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

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

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What other documents will be available? Study protocol

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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.

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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.

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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)