Assessing functional capacity in directly and remotely monitored home-based settings in individuals with chronic respiratory diseases: A protocol for a multinational validation study

Alec Bass, Sarah Géphine, Mickaël Martin, Marianne Belley, Manon Robic, Claudine Fabre, Jean-Marie Grosbois, Geneviève Dion, Didier Saey, Arnaud Chambellan, François Maltais

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Abstract

Background: Pulmonary rehabilitation is widely recommended to improve functional status and as secondary and tertiary prevention in individuals with chronic pulmonary diseases. Unfortunately, access to timely and appropriate rehabilitation services remains limited. To help close this inaccessibility gap, telerehabilitation models of care have been proposed. However, to ensure effective and safe exercise prescription during rehabilitation, exercise testing is necessary. Current gold standard tests, such as maximal cardiopulmonary exercise testing (CPET) and the 6-minute walk test (6MWT), are poorly adapted to home-based or telerehabilitation settings. This has been highlighted as an obstacle to the continuity of services during the COVID-19 pandemic. It is therefore essential to validate tests adapted to these new realities, such as the 6-minute stepper test (6MST).

Objective: To evaluate the metrological qualities of 6MST by: (1) establishing concurrent validity and agreement between the 6MST and CPET, as well as with the 6MWT; (2) determining test-retest reliability in a home-based setting with direct and remote (videoconferencing) monitoring; and (3) documenting adverse events and participant perspectives when performing the 6MST in home-based settings.

Methods: Three centers (CR-IUCPQ in Québec, and GHICL and FormAction Santé in France) will be involved in this multinational project which is divided into two studies. For study 1 (objective 1), 30 participants (Québec = 15, France = 15) will be recruited. Two laboratory visits will be performed for assessing anthropometric data, pulmonary function, and the three exercise tolerance tests (CPET, 6MWT, 6MST). Concurrent validity (paired sample t-tests and Pearson correlations) and agreement (Bland-Altman plots with 95% agreement limits) will be evaluated. For study 2 (objectives 2 and 3), 52 participants (Québec = 26, France = 26) will be recruited. Following a familiarization trial (trial 1), the 6MST will be conducted on two separate occasions (trials 2 and 3), once under direct supervision and once under remote supervision, in a randomized order. Paired sample t-test, Bland-Altman plots, and intraclass correlations will be used to compare trials 2 and 3. A semi-structured interview will be conducted after the third trial to collect participants' perspectives.

Results: Ethical approval was received for this project and the first participant was recruited in February 2024.

Conclusions: This study innovates by being among the first to validate a new clinical test necessary for the development and implementation of new models of rehabilitation adapted to home and telerehabilitation contexts. This study also aligns with the United Nations Sustainable Development Goals by contributing to augmenting healthcare service delivery (goal 3) and reducing healthcare access inequalities (goal 11).

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Research Protocol

Assessing functional capacity in directly and remotely monitored home-based settings in individuals with chronic respiratory diseases: A protocol for a multinational validation study

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Abstract (444/450)

Background: Pulmonary rehabilitation is widely recommended to improve functional status and as secondary and tertiary prevention in individuals with chronic pulmonary diseases. Unfortunately, access to timely and appropriate rehabilitation services remains limited. To help close this inaccessibility gap, telerehabilitation models of care have been proposed. However, to ensure effective and safe exercise prescription during rehabilitation, exercise testing is necessary. Current gold standard tests, such as maximal cardiopulmonary exercise testing (CPET) and the 6-minute walk test (6MWT), are poorly adapted to home-based or telerehabilitation settings. This has been highlighted as an obstacle to the continuity of services during the COVID-19 pandemic. It is therefore essential to validate tests adapted to these new realities, such as the 6-minute stepper test (6MST). This test, strongly inspired by 6MWT, consists of taking as many steps as possible on a "stepper" for 6 minutes.

Objective: To evaluate the metrological qualities of 6MST by: (1) establishing concurrent validity and agreement between the 6MST and CPET, as well as with the 6MWT; (2) determining test-retest reliability in a home-based setting with direct and remote (videoconferencing) monitoring; and (3) documenting adverse events and participant perspectives when performing the 6MST in home-based settings.

Methods: Three centers (CR-IUCPQ in Québec, and GHICL and FormAction Santé in France) will be involved in this multinational project which is divided into two studies. For study 1 (objective 1), 30 participants (Québec = 15, France = 15) will be recruited. Two laboratory visits will be performed for assessing anthropometric data, pulmonary function, and the three exercise tolerance tests (CPET, 6MWT, 6MST). Concurrent validity (paired sample *t*-tests and Pearson correlations) and agreement (Bland-Altman plots with 95% agreement limits) will be evaluated. For study 2 (objectives 2 and 3), 52 participants (Québec = 26, France = 26) will be recruited. Following a familiarization trial (trial 1), the 6MST will be conducted on two separate occasions (trials 2 and 3), once under direct supervision and once under remote supervision, in a randomized order. Paired sample *t*-test, Bland-Altman plots, and intraclass correlations will be used to compare trials 2 and 3. A semi-structured interview will be conducted after the third trial to collect participants' perspectives.

Results: Ethical approval was received for this project (October 12, 2023 in Québec and September 25, 2023 in France) and the first participant was recruited in February 2024.

Conclusions: This study innovates by being among the first to validate a new clinical test necessary for the development and implementation of new models of rehabilitation adapted to home and telerehabilitation contexts. This study also aligns with the United Nations Sustainable Development Goals by contributing to augmenting healthcare service delivery (goal 3) and reducing healthcare access inequalities (goal 11).

Trial Registration: *Awaiting final APS approval*

Keywords: Chronic Obstructive Pulmonary Disease; Exercise Capacity Test; Interstitial Lung Diseases; Physiotherapy; Rehabilitation; Telerehabilitation; Validation Study; Stepper Test.

Introduction

Recent guidelines strongly recommend pulmonary rehabilitation for individuals with stable or acutely exacerbated chronic obstructive pulmonary disease (**COPD**), or with interstitial lung disease (**ILD**) [1]. Unfortunately, access to rehabilitation care remains limited in many countries, including in Canada and France. Indeed, latest available estimates indicate that only 0.4% of individuals in Canada and 8.6% of individuals in France with COPD have access to pulmonary rehabilitation programs [2, 3]. The development of new and innovative healthcare models, including in rehabilitation, is urgently needed to address this healthcare gap that is only expected to worsen with the aging populations in most advanced economies [2, 4]. Home-based and telerehabilitation are now increasingly considered as a solution to increase rehabilitation access in this population [1, 4, 5]. These programs are cost-effective alternatives to traditional ambulatory pulmonary rehabilitation models anchored in specialized hospital institutions [6, 7]. Moreover, the effectiveness of home-based and pulmonary telerehabilitation programs has been demonstrated and is comparable to traditional rehabilitation models in individuals with COPD [8]. Yet, clinicians report the lack of validated functional exercise capacity tests to these new models of care as a major barrier for their implementation [9, 10]. These tests are important to ensure safe, effective and personalized exercise prescription during rehabilitation, and to monitor and document its effects [11, 12].

The current gold standard for exercise capacity testing is maximal cardiopulmonary exercise testing (**CPET**), which is generally conducted on a cycle ergometer or a treadmill. These tests are designed to assess maximal physiological responses to exercise, and thus require expensive equipment (e.g., gas exchange analyzer, electrocardiogram, etc.) that are not easily accessible outside of specialized institutions. Moreover, these tests are not always representative of functional activities in daily life (e.g., cycling may not be an activity of daily life for many individuals) [13]. Thus, functional capacity tests have been widely adopted in ambulatory rehabilitation settings [13, 14]. To this effect, the 6-minute walk test (**6MWT**), which only requires an unobstructed corridor (≥30 metres), is among the most widely utilized [13, 15]. Despite its simplicity, the 6MWT is not adapted to the realities of home-based and telerehabilitation settings. Indeed, limited available space inhibits its realization and has been highlighted as a barrier to the continuity of rehabilitation services during the COVID-19 pandemic [9]. It is therefore essential to validate functional capacity tests adapted to this new reality, such as the 6-minute stepper test (**6MST**). This test, strongly inspired by 6MWT, consists of taking as many steps as possible on a “stepper” for 6 minutes [16, 17].

In individuals with COPD, initial studies indicate that the 6MST is reliable, as no significant difference in test results were found when repeated on consecutive days in a laboratory setting [16]. The 6MST is also valid, as the number of steps taken during the test is correlated with the total distance travelled during the 6MWT (r=0.56-0.87, p<0.01), peak power during CPET (r=0.46, p<0.01) and peak oxygen consumption during CPET (r=0.39, p<0.01) [17, 18]. Responsiveness to change following pulmonary rehabilitation has also been shown, with a minimally important difference estimated at 40 steps [19]. Finally, predictive equations have been computed to individualize aerobic training intensity using the 6MST [20]. However, to our knowledge, cardiorespiratory responses during the 6MST in individuals with COPD have not been formally compared to those during the 6MWT and CPET to date. This is particularly important when considering the development of home-based and telerehabilitation programs, as different cardiorespiratory responses to testing may elicit safety concerns. In individuals with ILD, there is limited evidence regarding the validity of the 6MST, as the number of steps taken during the test is correlated with the total distance travelled during the 6MWT (r=0.70, p<0.01) [21]. Interestingly, in individuals with ILD, cardiorespiratory responses during the 6MST have been compared to the 6MWT. In this population, the 6MST lead to greater heart rate and ventilatory responses, but reduced blood oxygen desaturation [21, 22]. Lastly, as the 6MST has only been validated in laboratory or

hospital settings, metrological properties in home-based settings with direct or remote (i.e., videoconferencing) monitoring are currently unknown in individuals with COPD or ILD.

Objectives and Hypotheses

The overall aim of this project is to provide further evidence regarding the metrological properties of the 6MST in individuals with COPD or ILD. Specific objectives and hypotheses are described below.

I. ***Objective 1*** is to determine concurrent validity and the level of agreement (or bias) between peak cardiorespiratory responses and reported symptomology during the 6MST and CPET, and the 6MST and 6MWT. The corresponding ***hypotheses*** are that peak cardiorespiratory responses and reported symptomology to the 6MST will be strongly correlated to those measured during CPET and the 6MWT (i.e., concurrent validity), and that these values will be systematically lower than those measured during CPET (i.e., presence of bias), but similar to those measured during the 6MWT (i.e., no bias).

II. ***Objective 2*** is to determine test-retest reliability for the 6MST in home-based settings under direct and remote (i.e., videoconferencing) monitoring. The corresponding ***hypothesis*** is that measurement error will be minimal and intraclass correlations will be good and similar between direct and remote supervision.

III. ***Objective 3*** is to determine the safety and the perception of the 6MST in individuals with chronic pulmonary diseases in home-based settings under direct and remote monitoring by collecting adverse events and qualitative feedback. The corresponding ***hypothesis*** is that the test will be safe (i.e., absence of serious adverse events) and individuals will report a good level of overall satisfaction with the test, irrespective of the type of supervision.

Methods

Research Design

This research project comprises two studies resulting from an international collaboration between the *Centre de recherche de l'Institut universitaire de cardiologie et de pneumologie de Québec* (**CR-IUCPQ**, Université Laval, Canada), the *Groupement des Hôpitaux de l'Institut Catholique de Lille* (**GHICL**, France) and *FormAction Santé* (France). ***Study 1*** (objective 1) is a prospective, multicentric, quantitative, validation study realized in an outpatient hospital setting at the CR-IUCPQ and the GHICL. ***Study 2*** (objectives 2 and 3) is a prospective, multicentric, mixed methods, validation study realized at the participants' home in Québec (CR-IUCPQ) and in northern France (FormAction Santé).

Participants and Inclusion and Exclusion Criteria

A quota sampling method, based on disease and sex (i.e., 1: 1), will be used. All sample sizes were calculated *a priori* with an open-source calculator available online or SPSS (IBM) [23]. Inclusion and exclusion criteria are summarized in Textbox 1.

For ***study 1***, a mean difference of 0.28 ± 0.32 L/min in maximal oxygen uptake between the 6MST and CPET was assumed, based on previous studies between the 6MWT and CPET [22, 24]. To detect a difference of this amplitude with a paired sample *t*-test, assuming a power of 80%, an alpha level of 0.05 and a drop-out rate of 15%, 15 participants are needed. Fifteen (15) individuals of each disease population (i.e., COPD=15 and ILD=15) will be included for a total of sample 30 participants (15 in Québec and 15 in France), since cardiorespiratory responses to exercise are different among these populations [25].

For ***study 2***, a minimal acceptable intraclass correlation coefficient of 0.5, and an expected intraclass correlation coefficient of 0.75, was assumed for test-retest reliability of the 6MST. Assuming a power of 80%, an alpha level of 0.05, and a drop-out rate of 15%, a total of 52 participants (26 in Québec and 26 in France) will be recruited. This calculated sample was taken as a whole, as test-retest reliability is not expected to be influenced by the type of respiratory disease.

Textbox 1. Inclusion and exclusion criteria

Inclusion criteria:

- Adult ≥ 40 years old
- Diagnosis of chronic obstructive pulmonary disease (GOLD[a] 2 to 4) or of interstitial lung disease (> 6 months)
- Clinically stable for ≥ 4 weeks

Exclusion criteria:

- Interstitial lung disease associated with connective tissue disease and sarcoidosis (often accompanied with multisystemic effects)
- Unstable or severe cardiac condition
- Invalidating rheumatologic or neurologic condition
- Weight exceeding maximal limits of exercise equipment (e.g., 130 kg for the stepper)
- Any other physical or medical condition limiting or contraindicating exercise testing
- Simultaneous participation in another study requiring changes in medication
- Recent pulmonary rehabilitation (≤1 year, potential learning bias for the 6-minute walk test and the 6-minute stepper test)
- *For study 1 only:* Use of oxygen therapy (unable to provide oxygen therapy during testing due to limitation of gas exchange analysis equipment)
- *For study 2 only:* Participation in study 1

[a]Global Initiative for Chronic Obstructive Lung Disease Diagnostic Criteria

Study 1: Procedures and Measurements

For study 1, in addition to a review of medical records, two 3-hour laboratory visits (separated by 6 to 18 days) will be conducted. Participants will be instructed to take all medications as usual, including inhalers. A summary of collected data and outcomes is presented in Table 1 and further described below.

Table 1. Data collected during study 1

Measurements	Medical records	Visit 1	Visit 2
Sociodemographic			
- Age	✓		
- Sex	✓		
- Pulmonary diagnosis	✓		
- Comorbidities and risk factors	✓		
Anthropometric			
- Mass (kg)		✓	
- Height (m)		✓	
- Composition (bioimpedance)		✓	
- Leg length (cm)		✓	
Pulmonary function			
- Spirometry		✓	
- Plethysmography		✓	
- DLCO[a]		✓	
CPET[b] on cycle ergometer			
- Dyspnea (/10)		✓	
- Leg fatigue (/10)		✓	
- Absolute oxygen uptake (L/min)		✓	
- Relative oxygen uptake (mL/kg·min)		✓	
- Carbon dioxide excretion (L/min)		✓	
- Minute ventilation (L/min)		✓	
- Tidal volume (L)		✓	
- Respiratory rate (breath/min)		✓	
- Heart rate (bpm)		✓	
- Blood oxygen saturation (%)		✓	
- Blood pressure (mmHg)		✓	
- Québec only: Inspiratory capacity (*pre* and *post*)		✓	
6-minute walk test			
- Total distance travelled (m)			✓
- Identical measurements as CPET			✓
6-minute stepper test			
- Total number of steps			✓
- Identical measurements as CPET			✓

[a]DLCO: Diffusing capacity of the lungs for carbon monoxide
[b]CPET: Maximal cardiopulmonary exercise testing

Review of Medical Records

Medical records will be reviewed, and the following information will be retrieved regarding participant sociodemographic characteristics: age, sex, pulmonary diagnosis, medications, comorbidities and cardiovascular risk factors. Physical activity level will be assessed using the Ricci and Gagnon questionnaire [26].

First Laboratory Visit

During the first laboratory visit, anthropometric measurements, pulmonary function tests and CPET on a cycle ergometer will be performed.

Anthropometric measurements will be composed of body mass, height, body composition (i.e., lean and fat mass), and leg length. A standardized medical scale and stadiometer will be used to measure

body mass and height, respectively. Body composition will be estimated by bioimpedance [27]. Leg length will be measured using a standard tape measure from the anterior superior iliac spine to medial malleoli [28, 29]. The mean of two measurements of the right leg will be used [28, 29].

Pulmonary function will be characterized by spirometry, lung volume assessment (plethysmography), and diffusing capacity of the lungs for carbon monoxide (DLCO), following current guidelines [30-32]. Spirometry will be conducted firstly [30]. Following a period of quiet breathing, participants will be instructed to inhale to total lung capacity and exhale quickly and forcefully to residual volume. Forced vital capacity and forced expiratory volume in one second will be recorded. The test will be repeated until an agreement of at least 5% is obtained for three measures of forced vital capacity. The mean values of these three tests will be recorded (forced vital capacity and forced expiratory volume in 1 second) [30]. Plethysmography will be conducted secondly [31]. Participants will be instructed to breath quietly, hands on their cheeks, until end-expiratory lung volume is stable. The shutter will be closed near functional residual capacity, and participants will be instructed to conduct a series of gentle pants (between 0.5 and 1 Hz) in order to obtain at least three with adequate technique. The shutter will then be opened, and the participant will exhale to residual volume, followed by an inspiratory slow vital capacity manoeuvre. The test will be repeated until an agreement of at least 5% is obtained for three measures of functional residual capacity. The mean value of these three tests will be recorded (total lung capacity, slow vital capacity, inspiratory capacity, functional residual capacity, expiratory reserve volume, residual volume) [31]. DLCO will be measured thirdly [32]. After a period of relaxed tidal breathing, participants will exhale slowly to residual volume, followed by a rapid inhalation to total lung capacity during which a standardized gas mixture will be provided (carbon monoxide, methane, oxygen, nitrogen). Participants will be instructed to hold their breath for 8 to 12 seconds before exhaling to residual volume. The test will be repeated following a 4-minute rest period. At least two acceptable tests will be obtained [32].

CPET will be performed on a cycle ergometer (Quinton Corival 400 in Québec, Ergoline Ergoselect 200 in France) in accordance with current recommendations [33]. The protocol used is presented in Textbox 2. Briefly, following a warm-up, work rate will increase by 10 to 15 watts per minute, following a ramp protocol, until criteria for maximality is reached. Criteria for maximality will be those recommended by the *American College of Sports Medicine* and include abnormal cardiovascular responses or signs of ischemia, signs or symptoms of cerebral hypoxemia, pulsed blood oxygen desaturation (SpO_2 ≤80 %), and at the request of the participant [34]. Participants will be asked to maintain a pedalling rate of 60±5 revolutions per minute. The modified Borg scale (/10) will be used to assess dyspnea and leg fatigue at rest before the test, during (every 2 minutes and at peak exercise) and after (5 minutes following the end of the test). Cardiorespiratory responses during the CPET will be monitored continuously using a breath-by-breath gas analyzer (Oxycon Mobile in Québec, Metamax 3B Cortex in France), electrocardiogram, and oximeter (Nonin). This equipment will provide data for absolute and relative oxygen uptake, carbon dioxide excretion, minute ventilation, tidal volume, respiratory rate, heart rhythm and rate, and pulsed oxygen saturation (SpO_2). Blood pressure will be measured manually before and after the test. In Québec only, inspiratory capacity will be measured *pre* and within 10 seconds of the end of the test (sitting on the cycle ergometer, hands gripping the handlebars) and a reduction of more than 150 mL will confirm the occurrence of dynamic hyperinflation [35].

Textbox 2. Protocol for maximal cardiopulmonary exercise testing on stationary cycle ergometer

Resting phase:
- Duration: ≥3 minutes (following equipment set-up)
- Resting measurements recorded during last minute of this phase

Warm-up phase:
- Duration: 3 minutes following resting phase
- Warmup at an equivalent of 20 Watts and at a pedaling rate of 60 ± 5 revolutions per minute

Incremental phase:
- Duration: 8 to 12 minutes
- Work rate: start at 20 Watts and increase by 10 to 15 Watts per minute (ramp)
- Pedaling rate: 60 ± 5 revolutions per minute *(stop test if individual falls under 50 revolutions per minute)*

Recovery phase:
- Total duration: 5 minutes
- Active phase (pedaling at 20 Watts) for 2 minutes, followed by passive phase (quiet sitting) for 3 minutes

Monitoring:
- Continuous: breath by breath gas analysis, electrocardiography, peripheral oxygen saturation *(stop test if pulsed oxygen saturation ≤80% with symptoms, such as dizziness, nausea, etc.)*
- During last minute of unloaded phase, every 2 minutes during incremental phase, immediately at completion, and at 5 minutes of recovery phase: blood pressure, dyspnea (/10) and leg fatigue (/10)
- Pre and post incremental phase (*Québec only*): inspiratory capacity

To address current international recommendations that require the test be repeated twice, the first laboratory visit will end with a familiarization trial of the 6MWT for individuals who have not done the test during the 12 months prior (the 6MWT is routinely conducted during medical follow-ops in the centers in this study) [36, 37]. Data from this familiarization trial will not be recorded (although vital signs will be monitored for safety).

Second Laboratory Visit

During the second laboratory visit, spirometry will be repeated to ensure stability of the participants health state (particularly relevant for individuals with COPD). Thereafter, the 6MST and 6MWT will be performed in a randomized order, separated by a rest period of at least 30 minutes.

The ***6MWT*** will be performed in a levelled, unobstructed corridor in accordance with current recommendations [36, 37]. Briefly, the 30-meter testing area will be marked at both extremities with brightly coloured cones. Standardized instructions will be given before beginning the test, and standardized encouragements will be provided every minute during (see Textbox 3 for French translation of instructions used in this study) [36]. Total distance travelled will be collected to the nearest meter. Dyspnea, leg fatigue and cardiorespiratory responses will be collected as described previously.

The ***6MST*** will be performed in accordance with the original description [16]. The test consists of taking the maximum number of steps on a stepper in 6 minutes. One step is counted for each complete flexion-to-extension movement of a lower extremity. The stepper used will be standardized and identical for all participants (Zinnor Mini Multifunctional Fitness Stepper in Québec, Athletic Go Sport in France). Participants will be able to lightly touch a stable surface (i.e., a wall) for balance, if needed. Participants will be allotted a 2-minute familiarization period, followed by rest (≥3 minutes seated), then will begin the test. Standardized validated instructions and

encouragements, adapted from those of the 6MWT, will be provided (Textbox 4) [16, 38]. Evaluators will ensure that complete lower extremity extension is reached during every step. Total number of steps will be automatically provided by the stepper. Dyspnea, leg fatigue and cardiorespiratory responses will be collected as described previously.

Textbox 3. Free translation of standardized instructions and encouragements during the 6-minute walk test [36]

Standardized instructions in French:
Le but de ce test est de marcher la plus grande distance possible pendant 6 minutes. Vous devrez réaliser des allers-retours dans ce couloir. Six minutes, c'est une longue durée, vous risquez de vous essouffler et de vous fatiguer. Vous pouvez choisir de ralentir ou d'arrêter, si nécessaire. Vous pouvez vous appuyer contre le mur pour vous reposer, mais recommencer la marche dès que possible.

Vous ferez des allers-retours en contournant les cônes orange. Vous devriez faire des virages rapides afin de poursuivre dans la direction opposée sans hésitation. Je vais vous montrer comment faire le virage, regardez-moi. *(Démonstration)*

Êtes-vous prêts à faire le test? Je vais compter le nombre d'aller-retour que vous faites et je vous dirai la durée restante toutes les minutes. Rappelez-vous, l'objectif du test est de marcher la plus grande distance possible pendant 6 minutes, mais vous ne devez pas courir. Je vais compter à trois et dire « GO ». Partez lorsque je dis « GO ».

Standardized encouragements in French:
- C'est bien. Il vous reste 5 minutes.
- Continuez comme ça. Il vous reste 4 minutes.
- C'est bien. Vous avez fait la moitié.
- Continuez comme ça. Il vous reste seulement 2 minutes.
- C'est bien. Il vous reste seulement 1 minute.

Textbox 4. Free translation of standardized instructions and encouragements during the 6-minute stepper test [16, 38]

Standardized instructions in French:
Le but de ce test est de réaliser le plus grand nombre de pas possible pendant 6 minutes. Six minutes, c'est une longue durée, vous risquez de vous essouffler et de vous fatiguer. Vous pouvez choisir de ralentir ou d'arrêter, si nécessaire. Vous pouvez vous appuyer contre le mur pour vous reposer, mais recommencer l'exercice dès que possible.

Vous devez étendre complètement la jambe pour réaliser chaque pas. Le step doit toucher la base du stepper à chaque pas. Je vais vous montrer le bon mouvement, regardez-moi. *(Démonstration)*

Êtes-vous prêts à faire le test? L'appareil va compter le nombre de pas que vous faites et je vous dirai la durée restante toutes les minutes. Rappelez-vous, l'objectif du test est de réaliser le plus grand nombre de pas pendant 6 minutes. Je vais compter à trois et dire « GO ». Partez lorsque je dis « GO ».

Standardized encouragements in French:
- C'est bien. Il vous reste 5 minutes.
- Continuez comme ça. Il vous reste 4 minutes.
- C'est bien. Vous avez fait la moitié.
- Continuez comme ça. Il vous reste seulement 2 minutes.
- C'est bien. Il vous reste seulement 1 minute.

Study 2: Procedures and Measurements

For study 2, in addition to a review of medical records, three 1-hour home visits (separated by 2 to 5

days) will be conducted. Participants will be instructed to take all medications as usual, including inhalers. Individuals who participated in study 1 will not be admissible for study 2 to reduce the risk of bias introduced by a possible learning effect with the 6MST. A summary of collected data and outcomes is presented in Table 2 and further described below.

Table 2. Data collected during study 2

Measurements	Medical records	Trial 1	Trial 2	Trial 3
Sociodemographic				
- Age	✓			
- Sex	✓			
- Pulmonary diagnosis	✓			
- Comorbidities and risk factors	✓			
Anthropometric				
- Mass (kg)	✓			
- Height (m)	✓			
General lower limb function				
- SPPB[a] (/12)		✓		
6-minute stepper test				
- Total number of steps		✓	✓	✓
- Dyspnea (/10)		✓	✓	✓
- Leg fatigue (/10)		✓	✓	✓
- Heart rate (bpm)		✓	✓	✓
- Pulsed oxygen saturation (%)		✓	✓	✓
Adverse events				
- Minor		✓	✓	✓
- Serious		✓	✓	✓
Semi-structured interview				
- Level of comfort during test				✓
- Perception of safety				✓

[a]SPPB: Short Physical Performance Battery

Review of Medical Records

Medical records will be reviewed, and the following information will be retrieved regarding participant sociodemographic characteristics: age, sex, pulmonary diagnosis, medications, comorbidities and cardiovascular risk factors. Physical activity level will be assessed using the Ricci and Gagnon questionnaire [26].

First Trial

The first trial of the 6MST (familiarization trial) will be conducted at the participant's home with the therapist present. Preceding this trial, the ***Short Physical Performance Battery*** (SPPB) will be performed to obtain a general assessment of lower limb function [39].

The ***6MST*** will be performed using a standardized portable stepper (same as in study 1) and following the same protocol as in study 1, including the 2-minute *pre*-test warm-up period. However, full cardiorespiratory responses will not be measured. Instead, an oximeter (Nonin) will be used to monitor heart rate and pulsed oxygen saturation continuously. Blood pressure, dyspnea and perceived exertion will be measured *pre* and *post*-test using the modified Borg scale (/10). For individuals on home oxygen therapy, oxygen flows will be titrated if SpO_2 falls bellow 88% during the test, with the aim of maintaining an SpO_2 between 88-92%, while always respecting the flow limits of the prescribing physician's parameters. As in study 1, the test will be terminated if blood saturation falls

to ≤80% accompanied with symptoms of hypoxia (such as dizziness, nausea, etc.).
All ***adverse events*** will be recorded and graded according to the *Common Terminology Criteria for Adverse Events Version 5* (United States Department of Health and Human Services), progressing from mild (1) to lethal (5) [40]. See Textbox 5 for the standardized grading used in this study. Adverse events are defined as any event that leads to (or could potentially lead to) prejudice to the participant or that inhibits the completion of the test. Examples include dyspnea, dizziness or nausea, close-call or fall events, musculoskeletal pain, chest pain, syncope, etc.

Textbox 5. Classification of adverse events based on the Common Terminology Criteria for Adverse Events version 5 [40]

Grade 1: Mild
Mild adverse events are asymptomatic or with mild symptoms, or do not require intervention. Such adverse events include:

- Musculoskeletal pain or injury (asymptomatic or mild)
- Joint effusion (asymptomatic or mild)
- Dyspnea with moderate exertion
- Productive cough with minimal production of sputum
- Wheezing with minimal symptoms
- Dehydration requiring increased oral fluid intake
- Hypoglycemia or hyperglycemia not requiring medical intervention
- Asymptomatic hypotension

Grade 2: Moderate
Moderate adverse events require minimal, local or non-invasive intervention, or limit age-appropriate instrumental activities of daily living (preparing meals, doing the groceries, managing money, etc.). Such adverse events include:

- Musculoskeletal pain or injury limiting instrumental activities of daily living
- Joint effusion limiting instrumental activities of daily living
- Dyspnea with minimal exertion limiting instrumental activities of daily living
- Productive cough with moderate production of sputum or limiting instrumental activities of daily living
- Wheezing with moderate symptoms or requiring medical intervention or limiting instrumental activities of daily living
- Dehydration requiring intravenous fluids
- Hypoglycemia or hyperglycemia requiring intervention but no long-term changes in medical management
- Hypotension requiring non-urgent intervention
- Chest pain of palpitations related to exertion subsiding with rest

Grade 3: Severe
Severe adverse effects are medically significant but not immediately life-threatening, or require hospitalization, or limit self-care activities of daily living (bathing, dressing, using the toilet, feeding self, etc.). Such adverse events include:

- Musculoskeletal pain or injury limiting self-care activities of daily living
- Joint effusion limiting self-care activities of daily living
- Dyspnea at rest limiting self-care activities of daily living
- Productive cough with copious production of sputum or limiting self-care activities of daily living
- Wheezing with severe symptoms limiting self-care activities of daily living, or requiring oxygen therapy or hospitalization
- Dehydration requiring hospitalization
- Hypoglycemia or hyperglycemia requiring hospitalization or long-term changes in medical management

- Hypotension requiring intervention or hospitalization
- Syncope

Grade 4: Life-threatening
Life-threatening adverse effects require immediate and urgent intervention to avoid death. Such adverse events include:

- Dyspnea (life-threatening) requiring urgent intervention
- Wheezing with life-threatening consequences, or requiring urgent intervention
- Dehydration with life-threatening consequences
- Hypoglycemia or hyperglycemia with life-threatening consequences
- Hypotension (life-threatening) requiring urgent intervention
- Cardiac arrest

Grade 5: Lethal
Lethal adverse effects lead to death and are generally a continuum of life-threatening events. Such adverse events include:

- Dyspnea leading to death
- Wheezing leading to death
- Dehydration leading to death
- Hypoglycemia or hyperglycemia leading to death
- Hypotension leading to death
- Cardiac arrest leading to death

Second and Third Trials

The second and third trials of the 6MST will be performed in a randomized order, with either direct (therapist present at the home) or remote (therapist present through videoconferencing software, as in a telerehabilitation setting) monitoring. For the remotely monitored trial, another person (i.e., family member, etc.) will be present to ensure safety in case of emergency. The ***6MST*** and ***adverse events*** will be respectively performed and collected as in the first trial (the only difference being the presence of the therapist via videoconferencing for one of the trials). The third trial of the 6MST will be followed by a ***semi-structured interview*** using a guide created *a priori*. This interview will focus on the two following themes: level of comfort executing the test (ease of execution, symptoms, anxiety), and perception of safety (regarding test, and home and telerehabilitation settings). The interview will be conducted in person or through videoconferencing software, depending on the randomization of the third trial.

Data Preparation and Analysis

All data will be stored in digital databases (REDCap in Québec, OpenClinica in France) on secured servers at the participating research facilities (CR-IUCPQ, GHICL) following local protocols. Using a standardized thesaurus, research teams will enter data directly in both databases through remote access. With regards to data analysis, descriptive statistics will be used to summarize participant characteristics. For quantitative data, normality will be verified with Shapiro-Wilk tests and Q-Q plots. All statistical analyses will be completed using SPSS Statistics Version 28 with a significance level set at $p<0.05$. Graphical analyses will be conducted using Excel version 2305 and qualitative analyses will be performed with Nvivio version 14.

For ***objective 1***, concurrent validity will be assessed using paired sample *t*-tests (or Wilcoxon signed-rank tests) to verify whether peak cardiorespiratory (e.g., oxygen consumption, minute ventilation, heart rate, etc.) and symptomology (i.e., dyspnea and leg fatigue) values obtained during the 6MST are comparable to the CPET and 6MWT. Pearson's correlation coefficients (r) will also be calculated to quantify the strength of association between peak cardiorespiratory and symptomology values

reached during the 6MST with those reached during the CPET and the 6MWT. Additional Pearson's correlation coefficients (*r*) will be calculated to determine the strength of the association between the number of steps taken during the 6MST and peak oxygen consumption and heart rate reached during all three tests. The level of correlation will be interpreted as poor (≤0.20), fair (0.21–0.40), moderate (0.41–0.60), good (0.61–0.80), and very good (0.81–1.00) [41]. Agreement will be assessed with Bland-Altman plots and 95% limits of agreement (mean difference ± 1.96 standard deviation of the difference) between peak cardiorespiratory and symptomology values reached during the 6MST and those reached during the CPET and the 6MWT [41].

For ***objective 2***, reliability (trial 2 versus 3) will be assessed using paired sample *t*-tests (or Wilcoxon signed-rank tests), Bland-Altman plots (with 95% limits of agreement), and intraclass correlations [42-44]. Intraclass correlations will be interpreted as poor (≤0.50), moderate (0.51–0.75), good (0.76–0.9), and very good (0.91–1.00) [44].

For ***objective 3***, all minor and serious adverse events, for all trials, will be reported. The semi-structured interviews will be voice-recorded and transcribed. Thematic content analysis will be used to analyze all verbatim [45]. Briefly, a combination of deductive (based on *a priori* interview guide) and inductive (based on data) approaches will be used to generate themes and subthemes. Coding will be conducted separately by two reviewers, who will compare their results and resolve discrepancies through discussion.

Ethical considerations

This research project received ethical approval at the CR-IUCPQ on October 12, 2023 (2024-4075, 22380), and at the GHICL on September 25, 2023 (2023-A01571-44). All participants will provide written free and informed consent prior to enrollment. All information is provided in French and will be translated to English if needed. All data collected will be stored anonymously (coded numeric ID) on secured servers at participating research facilities. Participants will receive financial compensation in accordance with local standardized fees in participating research centres (value of approximately 40 CAD per laboratory visit and 10 CAD per at-home visit).

Results

The first participant (study 1) was recruited on February 2, 2024, and will continue for a maximum of 12 months. Recruitment for study 2 is to follow the completion of study 1 and is expected to last for a maximum of 12 months. Data analysis will occur after, and results will be published in peer-reviewed journals.

Discussion

Overview

The aim of this stud is to provide further evidence regarding the metrological properties of the 6MST in individuals with COPD or ILD. The 6MST is a clinically relevant functional capacity test that is specifically adapted for home-based models of care.

This research project innovates by being among the first to extensively evaluate the metrological properties of the 6MST in a diversified sample of pulmonary lung diseases. Moreover, this study is the first to evaluate the validity and the safety of assessing exercise capacity using 6MST through direct and remote monitoring, mimicking home-based and telerehabilitation contexts. Since all the equipment required for the 6MST (i.e., stepper) can easily be transported by a therapist, or even shipped to the patient, and requires very minimal space, this test is highly applicable in home-based rehabilitation models of care.

Knowledge derived from this research project will therefore contribute to addressing barriers currently hampering the wider adoption of these new models of care. Ultimately, this research project

fits in a continuum of knowledge creation that aligns with the United Nations Sustainable Development Goals by contributing to augmenting healthcare service delivery (goal number 3) and reducing healthcare access inequalities (goal number 11).

Potential challenges and appropriate mitigation strategies

Certain potential changes were foreseen, and the following mediation strategies will be put into place:

1. Changes in a participant's health status during the study could introduce bias in the results of repeated measures. To help reduce this risk, repeated testing conducted in the laboratory will be preceded by spirometry to ensure stability in health status. For testing conducted in the home-based settings, signs and symptoms of exacerbations will be collected prior to each repeated testing.
2. The steppers used in this study use hydraulic pistons to simulate the stepping movements. The resistance provided by the pistons is greater when the fluid inside them is cold and decreases progressively with use as the pistons heat. To avoid inducing a potential bias during repeated tests, a standardized two-minute warm-up (familiarization) will be conducted followed be a standardized 3 minutes of rest before initiating the test trial. Participants will also be instructed not to use the stepper device other than when instructed to do so during testing.
3. Some participants may have trouble maintaining balance during the 6MST. Participants are allowed to touch a wall or other stable surface to assist in maintaining balance. Nevertheless, for home-based testing in absence of the therapist (i.e., videoconferencing), a third person (e.g., family member) will be present to ensure safety. This person will also be instructed on how to react in case of emergency.

Strengths and Limitations

This research project has strengths and limitations that warrant consideration. With regards to ***strengths***, firstly, sex-parity will be assured and help limit bias, particularly related to the under-representation of people of the female sex in the pulmonary rehabilitation literature [46]. Secondly, the *a priori* calculation of sample sizes required will ensure sufficient statistical power to address the study's objectives. Thirdly, the inclusion of several different and complementary statistical strategies will ensure adequate evaluation of the metrological properties of the included tests. Fourthly, the multicentre and multinational nature of this study will improve its external validity and generalizability. Fifthly, the inclusion of a mixed methods study design will help ensure that stakeholders (i.e., individuals with pulmonary diseases) have an input regarding the acceptability and utility of the physical tests being validated in this research project. Finally, the publication of this protocol *a priori* will ensure accountability and any changes made *a posteriori* will be public knowledge and require justification.

With regards to ***limitations***, firstly, only individuals with COPD and an ILD will be included in this study. This will limit its generalizability in the population with other pulmonary diseases (e.g., asthma, cystic fibrosis). This methodological choice was made in an effort to reconcile feasibility (limited time and budget) and generalizability (i.e., heterogeneity). Secondly, for study 1, participants will be required to perform several physical tests on the same day, potentially leading to fatigue that may alter performances. To address this, tests occurring on the same day are separate by a rest period and are randomized. Moreover, the research team has extensive experience with this type of protocol. Finally, regarding test-retest reliability in study 2, a learning effect is possible as the test will be conducted repeatedly. To limit this effect, the 1st trial of the test will exclusively serve as a familiarization trial. Moreover, a 2-minute warm-up period is allotted before each trial. Nonetheless, as the learning effect may not be completely eliminated, randomization of the second and third trials

is performed in order to limit a systemic effect on the test conditions (i.e., with therapist present or through videoconferencing software).

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Data availability

The data sets generated during and/or analyzed during this study are not publicly available to maintain participant confidentiality but are available from the corresponding author on reasonable request.

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Conflicts of Interest

None declared.

Abbreviations

6MWT: 6-minute walk test
6MST: 6-minute stepper test
COPD: Chronic obstructive pulmonary disease
CPET: Maximal cardiopulmonary exercise testing
CR-IUCPQ: Centre de recherche de l'Institut universitaire de cardiologie et de pneumologie de Québec
DLCO: Diffusing capacity of the lungs for carbon monoxide
ILD: Interstitial lung disease
GHICL: Groupement des Hôpitaux de l'Institut Catholique de Lille
GOLD: Global Initiative for Chronic Obstructive Lung Disease Diagnostic Criteria
SpO_2: Pulsed oxygen saturation
SPPB: Short Physical Performance Battery

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Supplementary Files

Multimedia Appendixes

Peer-review report.
URL: http://asset.jmir.pub/assets/b965023376f093770be565e4dabb142f.pdf