Feasibility of the A-STEP for the assessment of exercise capacity in people with cystic fibrosis

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Feasibility of the A-STEP for the assessment of exercise capacity in people with cystic fibrosis

Lisa M. Wilson BHSc[1,2,3] | Angela Potter[4] | Carol Maher PhD[5] | Matthew J. Ellis MD[3] | Rebecca L. Lane PhD[6] | John W. Wilson PhD[3,7] | Dominic T. Keating MD[3,7] | Shapour Jaberzadeh PhD[1] | Brenda M. Button PhD[2,3,7]

[1]Department of Physiotherapy, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Victoria, Australia

[2]Department of Physiotherapy, Alfred Health, Melbourne, Victoria, Australia

[3]Department of Respiratory Medicine, Alfred Health, Melbourne, Victoria, Australia

[4]Department of Physiotherapy, Women's and Children's Hospital, Adelaide, South Australia, Australia

[5]Department of Allied Health and Human Performance, Alliance for Research in Exercise, Nutrition and Activity (ARENA) Research Centre, University of South Australia, Adelaide, Australia

[6]Department of Physiotherapy, Victoria University, Melbourne, Victoria, Australia

[7]Department of Medicine, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Victoria, Australia

Correspondence

Lisa M. Wilson, BHSc, Department of Physiotherapy, Alfred Health, P.O Box 315, Prahran, Melbourne, VIC 3181, Australia.
Email: l.wilson@alfred.org.au

Abstract

Objectives: To evaluate feasibility of the Alfred Step Test Exercise Protocol (A-STEP) for the assessment of exercise capacity in adults and children with cystic fibrosis (CF); in adults to test whether demographics and/or lung function correlated with exercise capacity.

Methods: Adults and children with stable CF from two centres completed the A-STEP (a recently developed incremental maximal-effort step test). Feasibility was evaluated by: usefulness for exercise capacity assessment (measures of exercise capacity were: level reached, exercise-induced desaturation, and achievement of at least one maximal effort criteria); safety; operational factors; time to complete; floor and/or ceiling effects. We used multiple linear regression to test whether demographics and/or lung function correlated with exercise capacity.

Results: A total of 49 participants: 38 adults (18 male), percent predicted (pp) forced expiration in one second (FEV_1) 29–109, aged 22–48 years and 11 children (6 male), $ppFEV_1$ 68–107, aged 10–15 years were included. Levels reached (mean (*SD*) [range]) were 10.2 (2.4) [6–15] (adults), 10.1 (2.5) [7–14] (children); desaturation (change between baseline and peak-exercise SpO_2): was 8.4 (3.8 [0–15]% (adults), 2.0 (2.0) [0–7]% (children). A total of 8 (21%) adults and no children desaturated <90% SpO_2. At least one criterion for maximal effort was reached by 33 (84%) adults and 10 (91%) children. There were no adverse events. The A-STEP was straightforward to use and carried out by one operator. A total of 26 (68.4%) adults and 7 (63.6%) children completed the test within the recommended 8–12 min. All participants completed a minimum of 6 levels, and completed the test before the final 16th level. In adults, $ppFEV_1$ and ppFVC correlated with the level reached ($r = 0.55$; $p = <0.001$ and $r = 0.66$, $p = <0.0001$) and desaturation ($r = 0.55$, $p = <0.001$ and $r = 0.45$, $p = <0.005$).

Shapour Jaberzadeh and Brenda M. Button are equal last authors.

The study was carried out at the Department of Respiratory Medicine, Health, Melbourne, Australia and the Women's and Children's Hospital, North Adelaide, South Australia.

Conclusion: In adults and children with stable CF, the A-STEP was feasible, safe, and operationally easy to use for the assessment of exercise capacity, without floor or ceiling effects. In adults, lung function correlated with exercise capacity.

KEYWORDS

exercise testing, incremental test, maximal effort, maximal test, oxygen desaturation

1 | INTRODUCTION

Cystic fibrosis (CF) is a complex multisystem disease characterized by a progressive decline in lung function with increasing age. While some individuals with CF experience significant exercise impairment due to ventilatory limitation, cardiac and/or muscular factors, or physical deconditioning, others only experience mild impairment.[1–7] Forced expiration in one second (FEV_1) is the main lung function measure of disease progression and accounts for the majority of the variability in exercise capacity in people with CF (pwCF). Habitual physical activity, age, gender, nutritional factors and hypoxemia are other factors that may affect exercise capacity in these individuals.[3,6,8–12] High levels of physical activity in addition to good muscular and pulmonary functions have been associated with higher aerobic capacity in pwCF.[13]

Exercise testing is useful for screening adverse events such as hypoxaemia and for direct measurement of maximum oxygen consumption (VO_2peak). VO_2peak is an important prognostic marker of exercise capacity in pwCF.[14,15] As pulmonary function tests are unreliable in predicting exercise capacity or exercise-induced hypoxemia, especially in mild to moderate CF lung disease, exercise testing is particularly important.[1,16–19]

Exercise testing stresses the major body systems to give insight into the causes of exercise limitation and the factors that affect disease progression.[16] Over 10 years of age, cardiopulmonary exercise testing (CPET) is recommended as the gold-standard for the assessment of exercise capacity in pwCF.[16,20] The individual should ideally reach VO_2peak in 8–12 min (ATS/ACCP guidelines) during an incremental protocol with direct breath by breath gas analysis.[16,20–22] However, due to its complexity, CPET is underutilized in pwCF.[16,23]

In many CF centres, field tests are used as surrogate exercise tests as they are generally easy to carry out.[5] However, these tests have limitations in pwCF. The 6-min walk test is self-paced, thus dependent on participant motivation and often has a ceiling effect in milder CF lung disease.[24] The modified shuttle walk test (MSWT)[25] is an externally paced incremental test incorporating a walk/run on a 10 m course. The MSWT has a ceiling effect in many older children and adults with CF.[26] The MST-25,[26] (developed with additional levels to be a maximal test) may take much longer than the recommended duration for maximal exercise testing in fitter pwCF.[16,20] Finding a suitable track space for conducting these tests in a clinical environment that is safe and nondisruptive can be challenging.

Step tests are similar to typical activity patterns of stepping and are considered a good measure of exercise capacity and require less space than walk tests.[27] The 3-min step test[28] is an externally paced test performed at a constant workload. A ceiling effect has been demonstrated in individuals with mild to moderate CF.[18,28] The Chester step test [29–31] and *i-Step*[32] are incremental step tests used in adults and children with CF. Four of the 22 adults with CF in the study by Planner et al.[30] completed the Chester step test at the maximum 30 cm step height, suggesting a ceiling effect. Similarly, a study of 24 children with mild to moderate CF lung disease who undertook the *i-Step* reported that 50% of participants completed the entire test, with 66% of all participants achieving a near-maximal physiological response. This suggests a ceiling effect for the *i-Step*.[32] Floor effects may not have been evident in these studies as no participants with severe CF lung disease were included.

The Alfred Step Test Exercise Protocol (A-STEP) is a new incremental maximal effort step test developed to assess exercise capacity in pwCF.[33] The A-STEP has been designed for use across the range of lung function and fitness levels to avoid ceiling and floor effects.[33] While it has been tested in a small group of adults during its development, the A-STEP has not yet been tested in children. The primary aim of this study is to evaluate feasibility of the A-STEP for assessment of exercise capacity in adults and children with CF. The secondary aim, in adults with CF, is to test whether any participant demographics and/or lung function correlate with A-STEP measured exercise capacity.

2 | MATERIALS AND METHODS

In adults, ethical approval was obtained from the Alfred Hospital Research and Ethics Committee (Project Number: 205/16) and the Monash University Human Research Committees (Project Number: 0267). The study was registered on ClinicalTrials.gov in March 2016 (Registration Number: NCT02717650). Written informed consent was obtained from all participants before enrollment. Testing of adults was completed between 25th August 2016 and 22nd February 2018.

In children ethical approval was obtained from the Women's and Children's Health Network Human Research Ethics Committee (HRE01722) and the University of South Australia Human Research Ethics Committees (203685). The study was registered December 2020 on Research GEMS SA https://gems.sahealth.sa.gov.au/

registration number 2020/GEM02481. Parents provided written informed consent for their child to participate and children provided assent. Testing of children was completed between 1st March 2021 and 5th July 2021.

2.1 | Sample size calculation

The primary aim was to ascertain the feasibility of a new incremental maximal exercise test in pwCF. This study was not powered to identify change in secondary outcomes. A sample size of 30 or greater has been recommended for feasibility studies.[34] We therefore recruited 38 adult participants to capture a representative range of demographics including age, gender, height, body mass index (BMI), and disease severity to meet our aims. Although our group of children was small ($n = 11$) the demographics were considered representative of this group and may serve to provide preliminary feasibility data for a future study.

2.2 | Study design and setting

A cross-sectional observational study was carried out using convenience sampling. The study was undertaken in CF outpatient centres in two states: the Alfred Hospital, Adult CF Service, Melbourne, Victoria and the Women's and Children's Hospital, North Adelaide, South Australia.

2.3 | Participant selection

All participants had a diagnosis of CF based on elevated sweat chloride levels, and a compatible genotype, were ≥10 years of age, with a percent predicted (pp) $FEV_1 > 20$, and were clinically stable. Clinically stable was defined as no acute exacerbation, hospitalization, or changes in maintenance therapy for at least 30 days.[35] For all participants who met standard criteria for maximal exercise testing medical consent was obtained.[16,20] We screened participants and excluded those with the following: febrile illness, hemoptysis, uncontrolled asthma, pneumothorax, cardiac, hepatic (e.g., CF liver disease and on beta-blockers), vascular (e.g. diabetic neuropathy), or renal comorbidities; pulmonary hypertension; unstable CF-related diabetes (CFRD); relevant musculoskeletal problems (that would preclude them from stepping up and down); BMI < 17.5 kg/m^2; pregnancy; or unable to safely follow instructions.[16,20,33]

2.4 | Baseline information

Participant demographics of: age, gender, height, BMI; and lung function: $ppFEV_1$ and forced vital capacity (ppFVC) were recorded. $PpFEV_1$ and ppFVC were measured using spirometry before each exercise test according to the ATS-ERS standards.[36] Participants were categorized in three groups based on $ppFEV_1$: mild CF lung disease ($ppFEV_1 > 70\%$); moderate CF lung disease ($ppFEV_1$ ≥40 to ≤70%); severe CF lung disease ($ppFEV_1 < 40\%$).[37]

Use of CFTR modulators, organisms, diagnosis of CFRD, and bone density status (osteoporosis and/or osteopenia) were documented. Participants were asked to refrain from caffeine and exercise on the day of the test, take bronchodilators as prescribed, measure blood glucose as indicated and wear appropriate shoes and dress. All participants completed a consent form.[16,20,33]

2.5 | The A-STEP

The A-STEP is an incremental maximal effort step test consisting of 16 levels of progressive stepping. Each level continues for a duration of one minute, starting at 18 steps (level 1) up to a maximum of 48 steps (level 16) per minute. The A-STEP was carried out by trained, experienced CF physiotherapists using a standard portable 20 cm step and an interval timer and metronome played from an iphone. The interval timer and metronome were set up to the specifics of the A-STEP using the Circuit Training Timer Lite App by DenciSoft. Participants were required to wear comfortable clothing and appropriate footwear for the test, as necessary complete airway clearance prior, and be well hydrated for the exercise test.[33]

At baseline, peak exercise, and the end of a 5-min recovery period, SpO_2, HR and BP were assessed using a Philips SureSigns VS2$^+$ portable Vital Signs Monitor (Philips) in adult participants, and a Welch Allyn Vital Signs Monitor 6000 (Welch Allyn) in pediatric participants. Subjective Borg scores for dyspnea and leg fatigue were assessed using the 0–10 modified Borg scale in all participants.[38]

The test was discontinued if any signs or symptoms of exercise intolerance or significant exercise-induced hypoxemia ($SpO_2 < 80\%$) were evident.[14,16,20,33] Maximal effort was attained if the participant reached at least one of four recognized subjective or objective criteria for maximal effort[16,20,33]: ≥90% of HRmax (90% of 220-age) OR self-reported Borg dyspnea score of 9 or 10/10 OR Borg leg fatigue score of 9 or 10/10 OR patient exhaustion as determined by the assessor (i.e., unable to continue the test due to extreme exhaustion).

2.6 | Feasibility criteria

Feasibility was evaluated by: assessment of usefulness for exercise capacity (measures of exercise capacity were: the level reached, exercise-induced desaturation, and achievement of at least one maximal effort criteria); safety (evaluated by the absence of adverse events observed or reported during or after the A-STEP); operational factors (technicality and ease of use); time to complete (aiming within the 8–12 min recommended in the ATS/ACCP guidelines[20]); and the absence of floor and/or ceiling effects.

Exercise-induced desaturation was categorized into three groups: a fall in SpO_2 to <90%; OR a fall in SpO_2 of >4% ($SpO_2 \geq 90\%$); OR a fall in SpO_2 of ≤4%.[16]

2.7 | Statistical analysis

Prism 9.0 GraphPad statistical software was used for data analysis. Descriptive data and results were expressed as mean (*SD*) [range]. Exercise limitation in pwCF generally progress with age and lung disease severity, therefore, the two groups (adults and children) were analyzed separately. In adults only, we used multiple linear regression to assess whether participant demographics and/or lung function correlated with A-STEP measured exercise capacity. We reported on data with a minimum correlation coefficient of ≥0.4 (moderate positive relationship) for this study.[39] For the correlational analyses, desaturation was defined by the change between baseline and peak-exercise SpO_2.

3 | RESULTS

A total of 49 participants, 38 adults (18 male), and 11 children (6 male) with stable CF were included (Table 1). Three adults (8%) and five children (46%) were on CFTR modulator therapy. One child was on elexacaftor/tezacaftor/ivacaftor (Trikafta), no adults were on Trikafta. Pseudomonas aeruginosa was present in 33 (87%) adults (no children). Aspergillus fumigatus was present in 22 (58%) adults (no children). *Staphylococcus aureus* was present in 6 (16%) adults and 6 (55%) children. Seventeen (45%) adults had a diagnosis of CFRD (no children). Osteopenia and/or osteoporosis were found in 23 (61%) adults. The minute by minute results including measures at baseline, peak exercise, recovery and level reached for adults and children are shown in Table 2.

TABLE 1 Participant demographics and lung function (adults and children)

Demographic	Adults	Children
FEV_1 (% pred.)		
All	61.95 (21.09) [29–109] *n* = 38	91.25 (10.89) [68.30–107.3] *n* = 11
Male	60.94 (19.40) [29–109] 18 M	92.62 (13.90) [68.30–107.3] 6 M
Female	62.85 (22.97) [32–101] 20 F	89.60 (6.967) [78.40–97.40] 5 F
FVC (% pred.)		
All	77.21 (15.96) [45–111]	92.63 (12.00) [67.70–113]
Male	81.33 (11.28) [59–105]	92.78 (15.68) [67.70–113.0]
Female	73.50 (18.75) [45–111]	92.44 (7.260) [81.90–100.0]
Age (years)		
All	31.89 (7.53) [22–48]	12.55 (1.75) [10–15]
Male	34.39 (7.24) [22–48]	12.33 (1.97) [10–15]
Female	29.65 (7.23) [22–46]	12.80 (1.64) [11–15]
Height (cm)		
All	166.2 (8.36) [146–181.4]	156.3 (10.17) [142.0–174.3]
Male	170.08 (6.55) [156.3–181.4]	154.6 (9.67) [142.0–169.5]
Female	162.0 (7.72) [146–174]	158.4 (11.49) [143.5–174.3]
BMI (kg/m^2)		
All	22.04 (2.76) [17.70–30]	20.73 (4.101) [16–29]
Male	22.95 (2.21) [19.3–26.9]	19.17 (2.927) [16.00–24.00]
Female	21.22 (2.99) [17.7–30]	22.60 (4.827) [17.00–29.00]

Note: Results were reported as mean (*SD*) [range].
Abbreviation: FEV_1, forced expiration in one second.

3.1 | Feasibility

3.1.1 | Assessment of usefulness for exercise capacity

Level reached

For participants with severe lung disease (based on $ppFEV_1$) (*n* = 6 adults, *n* = 0 children) the average level reached was 7.3 (1.4) [6–9]. For participants with moderate lung disease (*n* = 21 adults and *n* = 1 child), the average level reached was 10.1 (3.0) [7–14] for adults, and 12 levels for the child. For participants with mild lung disease (*n* = 11 adults and *n* = 10 children) the average level reached by adults was 11.9 (1.9) [8–15] and 9.9 (2.5) [7–14] for children.

Exercise-induced desaturation

In adults, desaturation (change between baseline and peak exercise SpO_2) was 5.4 (3.7) [0–15]% and in children 2.0 (2.0) [0–7]%. Eight (21%) adults, $ppFEV_1$ 39.4 (8.5) [29–53] (and no children) experienced a fall in SpO_2 to <90%. A total of 10 (26%) adults, $ppFEV_1$ 65.1 (23) [38–100] and one child with moderate lung disease experienced a fall in SpO_2 of >4%. A total of 10 20 adults (53%) and the remaining 10 children demonstrated fall in SpO_2 of 4%.

Achievement of maximal effort criteria

At least one criterion for maximal effort was reached by 33 (84%) adults and 10 (91%) children. The most common criterion indicating

TABLE 2 A-STEP outcomes measures at exercise time points and highest level completed

Time point	A-STEP outcome measures	*n* =	Adults	*n* =	Children
Baseline (at rest before test)	SpO_2 (%)	*n* = 38	97.97 (1.72) [93–100]	*n* = 11	98.64 (0.67) [98–100]
	Heart rate (beats/min)		79.61 (13.30) [49–106]		81 (12.47) [60–98]
	Systolic BP		116.0 (15.07) [89–158]		111.2 (10.08) [98–132]
	Borg dyspnea		0.32 (0.70) [0–3]		0.05 (0.15) [0–0.5]
	Borg leg fatigue		0.32 (0.70) [0–3]		0.23 (0.61) [0–2]
Level 1	SpO_2 (%)	*n* = 38	98.00 (1.85) [93–100]	*n* = 11	97.09 (2.07) [94–100]
	Heart rate (beats/min)		106.9 (13.31) [84–144]		111.5 (18.10) [86–141]
Level 2	SpO_2 (%)		96.71 (2.48) [90–100]	*n* = 11	97.73 (1.10) [96–100]
	Heart rate (beats/min)		113.9 (13.99) [86–148]		123.9 (17.24) [101–155]
Level 3	SpO_2 (%)	*n* = 38	96.34 (2.80) [89–100]	*n* = 11	97.91 (1.45) [95–100]
	Heart rate (beats/min)		117.9 (14.19) [93–152]		132.5 (19.04) [100–164]
Level 4	SpO_2 (%)	*n* = 38	96.13 (3.12) [87–100]	*n* = 11	98.27 (1.49) [96–100]
	Heart rate (beats/min)		123.3 (14.87) [99–159]		134.5 (19.82) [103–171]
Level 5	SpO_2 (%)	*n* = 38	95.42 (3.73) [84–100]	*n* = 11	97.18 (1.94) [93–100]
	Heart rate (beats/min)		130.5 (15.54) [103–170]		141.5 (17.87) [115–170]
Level 6	SpO_2 (%)	*n* = 38	94.82 (4.53) [80–100]	*n* = 11	97.36 (1.69) [94–100]
	Heart rate (beats/min)		138.1 (14.94) [112–172]		149.5 (18.68) [118–179]
Level 7	SpO_2 (%)	*n* = 36	94.78 (4.09) [82–100]	*n* = 11	97.55 (2.07) [94–100]
	Heart rate (beats/min)		143.7 (14.02) [116–175]		154.3 (19.67) [121–188]
Level 8	SpO_2 (%)	*n* = 30	95.13 (3.47) [86–100]	*n* = 9	97.89 (1.97) [93–100]
	Heart rate (beats/min)		151.7 (14.04) [124–181]		151.2 (15.55) [125-172]
Level 9	SpO_2 (%)	*n* = 27	94.70 (3.87) [86–100]	*n* = 8	97.13 (1.46) [94–100]
	Heart rate (beats/min)		156.8 (13.32) [132–182]		157 (18.91) [129–183]
Level 10	SpO_2 (%)	*n* = 23	92.00 (3.27) [86–100]	*n* = 6	96.83 (1.60) [94–100]
	Heart rate (beats/min)		161.1 (13.51) [133–180]		164.7 (22.27) [127–190]
Level 11	SpO_2 (%)	*n* = 19	95.26 (3.71) [85–100]	*n* = 4	93.50 (5.26) [86–98]
	Heart rate (beats/min)		166.2 (11.40) [142–182]		159.5 (26.54) [127–187]
Level 12	SpO_2 (%)	*n* = 13	95.38 (3.95) [84–100]	*n* = 3	93.67 (3.51) [90–97]
	Heart rate (beats/min)		171.2 (13.59) [144–190]		153 (23.90) [127–174]
Level 13	SpO_2 (%)	*n* = 4	95.75 (0.96) [95–97]	*n* = 2	94.33 (2.52) [92–97]
	Heart rate (beats/min)		170.6 (5.68) [165–178]		154.5 (38.89) [127–182]
Level 14	SpO_2 (%)	*n* = 4	96.00 (1.16) [95-97]	*n* = 2	94.50 (0.71) [95–95]
	Heart rate (beats/min)		176.3 (7.06) [170–184]		154 (38.18) [127–181]
Level 15	SpO_2 (%)	*n* = 1	97%	*n* = 0	–
	Heart rate (beats/min)		173		–
Level 16	–	*n* = 0	–	*n* = 0	–
Peak exercise	SpO_2 (%)		92.61 (4.60) [80–99]		96.64 (2.11) [92–99]
	Heart rate (beats/in)		166.9 (13.16) [131–190]		171.1 (16.31) [144–190]
	% HRmax		88.87 (7.19) [75–105]		87.74 (8.35) [73.90–97.40]

TABLE 2 (Continued)

Time point	A-STEP outcome measures	*n* =	Adults	*n* =	Children
	Systolic BP		146.2 (19.30) [109–196]		123.9 (11.66) [106–142]
	Borg dyspnea		8.21 (1.23) [5–10]		8.18 (1.78) [5–10]
	Borg leg fatigue		8.45 (1.37) [5–10]		9.09 (1.04) [7–10]
	Levels (exercise time)		10.16 (2.40) [6–15]		10.09 (2.47) [7–14]
	Levels (males)		10.72 (1.99) [7–14]		10.33 (2.25) [8–14]
	Levels (females)		9.65 (2.66) [6–15]		9.80 (2.95) [7–14]
Recovery (after the 5-min recovery period)	SpO_2 (%)		97.92 (1.38) [96–100]		97.45 (1.04) [96–99]
	Heart rate (beats/min)		103.7 (16.38) [73–135]		102.0 (16.45) [79–126]
	Systolic BP		119.1 (12.60) [92–148]		114.8 (8.15) [103–127]
	Borg dyspnea		0.29 (0.69) [0–3]		0.36 (0.64) [0–2]
	Borg leg fatigue		1.18 (1.2) [0–4]		0.41 (0.63) [0–2]

Note: Results are reported as mean (*SD*) [range].

Abbreviation: A-STEP, Alfred Step Test Exercise Protocol.

maximal effort was reaching ≥9/10 leg fatigue on the Borg scale (reached by 21 (55%) adults and 8 (73%) children; then ≥9/10 dyspnea on the Borg scale (reached by 17 (45%) adults and 7 (64%) children) followed by ≥90% HRmax (reached by 14 (37%) adults (Figure 1, panel 3) and 3 (27%) children. Patient exhaustion was evident in 18 (47%) adults and 7 (64%) children. For two adults and no children patient exhaustion was the only maximal criteria reached.

Of the six participants (five adults and one child) who did not achieve any criteria for maximal effort, two adults with severe lung disease demonstrated significant desaturation to 80% and 85%, respectively. These two and a further two adults, achieved ≥87.5% of HRmax. The other adult did not achieve close to 90% of HRmax. One child who did not achieve a maximal effort test had challenges with motivation and reporting symptoms using the Borg scale. Equal to or greater than 85% of HRmax was reached in 30 (79%) adults (Figure 1, panel 3) and 5 (46%) children.

Safety

There were no adverse events observed or reported in any participants during or after the test.

As per the published protocol, one participant was stopped by the operator because of significant exercise-induced hypoxaemia (SpO_2 < 80%).[33] The participant recovered to 92% SpO_2 within one minute without supplemental oxygen.

Operational factors (technicality and ease of use)

The A-STEP was observed to be a straightforward test to administer and could easily be carried out by one trained, experienced CF physiotherapist in a suitable clinical space. All participants were able to perform the required stepping technique. The A-STEP used standard simple equipment and readily available hospital equipment and devices (recording sheet, hospital vital signs monitor, a freely available smartphone metronome/timer App, and a standard portable step).[33]

Time to complete; floor and/or ceiling effects

The A-STEP was completed within the ATS/ACCP's recommended 8–12 min[20] in 26 (68.4%) adults (Figure 1) and 7 (63.6%) children. The minimum level reached was 6, and the maximum was 15, suggesting there were no floor or ceiling effects.

Relationship between participant demographics and lung function and A-STEP measured exercise capacity

In adults, $ppFEV_1$ moderately correlated with the level reached ($r = 0.55$; $p = <0.001$) (Figure 1, panel 1) and ppFVC also strongly correlated with the level reached ($r = 0.45$, $p = <0.005$). $ppFEV_1$ moderately correlated with desaturation ($r = 0.55$, $p = <0.001$) (Figure 1, panel 2) and ppFVC also moderately correlated with desaturation ($r = 0.45$, $p = <0.005$). There were no correlations between performance and participant demographics of age, height or BMI. We did not look for correlations in children because of the small sample size.

4 | DISCUSSION

The A-STEP is a feasible incremental maximal effort step test in adults and children across the range of CF lung disease in stable state.

The new A-STEP protocol was found to be viable in terms of assessment of exercise capacity, patient safety, and with no significant adverse events. The A-STEP was operationally feasible being a straightforward test to administer with all participants able to perform the test when carried out by one trained, experienced CF physiotherapist. The A-STEP was performed using standard technology and simple easily cleaned equipment. When considering time taken to complete the test, the A-STEP was completed in the 8–12 min recommended in ATS/ACCP guidelines[20] by 68% of adults and 64% of children, with minimal preparation time of 10 min. There

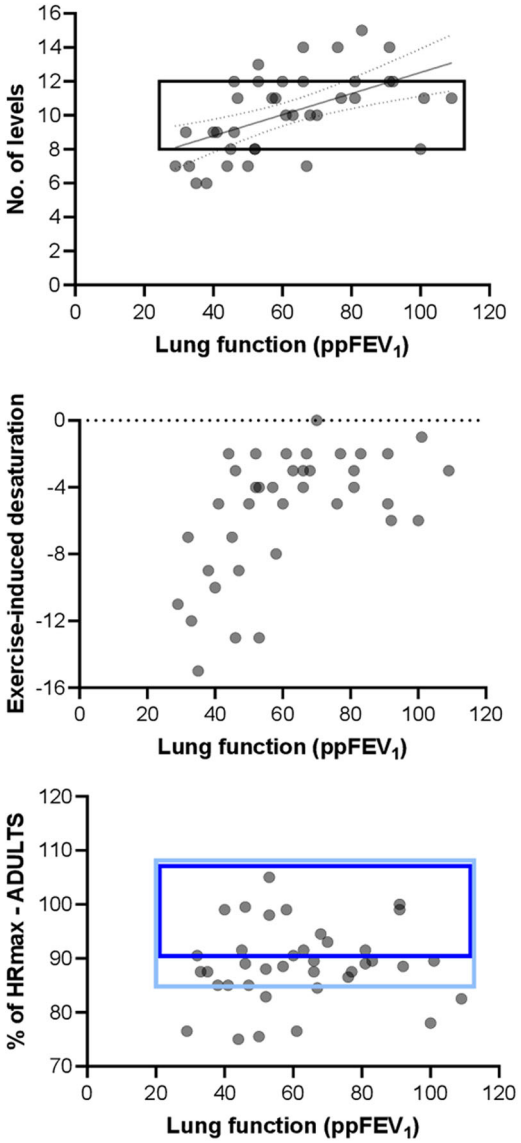

FIGURE 1 *Panel 1*: Correlation between ppFEV$_1$% pred. and level reached: $r = 0.55$, $p = <0.001$. Data points in the boxed area are adults who completed the A-STEP within the recommended 8–12 min. *Panel 2*: Correlation between ppFEV$_1$ AND desaturation: $r = 0.22$, $p = <0.001$. *Panel 3*: Percent of age-predicted HRmax achieved in adults: Data points in the upper box= ≥90% age pred. HRmax. Data points in the box= ≥85% age pred. HRmax. A-STEP, Alfred Step Test Exercise Protocol; FEV$_1$, forced expiration in one second

was neither a floor effect observed, with all participants completing a minimum of 6 levels, nor a ceiling effect, with all participants completing the test before reaching the final 16th level. Given the wide variation in lung disease severity and fitness level, as expected, some individuals completed the test outside the recommended duration of 8–12 min, up to a maximum of 15 min (an acceptable maximal time for a maximal effort test).[21]

The A-STEP was useful in assessing exercise-induced desaturation and in adults, lung function measures correlated with desaturation.[16–18] Two adults with severe lung disease and significant desaturation did not achieve ≥90% of HRmax. Ventilatory limitation was the most likely limiting factor to exercise in these two individuals, causing them to stop before peak cardiac output could be achieved and prevented achievement of a maximal effort test.[5,40] Fewer than half the adult participants (37%) achieved a HRmax ≥90% during the A-STEP, whilst the vast majority achieved a HRmax of ≥85%. Ventilatory limitation and deconditioning are likely to be the primary limitations to exercise in the majority of this cohort. Therefore, HRmax may not be a good marker of determining if peak exercise was achieved in pwCF.[25,40]

As expected, lower exercise capacity (fewer levels reached and more desaturation) was observed in participants with more severe lung disease.[1,19] This may have been related to ventilatory limitation, deconditioning and or differences in muscle mitochondria.[4,5] While there were moderate to strong correlations between lung function measures and level reached, the level reached was more variable in those with moderate and mild lung disease. This may be due to differences in fitness levels and habitual exercise amongst individuals. Our findings were consistent with other studies where oxygen desaturation and exercise capacity were not predicted from FEV$_1$ in mild to moderate CF lung disease.[2,12,19] Exercise capacity did not appear to be related to age, BMI or height in this study.

The minute by minute results observed for SpO_2 and heart rate along with Borg scores, level reached and desaturation may be clinically useful for exercise prescription, regular assessment of exercise capacity, for physical activity counseling, assessing physical response to new therapies, and evaluating training programs.[16]

4.1 | Limitations of the study

The main limitation of the study was the small sample size for each group of lung disease severity and gender in adults, and the small sample size in children. Individuals participating in this study were of a convenience sample that did not include a balanced comparison of participants across groups. However, the group size and comparisons performed in this study are consistent with other exercise studies in CF.[6,7,40] Given the variability of clinical presentation of pwCF, it will be important to confirm findings in larger samples in future. While the small sample of children predominantly had mild lung disease, we considered the sample representative of children with CF, as lung function is known to be better preserved in this group. Baseline fitness levels or habitual exercise participation was not quantified in this study.

4.2 | Implications of findings

Our results demonstrated the A-STEP, a new incremental maximal effort step test was feasible for use in adults and children with CF (≥10 years). The group of children though small was included to provide preliminary data of the applicability of the A-STEP and the ability to step up and down on a 20 cm step. This provides the clinician with an alternative maximal fitness test to CPET and other

field tests. This was a clinician-initiated study addressing a clinical gap, to develop a maximal test that could be performed in a small clinical space. This study provides early evidence regarding the feasibility of a new fitness test, which we hope will meet the needs of pwCF, who vary widely in terms of demographics, lung disease severity and overall fitness levels.

4.3 | Future directions

Results of this study need to be confirmed at other CF centers. Reliability, criterion validity, and responsiveness testing is required. Long-term follow-up studies in large CF populations at multiple international sites are needed to assess the prognostic and clinical usefulness of the A-STEP. Further investigation with breath by breath gas analysis is required to determine the maximal HR, dyspnea and leg fatigue scores reached at the point VO_2peak is achieved during the A-STEP in pwCF. In the future, we would encourage a review on the impact of newer CFTR modulators on exercise capacity using the A-STEP. For example, the protocol may require modification using a higher step in fitter patients with good lung function who are on CFTR modulators such as Trikafta.

5 | CONCLUSIONS

In adults and children with CF, the A-STEP was feasible, safe, and operationally easy to use for the assessment of exercise capacity, without floor or ceiling effects. In adults, lung function (ppFEV$_1$ and ppFVC) correlated with A-STEP measured exercise capacity (level reached and desaturation).

AUTHOR CONTRIBUTIONS

Lisa M. Wilson: conceptualization; investigation; writing—original draft; methodology; visualization; writing—review and editing; formal analysis; project administration. **Angela Potter**: writing—review and editing; project administration; investigation. **Carol Maher**: investigation; project administration; writing—review and editing. **Matthew J. Ellis**: writing—review and editing; methodology. **Rebecca L. Lane**: conceptualization; writing—review and editing. **John W. Wilson**: conceptualization; methodology; supervision; writing—review and editing. **Dominic T. Keating**: conceptualization; methodology; supervision; writing—review and editing. **Shapour Jaberzadeh**: methodology; writing—original draft; writing—review and editing; supervision; formal analysis; visualization. **Brenda M. Button**: conceptualization; investigation; writing—original draft; writing—review and editing; methodology; project administration; formal analysis; supervision; visualization.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Lisa M. Wilson http://orcid.org/0000-0003-2663-1049
Brenda M. Button http://orcid.org/0000-0002-3044-8872

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