions on retention-related, behavioural and mood outcomes: a systematic review with meta-analysis. *Health Psychol Rev*. 2021:1-37.

[40] Holland AE, Jones AW, Mahal A, et al. Implementing a choice of pulmonary rehabilitation models in chronic obstructive pulmonary disease (HomeBase2 trial): protocol for a cluster randomised controlled trial. *BMJ Open*. 2022;12:e057311.

[41] Rowbotham NJ, Smith S, Leighton PA, et al. The top 10 research priorities in cystic fibrosis developed by a partnership between people with CF and healthcare providers. *Thorax*. 2018;73:388-90.

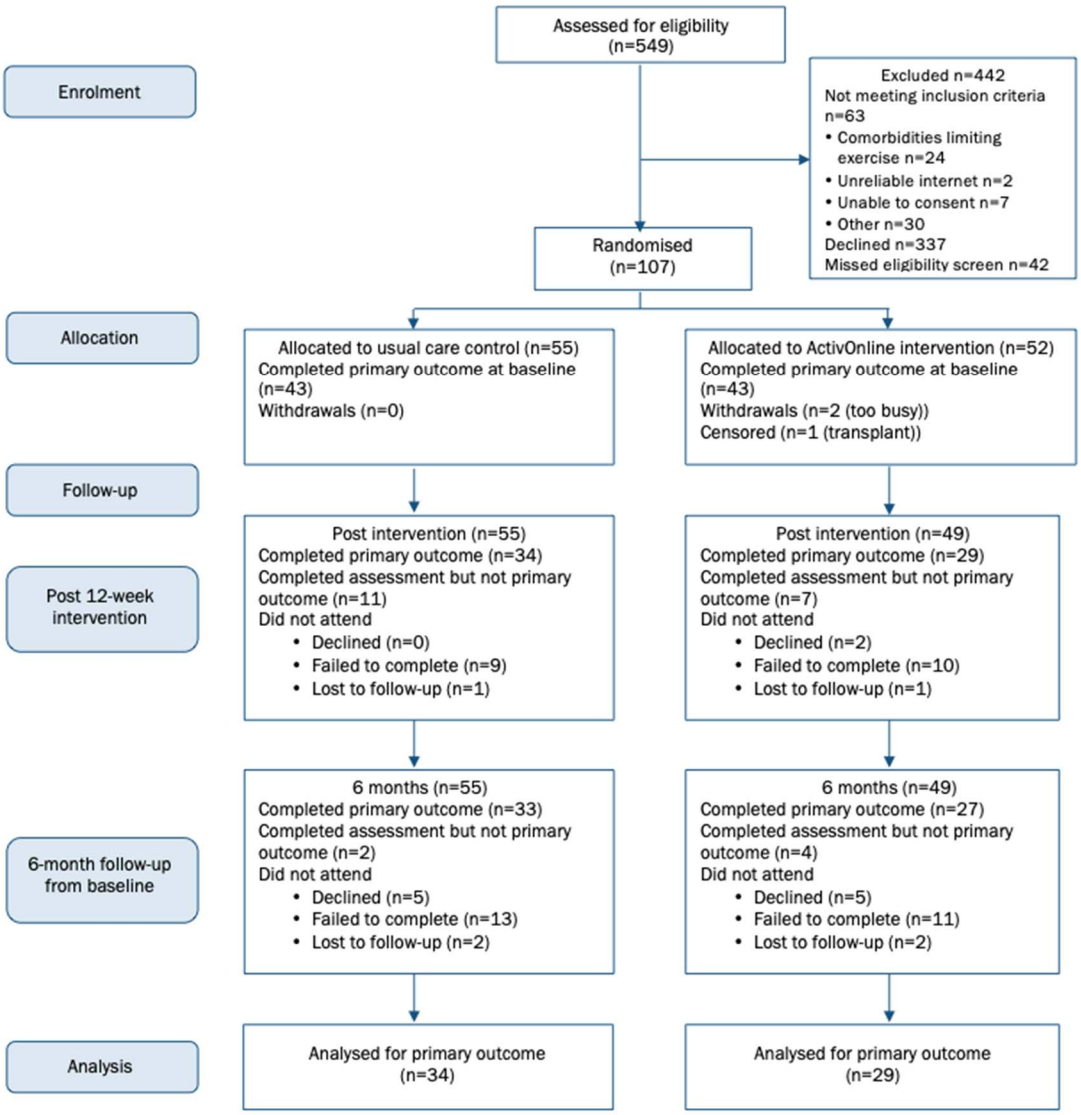
FIGURE LEGEND

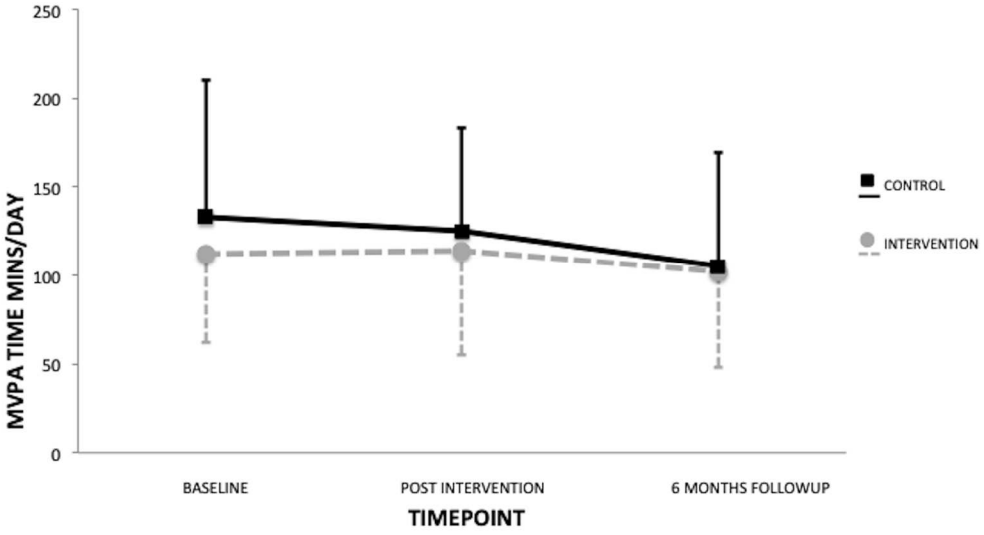
Figure 1. Consort flow diagram of participants in study

Figure 2. Physical activity levels by group and time-point

Legend: MVPA, moderate-to-vigorous physical activity; mins/day, minutes per day

Data are mean (SD)


Enrolment
Assessed for eligibility (n=549)
Excluded n=442
Not meeting inclusion criteria n=63
• Comorbidities limiting exercise n=24
• Unreliable internet n=2
• Unable to consent n=7
• Other n=30
Declined n=337
Missed eligibility screen n=42
Randomised (n=107)
Allocation
Allocated to usual care control (n=55)
Completed primary outcome at baseline (n=43)
Withdrawals (n=0)
Allocated to ActivOnline intervention (n=52)
Completed primary outcome at baseline (n=43)
Withdrawals (n=2 (too busy))
Censored (n=1 (transplant))
Follow-up
Post 12-week intervention
Post intervention (n=55)
Completed primary outcome (n=34)
Completed assessment but not primary outcome (n=11)
Did not attend
• Declined (n=0)
• Failed to complete (n=9)
• Lost to follow-up (n=1)
Post intervention (n=49)
Completed primary outcome (n=29)
Completed assessment but not primary outcome (n=7)
Did not attend
• Declined (n=2)
• Failed to complete (n=10)
• Lost to follow-up (n=1)
6-month follow-up from baseline
6 months (n=55)
Completed primary outcome (n=33)
Completed assessment but not primary outcome (n=2)
Did not attend
• Declined (n=5)
• Failed to complete (n=13)
• Lost to follow-up (n=2)
6 months (n=49)
Completed primary outcome (n=27)
Completed assessment but not primary outcome (n=4)
Did not attend
• Declined (n=5)
• Failed to complete (n=11)
• Lost to follow-up (n=2)
Analysis
Analysed for primary outcome (n=34)
Analysed for primary outcome (n=29)


250
200
150
100
50
0
MVPA TIME MINS/DAY
BASELINE
POST INTERVENTION
6 MONTHS FOLLOWUP
TIMEPOINT
CONTROL
INTERVENTION

Web-based physical activity promotion in young people with CF: a clinical trial

NS Cox, B Eldridge, S Rawlings, J Dreger, J Corda, J Hauser, B Button, J Bishop, A Nichols, A Middleton, N Ward, TJ Dwyer, R Dentice, R Lazarus, P O'Halloran, JYT Lee, C Mellerick, KA Mackintosh, MA McNarry, CA Williams, AE Holland

Online data supplement

METHODS

Sites:

Participants were recruited from eight specialist CF centres in Australia (Alfred Health, Monash Health and Royal Children's Hospital, Victoria; Royal Hobart Hospital, Tasmania; Royal Prince Alfred Hospital, Westmead Hospital and Children's Hospital at Westmead, New South Wales; Royal Adelaide Hospital, South Australia).

Eligibility criteria:

To be included potential participants had to have access to the internet via a computer or mobile device, and they (or their carer) able to provide written informed consent. Potential participants were excluded if they had a severe co-morbidity limiting activity participation (e.g. orthopaedic, cardiac or neurological condition), were pregnant or had been the recipient of a lung transplant.

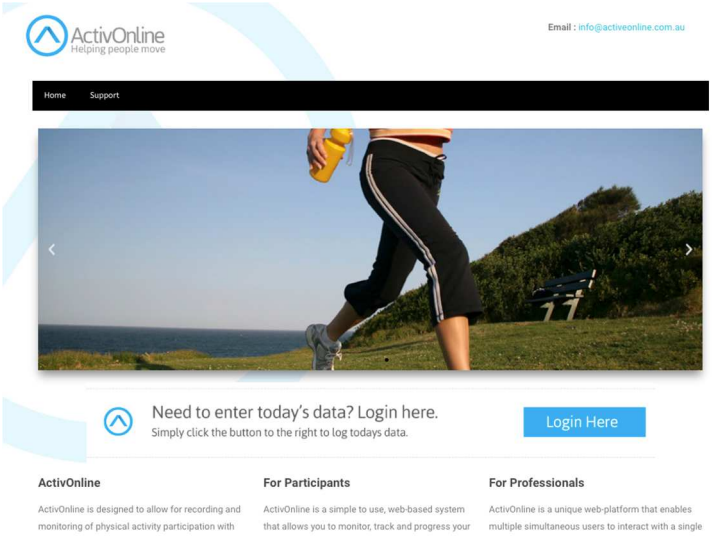
Usual care:

All participants received usual care. Physical activity and exercise recommendations on discharge from hospital were at the discretion of the treating CF service. All participants were provided with access to free, online, age appropriate information on physical activity guidelines, including daily recommendations for amount and intensity of physical activity (http://www.nhs.uk/Livewell/fitness/Pages/physical-activity-guidelines-foryoung-people.aspx)

Intervention:

Participants randomised to the ActivOnline intervention were provided with a unique user-name and password to access the online program (http://www.activonline.com.au)(Figure S1). The ActivOnline intervention was developed using principles of motivational interviewing and cognitive behavioural strategies, and was accessible from any internet enabled device. For the 12-week period of the intervention participants were encouraged to use the online program to set-goals, track their physical activity participation and monitor their progress.[1] Participants were issued with prompts when logging-on to remind them set weekly physical activity goals. Activity data entered by the participant were displayed in both graphical and numerical form to assist participants to self-monitor their performance.

Participants were able to communicate directly with the research team via the ActivOnline program through in-built messaging capability.



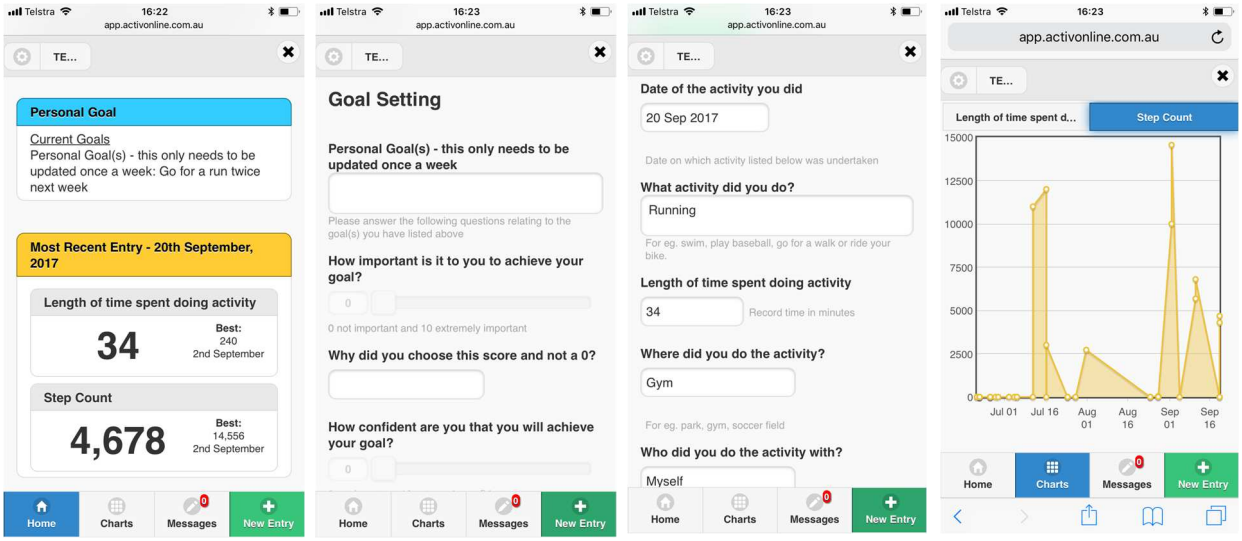


Figure S1. ActivOnline a) website portal and b) data entry screens

Primary outcome:

The primary outcome was change from baseline in time spent in moderate-vigorous physical activity (MVPA) at the end of the 12-week intervention. The primary outcome was assessed objectively using accelerometry (Actigraph Link, Actigraphcorp LLC, Pensacola FL, USA). The Actigraph Link ('the watch') is a wrist worn accelerometer, which was configured to display the time but provided no other feedback regarding activity participation. The accelerometer was configured prior to wear using proprietary software (ActiLife, v6.10.4; Actigraph, Pensacola, Fl, USA), initialised to sample at a rate of 100 Hz, and set to record for a minimum

period of 7 days. Participants were encouraged to wear the accelerometer both whilst awake and asleep. Pre-paid postage was provided for participants to return the activity monitor at the end of the wear period, particularly where this did not coincide with a scheduled clinic appointment.

Secondary outcomes were: self-reported physical activity participation (Habitual Activity Estimation Scale (HAES));[2] aerobic fitness (modified shuttle test 25 level version (MST-25));[3] determinants for exercise engagement (Behavioural Regulation in Exercise Questionnaire (BREQ-2));[4] health related quality of life (CF Questionnaire – Revised (CFQ-R));[5] psychological well-being (Center for Epidemiologic Studies – Depression scale (CES-D), and Hospital Anxiety and Depression scale (HADS));[6, 7] sleep quality (Pittsburgh Sleep Quality Index (PSQI));[8] and spirometry values for forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) according to standard procedures.[9]

Qualitative interviews

At the conclusion of their 6-month follow-up assessment (i.e. study completion for participants), all participants were invited to participate in a one-off semi-structured interview in order to examine attitudes to physical activity and experiences of the intervention. Interviews were undertaken by a researcher (SR) with over 10 years clinical expertise in caring for people with CF and experience in conducting telephone interviews with people with chronic respiratory disease of all ages. The interviewer was known to all participants in her role as blinded assessor for the study. Interviews were undertaken by telephone, at a time of the participant's choosing. Interviews were audio-recorded using a digital voice recorder and transcribed verbatim. For younger participants, a parent or carer could be present if desired. Two sets of 10 interview questions, underpinned by grounded theory, were compiled; one each for the intervention and control group. Questions were designed to understand participant perceptions of barriers and facilitators to physical activity participation, as well as the experience of using the ActivOnline program (intervention group) or other technologies to support activity participation (control group)(Table S1). All participant interviews and responses were coded to ensure participants could not be identified from their responses.

Data analysis

Physical activity data were analysed to report the average time (minutes) per day spent in MVPA. Activity monitors were downloaded using the ActiLife software. To be included in the analysis the a priori definition for activity data inclusion was a minimum of 3 days of wear,[10] for at least 10 valid wear time hours per day.[11] Valid wear time was established using the following ActiLife parameters for non-wear: more than 90 minutes of consecutive zero activity counts, with a spike threshold of 2 minutes and 100 counts per minute.[12] Pre-specified cut-points for wrist-worn accelerometry were applied to all valid data to determine time in MVPA. Activity intensity cut-points were applied separately for participants aged less than 18 years[13] and those aged 18 years and over.[14]

Table S1. Qualitative interview questions with follow-up prompts

Group	Questions
All participants	Can you tell me about your reasons for participating in this research program? - What were you hoping to gain or achieve from your participation? Can you tell me about your feelings toward performing physical activity and exercise? - Is exercise/activity something you aim for regularly? Why / why not? Do you enjoy it (what aspects of)? Do you not enjoy it (what don't you like)? Is it easy/difficult? Can you describe the things that make it hard for you to participate in physical activity? Can you describe the things that make it easier for you to participate in physical activity? Can you describe what effect doing regular physical activity has on your ability to complete your usual 'CF routine' (e.g. chest physio, nebulisers/pumps, having medcines etc.)?

	If you could change one thing in your life to make it easier to take part in physical activity, what would it be?
For participants in the ActivOnline intervention group	Can you describe aspects of ActivOnline that you felt were good or useful? - In what way did you find it good/useful e.g. motivating; easy to use Can you describe any features you found difficult or frustrating to use? - What could have made it better / easier / more engaging? Do you think using ActivOnline helped you to change your exercise/ physical activity behaviour? - How did it help you to change? If NO change, what kinds of intervention would help you in eliciting behaviour change? - Were you able to achieve the goals that you set in ActivOnline?
For participants in the usual care control group	Can you describe aspects of the research project and the online information you were provided that you felt were good or useful? - In what way did you find it good/useful? Can you describe any features you found difficult or frustrating? - What could have made it better / easier / more engaging? Do you think participating in this research helped you to change your exercise/ physical activity behaviour? - How did it help you to change? If no change, what kinds of interventions would help you in eliciting behaviour change?

	- Were you able to achieve any physical activity goals you may have?

RESULTS:

Participants were recruited from all eight participating specialist CF centres (Adult centres: Alfred Health n=4, Royal Prince Alfred Hospital n=13, Westmead Hospital n=10, Royal Adelaide Hospital n=8; Paediatric centres: Royal Children's Hospital n=24, Children's Hospital at Westmead n=10; Combined adult and paediatric centres: Monash Health n= 32, Royal Hobart Hospital n=6). Participant characteristics at baseline relative to those included in the ITT analysis or not are presented in Table S2.

Relatively few participants completed assessment of exercise capacity via the MST-25, precluding a between group comparison for this outcome. Raw data for MST-25 completion, by time-point, is presented in Table S3.

Physical activity participation by age (less than 18 years versus 18 years and older) and group are presented in Table S4. *Post-hoc* analysis of time spent in MVPA by age (<18 years versus ≥18 years) showed that younger participants accrued more MVPA at baseline (intervention group: Z=-2.75, p= 0.006; control group: Z=-3.4, p<0.01; Online Supplement Table S4). However, there was no significant change from baseline in MVPA between age groups (p≥0.06). There was no difference between intervention and control groups for physical activity participation by age (p≥0.1).

Use of the ActivOnline intervention, and characteristics of intervention groups participants who engaged with the ActivOnline web application are detailed in Table S5 and Table S6 respectively. A per protocol analysis for the primary and secondary outcomes is presented in Table S7. Participants who accessed the ActivOnline intervention were classified as adherent to protocol and included in the per protocol analysis. There was no difference between

groups at either time point for the primary outcome of time spent in MVPA. At 6-months follow-up participants in the control group self-reported more weekday active hours (MD -1.6 hours (95% CI-3.2 to -0.1)). There were no other between group differences for any other outcome in the per protocol analysis. A sensitivity analysis of intervention group participants who did or did not engage with the ActivOnline intervention was conducted (Table S8). Participants who did engage with the intervention had a decline in MVPA from baseline to post-intervention, but this was not significant between groups (mean Δ from baseline to post-intervention: engaged with intervention versus did not engage with intervention, Z=-1.7, p=0.1). Of note, only n=10 participants who did not engage with the intervention provided follow-up physical activity data.

Physical activity participation by modulator use and group are presented in Table S9. *Post-hoc* analysis of time spent in MVPA by modulator use showed no difference between groups for time spent in MVPA at any time point for those prescribed modulator therapy. There was no difference in MPVA time at any time point for those prescribed modulator therapy compared to those who were not.

Characteristics of participants who undertook qualitative interviews compared to those who did not are presented in Table S10. Representative participant quotes, arranged by theme, from qualitative interviews are presented in Table S11.

Table S2. Baseline outcome data of participants included in ITT analysis versus not in ITT analysis

	Group as a whole n=107	**Included in ITT analysis n=63**	**Not in ITT analysis n=44**
FEV_1, L	2.4 (1.0)	2.3 (0.9)	2.4 (1.0)
FEV_1, %predicted	67 (23)	68 (22)	67 (60)
FVC, L	3.4 (1.2)	3.3 (1.1)	3.5 (1.3)
FVC, %predicted	83 (19)	83 (19)	83 (20)
MVPA, mins·day^{-1}	115 (64)	123 (66)	96 (54)
HAES			
Weekday hrs active	3 (3)	2 (2)	4 (4)
Weekend hrs active	3 (4)	2 (3)	4 (4)
CFQ-R			
Respiratory domain	54 (23)	53 (23)	56 (24)
Physical	57 (28)	58 (28)	57 (29)
Treatment	50 (22)	49 (22)	51 (23)
Vitality	43 (20)	43 (19)	43 (21)
HADS anxiety	6 (4)	7 (4)	6 (5)
Case*, n (%)	22 (21)	12 (19)	10 (23)
HADS depression	4 (4)	4 (4)	4 (4)
Case*, n(%)	9 (8)	5 (8)	4 (9)
CES-D	15 (11)	16 (11)	15 (11)
Case¥, n(%)	45 (42)	25 (40)	20 (45)
PSQI	7 (4)	7 (4)	7 (4)
Case§, n(%)	61 (57)	34 (54)	27 (61)

BREQ-2			
Amotivation	0.4 (0.7)	0.4 (0.8)	0.4 (0.7)
External regulation	0.9 (0.9)	1.0 (0.8)	0.8 (1.0)
Introjected regulation	1.2 (1.2)	1.4 (1.2)	0.9 (1.0)
Identified regulation	2.6 (1.0)	2.5 (0.9)	2.3 (1.1)
Intrinsic regulation	2.2 (1.3)	2.2 (1.3)	2.2 (1.2)

LEGEND: Data are Mean (SD) unless indicated

n, number; hrs, hours; CF, cystic fibrosis; FEV_1, forced expiratory volume in one second; L, litres; %predicted, percentage of predicted normal; FVC, forced vital capacity; BMI, body mass index; CFRD, cystic fibrosis related diabetes; MVPA, moderate-to-vigorous physical activity; HAES, habitual activity estimation scale; CFQ-R, cystic fibrosis questionnaire – revised; HADS, hospital anxiety and depression scale; CES-D, centre for epidemiological studies depression scale; PSQI, Pittsburgh sleep quality index; BREQ-2, behavioural regulations in exercise questionnaire.

*HADS case definition score ≥11; ¥CES-D case definition score ≥16; §PSQI case definition score >5

Table S3. Modified shuttle test- 25 distance by group at each timepoint

	Baseline	Post intervention	6-month follow-up
Intervention	n=26	n=11	n=1
	888 (366) m	954 (388) m	
	[range 200-1760]	[range 350-1730]	
Control	n=24	n=16	n=8
	1107 (411) m	1058 (331) m	1078 (357) m
	[range 200-1960]	[range 530-1870]	[range 720-1800]

LEGEND: Data are mean (SD) and range.

Table S4. MVPA time by age and group

	ActivOnline intervention		Usual care control group		Between group difference (intervention vs control)	
Age less than 18 years	T1	135 [86, 175]	T1	143 [136, 209]	T1	*Z*=-1.6, p=0.1
	ΔT2	-7 [-39, 17]	ΔT2	-15 [-77, 2]	T2	*Z*=-1.2, p=0.2
	ΔT3	2 [-37, 14]	ΔT3	-32 [-68, -4]	T3	*Z*=-0.8, p=0.4
Age 18 years and older	T1	89 [72, 147]	T1	102 [61, 121]	T1	*Z*=-0.5, p=0.6
	ΔT2	-8 [-40, 24]	ΔT2	11 [-46, 50]	T2	*Z*=-1.2, p=0.2
	ΔT3	-20 [-41, 22]	ΔT3	-5 [-55, 17]	T3	*Z*=-0.04, p=0.9
Between group difference	T1	*Z*=-2.75, p=0.006	T1	*Z*=-3.4, p<0.01		
(<18 years vs ≥18 years)	T2	*Z*=-0.7, p=0.5	T2	*Z*=-1.9, p=0.06		
	T3	*Z*=-0.03, p=1.0	T3	*Z*=--0.7, p=0.5		

LEGEND: Data are median [interquartile range] at baseline (T1) and change from baseline to post-intervention (T2) and baseline to 6-month follow-up (T3). MVPA = moderate-vigorous physical activity; Δ = change. Between group differences assessed with Mann-Whitney U-test. p<0.05.

Table S5. ActivOnline usage data

ActivOnline usage data	
Unique users, n (%)	21 (40%)
Entries	
Total entries logged, n	633
Entries per participant, median [IQR]	18 [IQR 3 to 40]
Entries per participant, range	1 to 179
Individual goal-setting	
Total goals set, n	54
Goals set per participant, median [IQR]	1 [IQR 1 to 4]
Goals per participant, range	0 to 10

Table S6. Baseline characteristics of participants who did engage with ActivOnline intervention

	ActivOnline users n=21
Male:Female, n	9:12
Age, years	24 (8)
Age <18 years, n	7
FEV_1, L	2.2 (1.1)
FEV_1, %predicted	61 (27)
FVC, L	3 (1)
FVC, %predicted	79 (23)
MVPA, mins·day^{-1}	110 (53)
HAES	
Weekday hrs active	7 (4)
Weekend hrs active	7 (3)
CFQ-R	
Respiratory domain	53 (21)
Physical	51 (33)
Treatment	46 (19)
Vitality	43 (20)
HADS anxiety	7 (4)
Case*, n (%)	5 (24)
HADS depression	5 (3)
Case*, n(%)	1 (5)
CES-D	17 (11)
Case¥, n(%)	11 (52)
PSQI	8 (4)
Case§, n(%)	12 (57)
BREQ-2	

Amotivation	0.3 (0.6)
External regulation	1.0 (1.0)
Introjected regulation	1.0 (1.0)
Identified regulation	2.7 (0.7)
Intrinsic regulation	2.4 (1.2)

LEGEND: Data are Mean (SD) unless indicated

n, number; hrs, hours; CF, cystic fibrosis; FEV_1, forced expiratory volume in one second; L, litres; %predicted, percentage of predicted normal; FVC, forced vital capacity; BMI, body mass index; CFRD, cystic fibrosis related diabetes; MVPA, moderate-to-vigorous physical activity; HAES, habitual activity estimation scale; CFQ-R, cystic fibrosis questionnaire – revised; HADS, hospital anxiety and depression scale; CES-D, centre for epidemiological studies depression scale; PSQI, Pittsburgh sleep quality index; BREQ-2, behavioural regulations in exercise questionnaire.

[*]HADS case definition score ≥11; [¥]CES-D case definition score ≥16; [§]PSQI case definition score >5

Table S7. Clinical outcomes - Per protocol analysis

		Within group differences from baseline (95% CI)				Between group differences	
		ActivOnline n= 21		Usual care control n= 34		ActivOnline – Control (95% CI)	
		Post intervention	6 months	Post intervention	6 months	Post intervention	6 months
Primary outcome	MVPA, mins·day^{-1}	-13 (-45 to 19)	-107 (-132 to -81)*	-5 (-36 to 26)	-33 (-71 to 6)	-28 (-63 to 6)	-11 (-47 to 25)
Secondary outcomes	FEV_1L	0.0 (-0.2 to 0.2)	0.1 (-0.1 to 0.2)	-0.1 (-0.3 to 0.1)	0.0 (-0.1 to 0.1)	0.1 (-0.2 to 0.3)	0.1 (-0.1 to 0.3)
	FEV_1 %predicted	0.2 (-6.1 to 6.5)	-0.0 (-4.9 to 4.9)	-3.9 (-7.8 to 0.0)	-1.2 (-4.9 to 2.4)	1.7 (-5.0 to 8.3)	1.2 (-5.3 to 7.7)
	FVC, L	0.0 (-0.2 to 0.3)	0.1 (-0.0 to 0.3)	-0.2 (-0.3 to 0.0)	0.4 (-0.4 to 1.1)	0.3 (-0.4 to 1.0)	-0.2 (-0.9 to 0.5)
	FVC, %predicted	1.1 (-6.5 to 8.6)	1.4 (-3.6 to 6.4)	-3.5 (-7.3 to 0.3)	-3.3 (-9.1 to 2.4)	3.0 (-4.9 to 11.0)	5.0 (-2.9 to 12.8)
	CFQR-						
	Physical	20.4 (3.8 to 37.0)*	9.6 (-3.2 to 22.5)	11.3 (2.1 to 20.5)*	15.7 (4.9 to 26.4)*	5.3 (-8.7 to 19.3)	-10.2 (-24.2 to 3.7)
	Vitality	11.3 (-0.9 to 23.5)	6.8 (-3.8 to 17.3)	16.0 (6.1 to 25.8)*	12.9 (2.6 to 23.2)*	-2.9 (-16.9 to 11.0)	-6.5 (-20.2 to 7.3)
	Treatment	4.6 (-2.4 to 11.6)	0.0 (-8.0 to 8.0)	6.9 (0.1 to 13.7)*	11.1 (1.5 to 20.7)*	-2.2 (-12.6 to 8.2)	-9.4 (-19.7 to 0.9)
	Respiratory	6.0 (-4.8 to 17.0)	5.7 (-2.0 to 13.4)	7.5 (0.2 to 14.9)*	10.2 (-1.3 to 21.7)	0.0 (-12.3 to 12.3)	-2.1 (-14.4 to 10.1)
	HAES-						
	Weekday somewhat active, hrs	0.5 (-0.6 to 1.5)	0.1 (-1.0 to 1.1)	0.3 (-1.0 to 1.6)	-0.2 (-1.5 to 1.1)	0.1 (-1.6 to 1.3)	0.4 (-1.1 to 1.8)
	Weekday active, hrs	0.3 (-1.3 to 2.0)	0.0 (-1.2 to 1.3)	1.1 (0.0 to 2.2)*	1.6 (0.6 to 2.7)*	-0.5 (-2.1 to 1.0)	-1.6 (-3.2 to -0.1)*

Weekday total activity, hrs	0.8 (-0.4 to 2.0)	0.1 (-1.7 to 1.9)	1.5 (-0.2 to 3.1)	1.4 (0.1 to 2.8)	-0.6 (-2.7 to 1.6)	-1.6 (-3.7 to 0.5)
Weekend somewhat active, hrs	-0.4 (-2.5 to 1.7)	0.2 (-1.8 to 2.1)	-1.2 (-2.5 to 0.7)	-0.2 (-1.2 to 0.8)	-1.4 (-3.2 to 0.5)	0.5 (-1.3 to 2.3)
Weekend active, hrs	0.2 (-0.6 to 1.0)	-2.7 (-4.9 to -0.6)*	1.3 (-0.3 to 2.8)	0.8 (-0.1 to 1.7)	-0.7 (-2.3 to 1.0)	-0.8 (-2.4 to 0.8)
Weekend total activity, hrs	-0.2 (-2.5 to 2.1)	0.3 (-2.0 to 2.5)	0.2 (-1.7 to 2.1)	0.5 (-0.8 to 1.9)	0.7 (-1.8 to 3.2)	-0.3 (-2.7 to 2.1)
BREQ-2-						
Amotivation	0.1 (-0.1 to 0.3)	0.1 (-0.2 to 0.4)	0.0 (-0.2 to 0.2)	-0.1 (-0.2 to 0.1)	0.0 (-0.3 to 0.3)	0.1 (-0.2 to 0.4)
External	0.2 (-0.3 to 0.7)	0.1 (-0.4 to 0.6)	-0.1 (-0.4 to 0.2)	-0.2 (-0.5 to 0.1)	0.3 (-0.3 to 0.8)	0.4 (-0.2 to 0.9)
Introjected	0.2 (-0.1 to 0.5)	-0.1 (-0.5 to 0.2)	-0.0 (-0.3 to 0.3)	-0.0 (-0.5 to 0.5)	0.1 (-0.4 to 0.6)	-0.2 (-0.7 to 0.4)
Identified	-0.0 (-0.4 to 0.3)	0.0 (-0.2 to 0.3)	-0.1 (-0.4 to 0.2)	-0.3 (-0.6 to 0.1)	-0.1 (-0.6 to 0.4)	0.0 (-0.5 to 0.5)
Intrinsic	-0.4 (-1.4 to 0.7)	-0.2 (-1.1 to 0.7)	0.5 (-0.2 to 1.2)	0.4 (-0.3 to 1.1)	-0.6 (-1.1 to -0.1)*	-0.3 (-0.8 to 0.3)
CES-D	-1.9 (-6.0 to 2.3)	-1.3 (-6.4 to 3.7)	-2.4 (-5.5 to 0.8)	-3.0 (-8.1 to 2.1)	0.3 (-5.4 to 6.1)	2.2 (-3.5 to 7.9)
HADS -A	-0.2 (-1.8 to 1.3)	-0.6 (-2.6 to 1.4)	-0.6 (-2.1 to 0.9)	-0.7 (-2.4 to 0.9)	-0.1 (-2.6 to 2.3)	0.1 (-2.4 to 2.6)
HADS -D	-1.0 (-2.4 to 0.4)	-0.7 (-2.1 to 0.8)	-0.4 (-1.8 to 1.1)	-0.3 (-2.2 to 1.5)	-0.1 (-2.3 to 2.1)	0.3 (-1.9 to 2.5)
PSQI	-1.1 (-2.4 to 0.2)	-0.5 (-1.6 to 0.7)	-0.4 (-1.8 to 0.9)	-1.0 (-2.2 to 0.2)	0.1 (-2.0 to 2.2)	1.0 (-1.0 to 3.0)

LEGEND:

Data are mean difference and 95% CIs adjusted for baseline values.

*p<0.05

MVPA, moderate-to-vigorous physical activity; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; CFQ-R, Cystic Fibrosis Questionnaire – revised version; HAES, Habitual Activity Estimation Scale; hrs, hours; BREQ-2, exercise regulation questionnaire; CES-D, Centre for Epidemiological Studies – Depression scale; HADS-A, Hospital Anxiety and Depression Scale – Anxiety; HADS-D, Hospital Anxiety and Depression Scale – Depression; PSQI, Pittsburgh Sleep Quality Index

Table S8. Sensitivity analysis – Physical activity outcome data for intervention group participants who did versus did not engage with ActivOnline intervention

	ActivOnline intervention did engage		ActivOnline intervention did *not* engage		Between group difference (engaged vs did not)	
MVPA	T1	108 (54)	T1	118 (43)	T1	*Z*=-0.8, p=0.5
	T2 n=17	95 (49)	T2 n=10	139 (67)	T2	*Z*=-2.1, p=0.04
	T3	95 (50)	T3	101 (62)	T3	*Z*=-0.1, p=0.9
HAES Weekdays hours active	T1	2.6 [0.5, 3.8]	T1	0.6 [0. 2.3]	T1	*Z*=-0.5, p=0.6
	T2	3.0 [0, 4.8]	T2	1.7 [0.3, 3.2]	T2	*Z*=-0.4, p=0.7
	T3	2.7 0, 5.5]	T3	1.4 [0, 2.7]	T3	*Z*=-0.8, p=0.5
HAES Weekend hours active	T1	2.1 [0, 4.4]	T1	0.5 0, 1.3]	T1	*Z*=-1.1, p=0.3
	T2	2.3 [0, 4.9]	T2	1.7 [0, 3.1]	T2	*Z*=-0.1, p=1.0
	T3	2.0 [0, 4.5]	T3	1.6 [0, 3.1]	T3	*Z*=-0.0, p=1.0

LEGEND: Data are mean (SD) or median and interquartile range [IQR] as indicated, at baseline (T1) and post-intervention (T2) and 6-month follow-up (T3). MVPA = moderate-vigorous physical activity. Between group differences assessed with Mann-Whitney U-test. $p<0.05$.

Table S9. MVPA time by modulator use and group

	ActivOnline intervention		Usual care control group		Between group difference (intervention vs control)	
Modulator therapy prescribed	T1	97 60, 150]	T1	175 [58, 195]	T1	*Z*=-0.9, p=0.3
	ΔT2	-17 [-47, 23]	ΔT2	20 [-88, 71]	T2	*Z*=-0.4, p=0.7
	ΔT3	4 [-52, 26]	ΔT3	-60 [-91, 47]	T3	*Z*=-0.8, p=0.4
Not prescribed modulator therapy	T1	89 [64, 135]	T1	115 [65, 143]	T1	*Z*=-1.2, p=0.2
	ΔT2	-5 [-18, 21]	ΔT2	1 [-34, 27]	T2	*Z*=-0.1, p=0.9
	ΔT3	-18 -40, 6]	ΔT3	-5 [-52, 8]	T3	*Z*=-0.2, p=0.8
Between group difference	T1	*Z*=-0.7, p=0.5	T1	*Z*=-0.6, p=0.5		
(<18 years vs ≥18 years)	T2	*Z*=-0.8, p=0.4	T2	*Z*=-0.3, p=0.8		
	T3	*Z*=-0.6, p=0.5	T3	*Z*=-0.6, p=0.5		

LEGEND: Data are median [interquartile range] at baseline (T1) and change from baseline to post-intervention (T2) and baseline to 6-month follow-up (T3). MVPA = moderate-vigorous physical activity. Δ = change. Between group differences assessed with Mann-Whitney U-test. p<0.05.

Table S10. Characteristics of participants who undertook qualitative interviews versus those who did not

	Interview participants n=44	Non-interview participants n=63
Male:Female, n	20:24	27:36
Age, years	19 (6)	22 (6)
Age <18 years, n	25	21
FEV_1, L	2.3 (1)	2.4 (1)
FEV_1, %predicted	67 (21)	68 (24)
FVC, L	3.2 (1.2)	3.6 (1.2)
FVC, %predicted	81 (18)	84 (20)
MVPA, mins·day^{-1}	128 (56)	103 (68)
HAES		
Weekday hrs active	3 (3)	3 (3)
Weekend hrs active	3 (3)	3 (4)
CFQ-R		
Respiratory domain	56 (19)	54 (25)
Physical	62 (25)	55 (30)
Treatment	51 (20)	49 (23)
Vitality	44 (17)	43 (21)
HADS anxiety	7 (4)	6 (5)
Case*, n (%)	10 (23)	12 (19)
HADS depression	4 (4)	4 (4)
Case*, n(%)	2 (5)	7 (11)
CES-D	14 (10)	16 (12)
Case¥, n(%)	15 (34)	30 (48)
PSQI	6 (4)	8 (4)
Case§, n(%)	23 (52)	38 (60)

BREQ-2		
Amotivation	0.4 (0.7)	0.4 (0.8)
External regulation	0.9 (0.8)	0.9 (1.0)
Introjected regulation	1.1 (1.0)	1.3 (1.2)
Identified regulation	2.5 (0.9)	2.6 (1.1)
Intrinsic regulation	2.1 (1.3)	2.4 (1.2)

LEGEND: Data are Mean (SD) unless indicated

n, number; hrs, hours; CF, cystic fibrosis; FEV_1, forced expiratory volume in one second; L, litres; %predicted, percentage of predicted normal; FVC, forced vital capacity; BMI, body mass index; CFRD, cystic fibrosis related diabetes; MVPA, moderate-to-vigorous physical activity; HAES, habitual activity estimation scale; CFQ-R, cystic fibrosis questionnaire – revised; HADS, hospital anxiety and depression scale; CES-D, centre for epidemiological studies depression scale; PSQI, Pittsburgh sleep quality index; BREQ-2, behavioural regulations in exercise questionnaire.

*HADS case definition score ≥11; ¥CES-D case definition score ≥16; §PSQI case definition score >5

Table S11. Qualitative interviews, participant quotes by theme

Theme	Example participant quotes
Using the app	'feel like the app is a good way to track, um, and it sort of, can help build motivation'
	'it pushed me to get my limit, because…I didn't want to, I wanted to show you guys that I was able to do it'
	'[use a different app] and it gives you, like, rewards. Um, and I find that, like, I actually use it every day….. stuff like that I'm more interested in, because, like, it reminds you just to do certain things.'
	'some common activities could be as a drop-down menu. …Um, you know, or maybe icons, picture icons, because kids are always, uh, emoji's seem to be big in their world.'
	'[if it] monitors heart rate, to me that's definitely a better indication of the activity that I'm doing'
The 'watch' as a physical reminder	'with the watch I also had, like, more motivation to do more'
	'wearing a watch made me consciously aware of how much I was doing'
	'the watch was a bit bulky…..it was a little bit annoying when I was doing things'
	'Because I was wearing it, I felt like I needed to do more'
	'I feel like the watches weren't like, I don't know, I just don't think they were very good to look at'
	'I did notice each time I wore the watch, I concentrated more on my physical activity'
	'I think I've been out more with the watch'
	'The week of wearing a watch made me consciously aware of how much I was doing'

	‘I feel like if it had, like, a step counter on it or something, or like something visual that you can look at, like on the watch…’ ‘found the watch a little bit frustrating to wear….They’re very chunky and very obvious’. ‘maybe having, like, the watch more interactive?’
The impact of symptoms	‘I try to go to the gym, if I’m feeling up to it. But some days after being at school all day, I just can’t. I don’t have the energy to do it.’ ‘if I’m having a good day I’ll have a good workout, if I’m bad day I kind of have to take it a bit slower and have to have more rests.’ ‘it’s something I wish I could do a lot more but generally tend to avoid doing because of the struggle.’ ‘it makes me feel out of breath and stuff and it’s not very nice.’ ‘sometimes I run out of breath or, or I get too tired during the game’ ‘I just get really tired after work and so that impacts my ability to participate’
Motivation for activity and exercise	‘I don’t like going to the gym by myself. So when I go with somebody it’s definitely a lot easier’ ‘when friends do it it’s easier and more enjoyable’ ‘there’s gotta be something distracting me’ ‘I enjoy the benefits and I enjoy like, my main exercise is getting my dogs out’ ‘with other people generally makes… it makes it seem easier anyway’ ‘I just don't have any motivation to exercise and to do physical activities’

	‘releasing stress from school and everything. Um, it just gives me a bit of boost to keep going’ ‘it makes me want to do it so like I keep healthy and stuff’
Time	‘I feel like, if I wasn’t at school, I’d probably do a lot more’ ‘I just didn’t have time to think about all the things I’d done that day and do it in there [the app].’ ‘What would make it easier? Um, ah, a nice free schedule always makes it easier’ ‘It’s definitely easier to fit it in in school holidays because I don’t have much school. So it’s just fitting it around work.’ ‘probably not have to spend so much time doing, like, own, like, doing like nebulisers and physio and stuff. Yeah, because it’d free up some time in my day.’ ‘it is that struggle for time, having to study … as well as all my medications and nebulizers and trying to fit exercise in with all of that.’

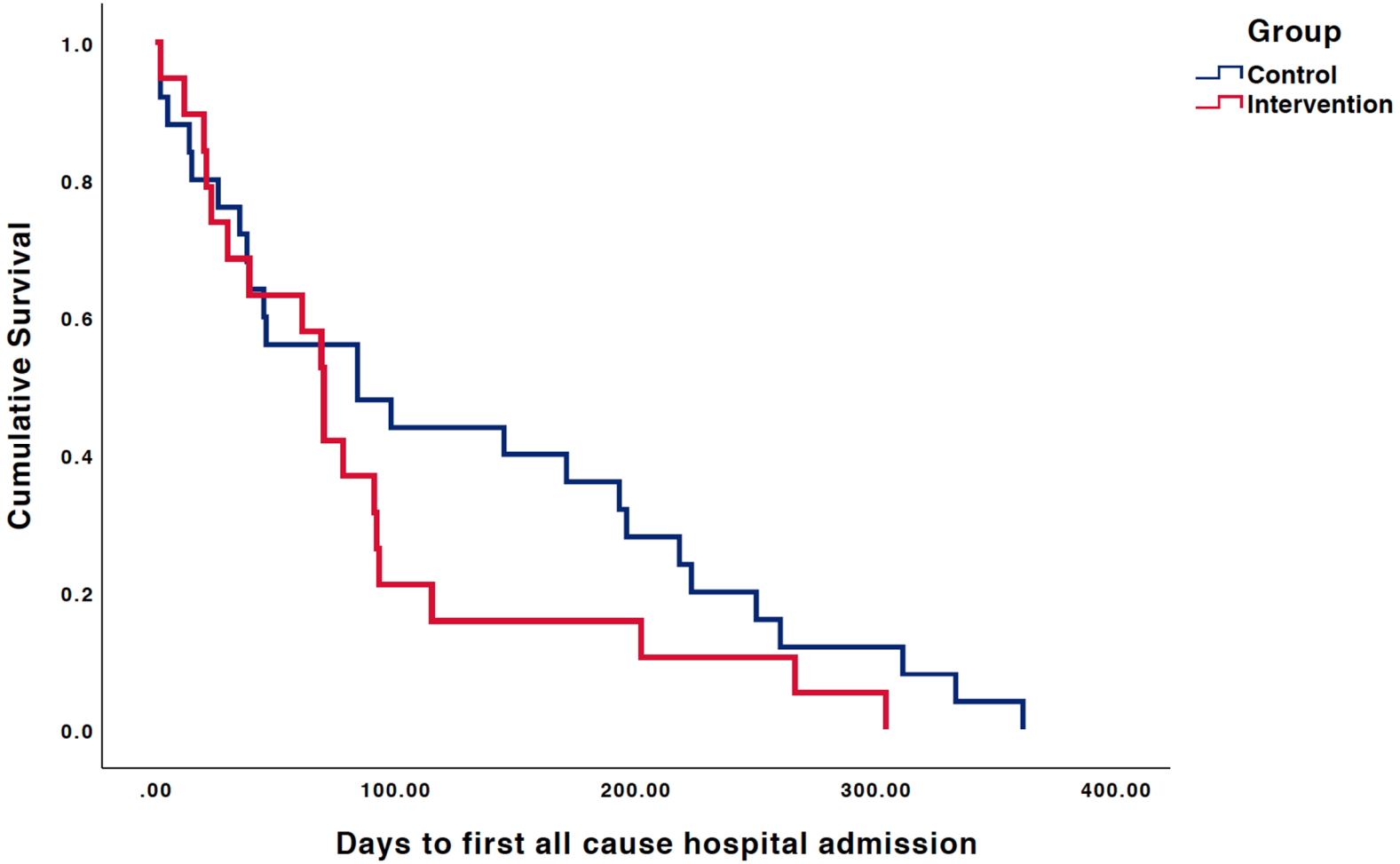

Group
Control
Intervention
Cumulative Survival
1.0
0.8
0.6
0.4
0.2
0.0
.00
100.00
200.00
300.00
400.00
Days to first all cause hospital admission

Fig S2. Kaplan Meier curve, days to first all cause hospitalisation

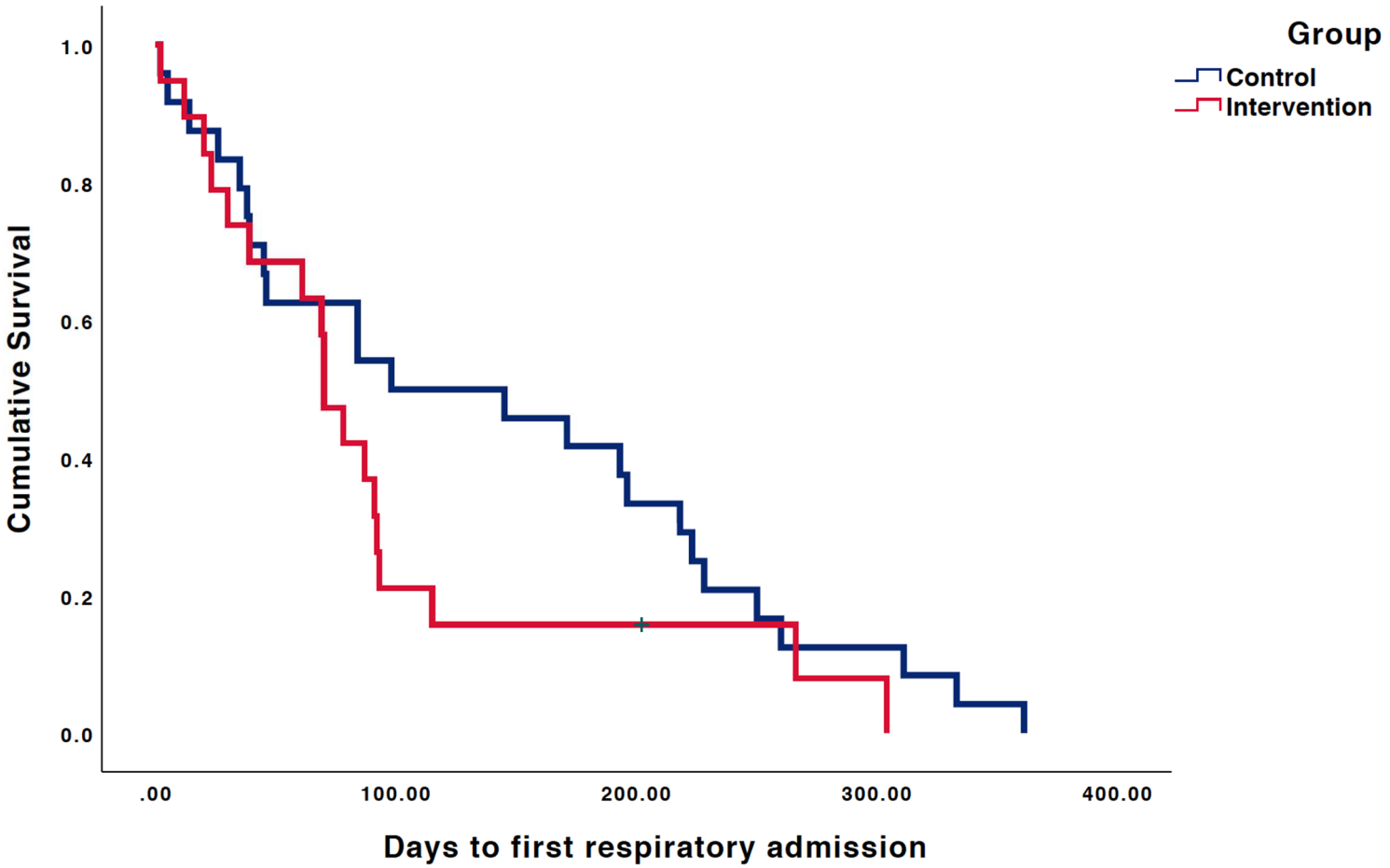


Fig S3. Kaplan Meier curve, days to first respiratory admission

REFERENCES:

1. Cox NS, Eldridge B, Rawlings S, Dreger J, Corda J, Hauser J, Button B, Bishop J, Nichols A, Middleton A, Ward N, Dwyer T, Tomlinson O, Denford S, Barker A, Williams CA, Kingsley M, O'Halloran P, Holland AE. A web-based intervention to promote physical activity in adolescents and young adults with cystic fibrosis: protocol for a randomized controlled trial. BMC Pulm Med 2019: 19: 253.
2. Wells G, Wilkes DD, Schneiderman-Walker J, Elmi M, Tullis E, Lands L, Ratjen F, Coates AL. Reliability and validity of the Habitual Activity Estimation Scale (HAES) in patients with cystic fibrosis. Ped Pulm 2008: 43: 345-353.
3. Elkins M, Dentice R, Bye PT. Validation of the MST-25: an extension of the modified shuttle test (MST) [Abstract]. Journal of Cystic Fibrosis 2009: 8(Supplement 2): S70.
4. Markland D, Tobin V. A Modification to the Behavioural Regulation in Exercise Questionnaire to Include an Assessment of Amotivation. J Sport Exerc Psychol 2004: 26: 191-196.
5. Quittner AL, Buu A, Messer MA, Modi AC, Watrous M. Development and validation of The Cystic Fibrosis Questionnaire in the United States: a health-related quality-of-life measure for cystic fibrosis. Chest 2005: 128: 2347-2354.
6. Radloff LS. The CES-D scale a self-report depression scale for research in the general population. Applied Psychol Meas 1977: 1: 385-401.
7. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatrica Scand 1983: 67(6): 361-370.
8. Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psych Res 1989: 28(2): 193-213.
9. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten CPM, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay R, Navajas D, Pedersen OF, Pellegrino R, Viegi G, Wanger J. Standardisation of spirometry. Eur Respir J 2005: 26(2): 319-338.
10. Trost S, McIver K, Pate RR. Conducting Accelerometer-Based Activity Assessments in Field-Based Research. Med Sci Sports Exerc 2005: 37: S531-S543.
11. Cox NS, Alison JA, Button BM, Wilson JW, Morton JM, Holland AE. Physical activity participation by adults with cystic fibrosis: An observational study. Respirology 2016: 21: 511-518.

12. Evenson KR, Wen F, Howard AG, Herring AH. Applying latent class assignments for accelerometry data to external populations: Data from the National Health and Nutrition Examination Survey 2003–2006. Data in Brief 2016: 9: 926-930.

13. Lin H-P, Lynk N, Moore L, Cabral H, Heffernan K, Dumas A, Hruska B, Zajdel R, Gump B, Spartano N. A pragmatic approach to the comparison of wrist-based cutpoints of physical activity intensity for the MotionWatch8 accelerometer in children. PLOS ONE 2020: 15: e0234725.

14. Montoye A, Clevenger K, Pfeiffer KA, Nelson M, Bock J, Imboden M, Kaminsky L. Development of cut-points for determining activity intensity from a wrist-worn Actigraph accelerometer in free-living adults. Journal of Sports Sciences 2020: 38: 2569-2578.