Quality of Home Spirometry Performance amongst Adults with Cystic Fibrosis

Jody Bell

A thesis submitted to fulfil requirements for the degree of Master of Philosophy

Faculty of Medicine & Health
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Statement of originality

This is to certify that to the best of my knowledge, the content of this thesis is my own work. This thesis has not been submitted for any degree or other purposes.

I certify that the intellectual content of this thesis is the product of my own work and that all the assistance received in preparing this thesis and sources have been acknowledged.

Jody Bell

16 December 2024

Author attribution

The work contained in the body of this thesis, except otherwise acknowledged, is the result of my own investigations.

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Abstract

Spirometry is usually performed under the supervision of a trained respiratory scientist to ensure acceptability and repeatability of results. To evaluate the quality of spirometry performance by adult cystic fibrosis (CF) patients with and without observation by a trained respiratory scientist, an observational, single centre study was conducted between February to December 2020. 74 adults were recruited and instructed to perform spirometry without supervision within 24 hours of their remote CF clinic consultation. Spirometry was repeated at their consultation, supervised by a respiratory scientist using video conferencing. The majority of patients achieved grade A (excellent) or B (very good) spirometry quality with (95%) and without supervision (93%) independent of lung function severity. Similarly, forced expiratory volume in 1 second demonstrated no significant differences with paired spirometry performed within a 24-hour period. For a large proportion of adult CF patients, unsupervised portable spirometry produces acceptable and repeatable results.

As supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

Dr. Sheila Sivam, 1st, December 2024.

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Abbreviations

ATS	American Thoracic Society
BE	Bronchiectasis
BOS	Bronchiolitis obliterans syndrome
CF	Cystic fibrosis
CFTR	Cystic fibrosis transmembrane conductance regulator
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
ERS	European Respiratory Society
FEV_1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
GVHD	Graft versus host disease
ICC	Intraclass correlation coefficient
ILD	Interstitial lung disease
IPF	Idiopathic pulmonary fibrosis
LOA	Limits of agreement
PPE	Personal protective equipment
$ppFEV_1$	Forced expiratory volume in 1 second, percent predicted
ppFVC	Forced vital capacity, percent predicted
pwCF	People with cystic fibrosis
RPA	Royal Prince Alfred Hospital
SD	Standard deviation
SSc-ILD	Systemic sclerosis-associated interstitial lung disease

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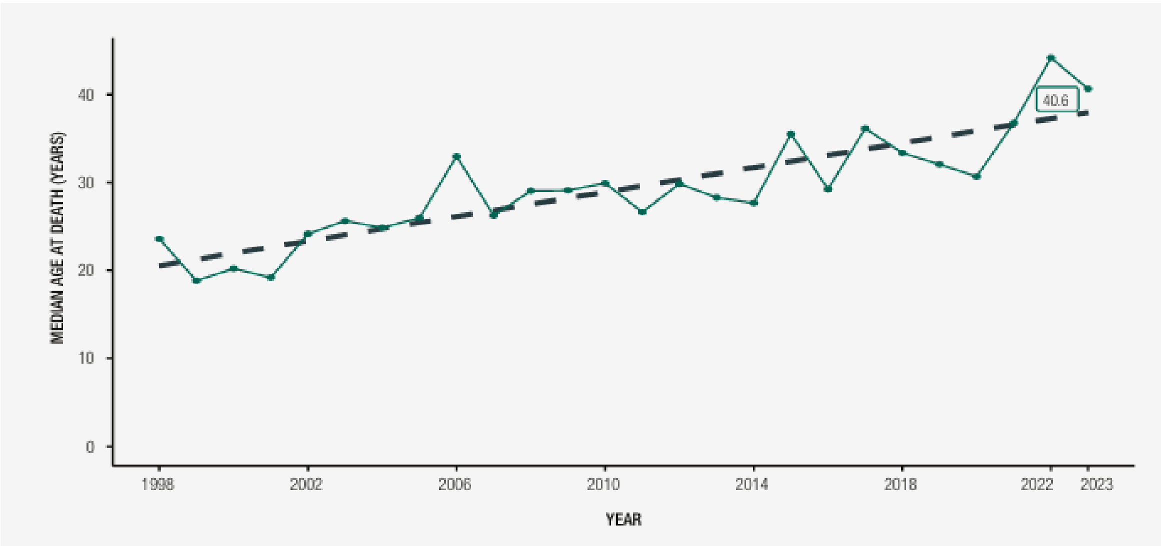
Chapter 1
Literature review

1. Cystic Fibrosis

Background and disease population

Cystic fibrosis (CF) is an inherited autosomal recessive disease (Ruseckaite et al., 2022; Shteinberg et al., 2021), estimated to be affecting anywhere from 163,421 to 209,204 people across 96 countries (Guo et al., 2024). In Australia in 2023 there were 3798 people with CF (pwCF) registered with the Australian Cystic Fibrosis Data Registry, however this number is likely higher as not all pwCF are registered. CF is a complex multi-system disease, characterised by lung disease (bronchiectasis with chronic pulmonary infection and inflammation), and extra pulmonary disease including pancreatic exocrine and endocrine (diabetes mellitus) dysfunction, liver disease, and male infertility. It is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, which results in dysfunction of a protein in the secretory epithelial cells that regulates sodium and chloride transport (Kerem et al., 2005). In the lung, mutations in the CFTR protein channels impair the mucociliary cells and cause build-up of thick secretions. This leads to infection and inflammation which can cause acute exacerbations and eventually structural lung damage (Shteinberg et al., 2021). Although life expectancy in the last 4 decades has dramatically improved (Figure 1), respiratory failure is still reported as the most common cause of premature death in pwCF. Poorer quality of life and a large burden of care for most pwCF and their families is still an ongoing issue (Bell et al., 2020; Castellani et al., 2018; Ruseckaite et al., 2022), however the recent advancement of CFTR modulator therapy has begun to decrease this burden (Middleton et al., 2019; Taylor-Cousar et al., 2023).

Figure 1: 1998 – 2023 Australian Cystic Fibrosis Data Registry Median Age of Death



Straight dashed line represents the overall trend estimated by a linear regression model

(*Australian Cystic Fibrosis Data Registry Annual Report*, 2023; *https://www.cysticfibrosis.org.au/cf-data-registry/*, 2023)

Standard of care

Once diagnosed, pwCF require support from a health care service. The current standard of care is for pwCF to be seen in a specialised CF centre every 3 months by a multidisciplinary team of physicians, specialist nurses, dieticians, physiotherapists, and psychologists. If possible, each visit should include a routine physical examination, weight measurement, oximetry, sputum sample and a lung function test (Castellani et al., 2014; Kerem et al., 2005; Shteinberg et al., 2021). While regular clinic attendances are considered the standard of care, an ongoing concern is infection control. Bacterial lung infections are frequent in pwCF, and respiratory viruses can also cause acute exacerbations. Frequent use of antibiotics to treat these infections can lead to the development of antimicrobial resistance and subsequently, more rapid progression of lung disease (Kerem et al., 2005). CF clinics must ensure no patient-to-patient contact occurs within clinic settings in an effort to prevent cross infection, which can occur via multiple routes including coughing, airway clearance, spirometry and fomite transmission from contaminated surfaces. PwCF are required to wear a face mask, while clinicians who come in contact with pwCF are required to wear personal protective equipment (PPE). Cleaning of hard surfaces must be completed after each person with CF is reviewed in clinic and increase air exchange regimens are preferred in clinic consulting rooms. In addition, some strains of microbiota require the patient come to a separate clinic either on a different day or at the end of the day to avoid cross-infection between patients (Shteinberg et al., 2021).

2. Spirometry

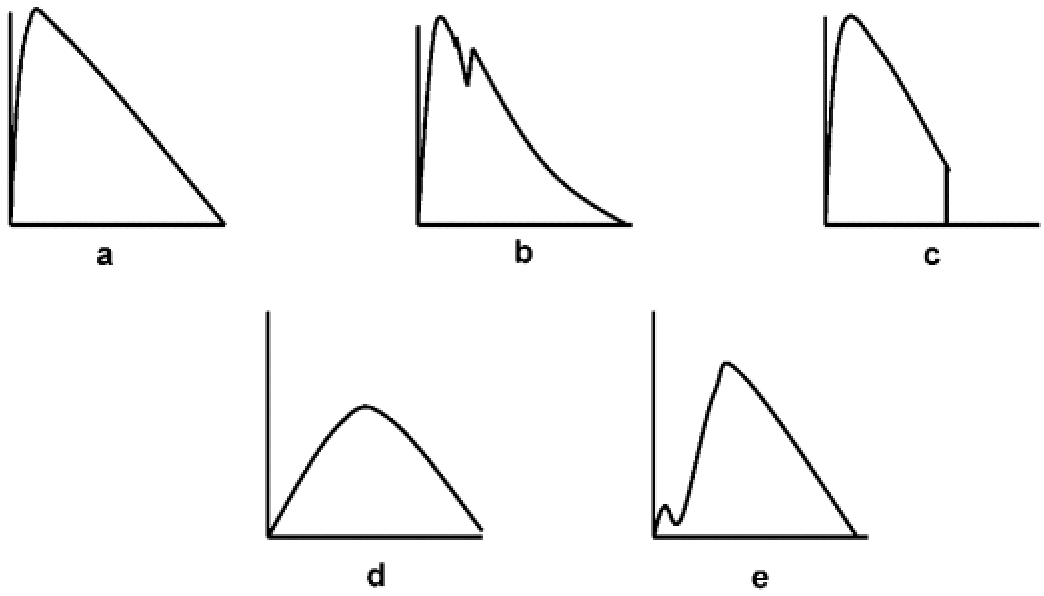
What is spirometry

Spirometry is a physiological lung function test that measures the inhalation and exhalation of breath in volume and flow as a function of time. It requires a maximal effort of inspired and expired breath. The test involves the patient breathing into a machine through a mouthpiece with a nose clip blocking the nostrils. The patient must take in a full inhalation of air then blast the air out as forcefully as possible until it is fully expired, with an inhalation required to complete the test. The two main measurements obtained are forced expiratory volume (FEV_1) which measures the maximal forced breath out in the first second and forced vital capacity (FVC) which is the total amount of air expired at force. Results are given in litres and as a percentage of a predicted value ($ppFEV_1$ and ppFVC), which is obtained from the patients age, sex at birth, and height, with ethnicity also having an influence (Mottram, 2023). Z-scores are also reported, which represent the number of standard deviations from the predicted value and identifies the upper and lower limits of normal (5^{th} and 95^{th} percentile limits, or Z-scores of -1.65 and 1.65 respectively) (Stanojevic et al., 2022). False-positive results are possible if this test is performed poorly, which can lead to an incorrect diagnosis and thus treatment (Mottram, 2023).Therefore, testing needs to be performed by personnel with adequate training, as patients need to be encouraged to perform these tests with maximal effort, and continuous instruction is often required to achieve accurate results (Miller et al., 2005).

Standards exist to ensure valid measurements

The American Thoracic Society and European Respiratory Society (ATS/ERS) provide guidelines and criteria for performing correct testing methodology. These guidelines provide the standards of lung function testing used by many countries and provide information on all aspects of testing, including calibration of machinery, patient details to be obtained and how to perform the test. A trained technician is required to coach the patient and observe if the criteria are met. The ATS/ERS criteria requires at least 3 acceptable spirometry manoeuvres are obtained with at least 2 having FEV_1 and FVC measurements within 150 mL of the best effort. Results are graded from A to F for both FEV_1 and FVC, with an A grade being achieved when these criteria are met and an F grade corresponding with no acceptable results being achieved (Table 1). Possible errors that can occur include slow or hesitant start of the blast, a cough during the first second, or early termination (Enright, 2003). Technique issues that will affect the results include the patient not blowing the air out as hard as they can and glottic closure (Figure 2). Other issues to be monitored which may require additional mouthpiece adaptors during testing include leaking around the mouth if the patient is unable to form a tight seal with their lips or obstruction of the mouthpiece by the tongue or teeth (Graham et al., 2019). These standards also state that it is the “responsibility of the operator to observe and engage with the patient to achieve optimal results, which requires a combination of training and experience” (Graham et al., 2019).

Figure 2: Acceptable and unacceptable spirometry flow-volume loops



Possible errors a) no errors, b) cough in first second, c) early termination, d) submaximal effort, e) hesitation at start of the blast (Lange et al., 2009)

Table 1: Spirometry grading system for FEV_1 and FVC

Grade	Criteria for age 7 years +	Criteria for age 6 years and under
A	Three or more acceptable manoeuvres with the top two FEV_1 and FVC values within 150 mL*	*Within 100 mL (or 10% of the highest value, whichever is greater)
B	Two acceptable manoeuvres with the top two FEV_1 and FVC values within 150 mL*	*Within 100 mL (or 10% of the highest value, whichever is greater)
C	Two or more acceptable manoeuvres with the top two FEV_1 and FVC values within 200 mL*	*Within 150 mL (or 10% of the highest value, whichever is greater)
D	Two or more acceptable manoeuvres with the top two FEV_1 and FVC values within 250 mL*	*Within 200 mL (or 10% of the highest value, whichever is greater)
E	Either two or more acceptable manoeuvres with the top two FEV_1 and FVC values less than 250 mL* Or only one acceptable manoeuvre	*>200 mL (or 10% of the highest value, whichever is greater)
F	No acceptable manoeuvres achieved	
U	Manoeuvres are usable but not acceptable	

FEV_1: Forced Expiratory Volume in 1 second; FVC: Forced vital capacity

Why is spirometry used

Diagnosis and Monitoring of lung diseases

Spirometry can be a useful tool in the diagnosis and monitoring of many lung diseases, as well as the evaluation of general respiratory health. Measurements obtained from spirometry manoeuvres can be used to assess airway responsiveness, monitor disease course, assess preoperative risk and determine a prognosis from many pulmonary conditions (Graham et al., 2019). Initial testing can be used in conjunction with other diagnostic tools to help diagnose pulmonary conditions including asthma, chronic obstructive pulmonary disease (COPD), and interstitial lung disease (ILD). Following that, it can be very effective in monitoring the progression of a lung disease over time, including recovery from exacerbations. It can also be used to monitor the response to medications (Graham et al., 2019).
In general, spirometric abnormalities can be grouped into two categories, restrictive or obstructive.

Restrictive lung diseases cause a reduction of the expansion of the lung which reduces the amount of air exhaled and results in a reduced FVC and/or FEV_1. ILD is a restrictive lung disease which includes idiopathic pulmonary fibrosis (IPF), pneumoconiosis and sarcoidosis and there are numerous other restrictive conditions including neuromuscular disorders and lung resection (Mottram, 2023; Robert L. Maynard, 2020). Respiratory muscle weakness can cause a reduction in FVC, which can be further exacerbated by being in the supine position. A combination of erect and supine spirometry can thus be used in the assessment of diagnosis of neurogenic, neuromuscular junction and muscular diseases (Robert L. Maynard, 2020).

Obstructive airways disease results in either a reduction in airflow into or out of the lungs, as shown by a reduction in FEV_1. An example is asthma, which is caused by inflammation of the airways and is characterised by reversible airway obstruction. This reversibility can be measured by performing spirometry before and after taking bronchodilators, which can result in an increase in FEV_1 or FVC. Further testing following the initiation of an inhaler can inform the prescriber if the inhaler has helped. Chronic obstructive pulmonary disease (COPD) describes long standing and persistent airway obstruction and airflow limitation, with causes including emphysema, chronic bronchitis, and non-reversible asthma. Spirometry can help determine the severity of airway obstruction when compared with healthy population data. The FEV_1 trend can be monitored over time. CF is also considered an obstructive disease (Mottram, 2023; Robert L. Maynard, 2020).

Spirometry can also be used to help detect bronchial hyperresponsiveness. There are several different bronchoprovocation tests available, which stimulate the airways using different mechanisms. Airways of healthy people will not be affected by the stimuli, but in a susceptible individual, direct or indirect stimuli can cause the contraction of the smooth muscle cells and a narrowing of the lumen. Spirometry is performed before, during and after the airways are aggravated, with FEV_1 being the common variable used to determine if there is airway hyperreactivity. These bronchoprovocation tests can help diagnose asthma and help to distinguish it from other diseases that cause airway inflammation or obstruction like COPD (Mottram, 2023; Robert L. Maynard, 2020).

Figure 3: Normal and abnormal flow volume pattern loops

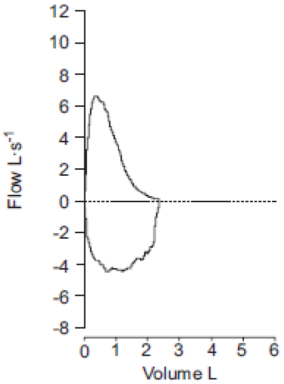


FIGURE 5. Flow–volume loop of a normal subject with end expiratory curvilinearity, which can be seen with ageing.

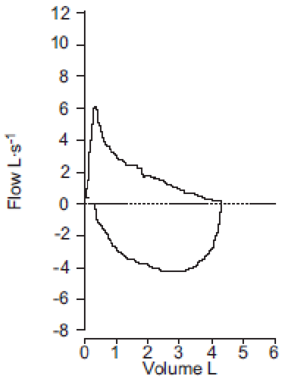


FIGURE 6. Moderate airflow limitation in a subject with asthma.

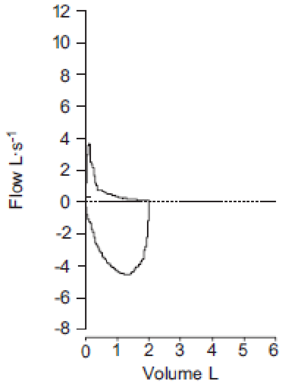


FIGURE 7. Severe airflow limitation in a subject with chronic obstructive pulmonary disease.

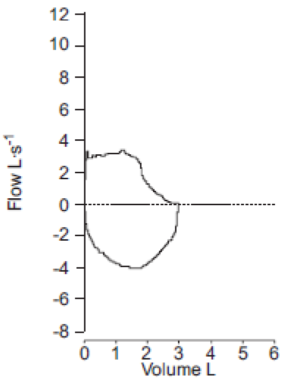


FIGURE 8. Variable intra-thoracic upper airway obstruction.

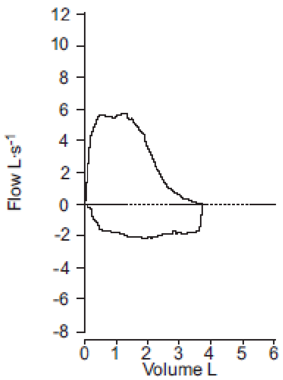


FIGURE 9. Variable extra-thoracic upper airway obstruction.

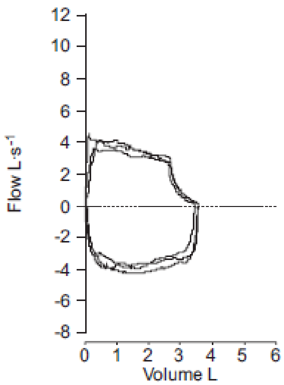


FIGURE 10. Fixed upper airway obstruction shown by three manoeuvres.

(Miller et al., 2005)

Cystic Fibrosis and spirometry

Spirometry (FEV_1) has been the key measure used to determine the state of the lungs, as it slowly declines over the lifespan of pwCF (Shteinberg et al., 2021). Moderate or severe pulmonary impairment can have a major impact on life expectancy. Those with $ppFEV_1 \geq 70\%$ are likely to have the best survival whereas those with a $ppFEV_1$ between 40-70% have a 50% chance of reaching the age 40 years. Those with an $ppFEV_1$ of < 40% have a poorer prognosis and a 50% likelihood of death before the age of 30 years (Durda-Masny et al., 2021). CF pulmonary exacerbations are equated with decreased quality of life, increased mortality risk and utilise more resources. Exacerbations can be defined by a drop in FEV_1 of 10% or more from a previously recorded value, along with symptoms including cough, shortness of breath, increased sputum and fatigue. The Fuchs criteria is often used in which 4 or more of the criteria being met (Table 2) is used to define an exacerbation (Shteinberg et al., 2021; VanDevanter et al., 2021).

FEV_1 can be used to guide day-to-day management, assess treatment response and determine if patients should be referred for lung transplantation assessment. Cooperation is needed from CF patients as maximal effort is required, with some finding it difficult to perform the test reliably, particularly young children (Shteinberg et al., 2021). Studies have shown that children as young as 2.5 years are capable of performing technically correct spirometry, (Marostica et al., 2002; Vilozni et al., 2007), however the Cystic Fibrosis Australia guidelines recommend children 5 years and over can reliably perform spirometry (Bell et al., 2008; Scott Bell, 2008). Most adult patients have been performing spirometry since they were young and so are experienced in the correct technique, meaning regular spirometry is a reliable way to monitor their lung function.

In line with CF standards of care, thorough cleaning is particularly important in the pulmonary function laboratory due to the aerosolization of bacteria and viruses that may occur when a patient performs spirometry. In addition, standard of care guidelines recommend that spirometry be performed in well-ventilated rooms with in-line filters (Castellani et al., 2014; Kerem et al., 2005).

Post transplant monitoring

Another group who benefits from the monitoring of spirometry are lung transplant recipients. Improved survival is associated with the normalisation of spirometry 12 months after a lung transplant, with each 10% decrease in FEV_1 increasing the risk of death (Paraskeva et al., 2021). Spirometry can also assist in the early detection of lung complications in allogeneic hematopoietic cell transplant patients, thus improving survival and preventing significant and possibly permanent loss of lung function (Sheshadri et al., 2022).

Table 2: Fuchs sign and symptom criteria

- Increased cough
- Change in sputum
- New or increased hemoptysis
- Increased dyspnea
- Malaise, fatigue or lethargy
- Temperature above 38°C
- Anorexia or weight loss
- Sinus pain or tenderness
- Change in sinus discharge
- Change in physical examination of the chest
- Decrease in pulmonary function by 10% or more from a previously recorded value
- Radiographic changes indicative of pulmonary infection

(VanDevanter et al., 2021)

3. Introduction of Portable Home Spirometers and Telehealth Appointments to the CF Clinic

As per CF standard of care, pwCF should be seen by a multidisciplinary team every 3 months (Kerem et al., 2005). In recent years, there has been an increase in the number of adults attending CF clinics (Dixon et al., 2022). This makes 3 monthly visits challenging with infection control limiting the turnaround time of consult rooms. A solution has been to introduce telehealth appointments as part of a regular CF clinic, which allows some patients to attend CF clinic via video conferencing from home or work. Although it requires more organising and adds to the administrative burden, the addition of telehealth has had many advantages for both the patient and the clinic (Dixon et al., 2022). This transition to telehealth has also been made feasible due to the more widespread use of portable spirometers.

At Royal Prince Alfred Hospital (RPA), Sydney, Australia, the COVID-19 pandemic escalated the use of telehealth appointments as all face-to-face appointments were cancelled. Patients understood the need to stay home and isolate to reduce exposure to COVID-19. As a result, the transition to appointments via video conferencing was relatively smooth (Bell et al., 2023). Multiple publications have demonstrated similar successful transitions in other centres (Dixon et al., 2022; Edmondson & Lechtzin, 2023; Vagg et al., 2021).

Advantages of telehealth appointments

Changing population leading to larger adult clinics

The first CFTR modulator drugs were approved in 2012, and each successive generation has become more effective in correcting the underlying cause of the disease, with the latest triple therapy combination resulting in substantial multi-system benefits (Taylor-Cousar et al., 2023). Although an increase in the average age of pwCF was already occurring before this, further improvement is expected with this therapy (Gramegna et al., 2024). This has resulted in the adult population of pwCF now outnumbering the paediatric population in many countries (Hisert et al., 2023). In 2022, 57% of pwCF in Australia were over the age of 17, with the median survival age increasing to 58, up 11 years since 2012 (*https://www.cysticfibrosis.org.au/cf-data-registry/*, 2023). In the United States, the median survival has increased by 20 years to 56.6 since 2006 (Gramegna et al., 2024). This increase in survival has also led to the population experiencing more age associated co-morbidities such as hypertension, cardiovascular disease (Prickett et al., 2023) and menopause (Gramegna et al., 2024). The addition of telehealth appointments in combination with face to face has allowed pwCF to maintain their 3 monthly appointments, with the telehealth consults sufficient to maintain care when they are feeling more well, which is more likely now with the widespread use of the modulator therapy (Prickett et al., 2023). In 2022 69% of Australian adults were on CFTR modulator therapy, up from 38% in 2019 (*https://www.cysticfibrosis.org.au/cf-data-registry/*, 2023).

Travel, cost and time reduction

One of the biggest advantages of telehealth appointments for pwCF is the elimination of travel time to attend CF clinic at a tertiary centre, which also leads to a reduction in cost (Bell et al., 2023; Dixon et al., 2022). Previous studies have shown that patients living in regional areas with long travel times were enthusiastic about integrating telehealth appointments into regular CF clinics (Logie et al., 2020). Surveys completed by 75 adults with CF in an Australian hospital found an average saving of $272.20 per patient per clinic when face-to-face appointments are replaced with telehealth (Bell et al., 2023). The time saved by regional pwCF was an average of 237 minutes (SD132 to 341) per clinic, and 70 minutes (SD 42 to 98) for those living in nonregional areas.

As pwCF feel more well, there is an increased chance they will be working or studying full time. Telehealth appointments mean they only need time off for the actual appointment, saving time from the travel it would have taken to attend in person. In addition to this, the latest CFTR therapy has resulted in an increase in the number of pregnancies (up 18% from 2019 to 2022 in Australia (*https://www.cysticfibrosis.org.au/cf-data-registry/*, 2023)), adding further time constraints to attending face to face clinics (Gramegna et al., 2024). Telehealth appointments allow the continued support of the CF team without the extra burden of traveling to the CF centre.

Infection control

Despite the widespread use of standardised infection control precautions, many pwCF are still concerned about the risk of cross-infection when attending CF clinic (Prickett et al., 2023). The reduction of this risk with the use of telehealth is a major benefit for patients and clinics (De Biase et al., 2020; Dixon et al., 2022). PwCF that have certain infectious pathogens who need to be seen apart from other patients, can sometimes miss out on seeing select members of the multi-disciplinary team (Shteinberg et al., 2021). For this group, maintaining telehealth appointments allows for a more flexible schedule as they can be seen at any time in the clinic and can be seen by all members of the team. Telehealth appointments in this group also benefit the clinic as there is a reduction in the amount of cleaning required after face-to-face appointments resulting in cost savings. There is also a reduction in the amount of personal protective equipment (PPE) used in each clinic (Bell et al., 2023).

Portable spirometers allow continued monitoring for patients not attending clinics face to face

The introduction of portable spirometry devices has made telehealth a more viable option as lung function can continue to be monitored regularly. As the CF standard of care, spirometry should be measured at each clinic visit due to it being the strongest clinical predictor of mortality (Kerem et al., 2005). These devices require a smart phone with Bluetooth capability and are generally easy to use. Patient satisfaction with these devices is generally high amongst pwCF as well as in several other disease cohorts (Davis et al., 2022; Fettes et al., 2022; Ilić et al., 2023; Kupczyk et al., 2021; Moor et al., 2021). PwCF are also able use their device to self-monitor their lung function between visits and can contact the CF team if they are concerned with the results.

Potential barriers in care with a virtual clinic

What cannot be monitored

The rapid adoption of telehealth provided its own challenges. CF standard of care recommends that at each visit the patient has a physical examination, height and weight measured, oximetry, spirometry and sputum samples obtained (Kerem et al., 2005). Whilst some of these requirements could be met in the home setting, others cannot. If patients have scales at home, weight can still be recorded. Sputum samples are required to test for airway microbial colonization. Sputum collection jars can be sent to patients' homes with samples analysed at local pathology centres, thus while this can still be monitored, it takes time and effort from the CF staff as well as the patient to organise. If the patient does not own a portable spirometer, lung function cannot be recorded.

Technical issues

There are many points where technical issues can arise, with smart phones, home computers and iPads, internet and devices which connect via Wi-Fi and Bluetooth. These needed to be worked through with the introduction of telehealth appointments. A secure video conferencing platform is required. Reliable internet is not always available in remote areas and can result in unreliable or lost connections. Portable spirometers require a smartphone and an associated spirometer app which needs to be on during the spirometry efforts. A second device is required for the video link to allow monitoring of spirometry technique. Any issues with the internet and portable spirometer can result in missing data for clinicians, potentially making the telehealth appointment less valuable.

Accuracy of home spirometers

Portable spirometers can be costly if the patient must pay for it out of their own pocket. There is also the question of how accurate the portable spirometry devices are compared to calibrated in-lab spirometers. Potential issues include device overreading where a clinical decline may be missed, or underreading, leading to unnecessary treatment (Dixon et al., 2022).

4. Are Portable Home Spirometers Accurate compared to In-Lab Spirometers

Types of spirometers

In-lab spirometers

The predominant method spirometry is measured is through ‘flow-measuring’ devices. The most used flow-measuring device used in respiratory laboratories is a pneumotachograph, which records air flow in terms of a reduction of flow across a resistance. (Mottram, 2023; Robert L. Maynard, 2020). Daily calibrations are required to assure devices measure accurately (Graham et al., 2019).

Portable home spirometers

There are 2 types of portable spirometers predominantly used for home use.

Turbine spirometers are the simplest type of flow-sensing devices, where air flow causes the rotation of a vane at a speed proportional to the flow. It is unable to measure very low or high flows accurately due to distortion at high speed and lack of rotation at low speeds. Secretions can also affect the rotor if no filter is used (Mottram, 2023; Robert L. Maynard, 2020).

Ultrasonic spirometers detect gas flow via sound waves. The ultrasonic transducers are protected by disposable flow tubes which have a transparent barrier keeping the gas from the transducer. This device has the advantage of no moving parts that can be affected by secretions (Mottram, 2023; Robert L. Maynard, 2020).

Studies comparing devices

Observed in-lab compared to observed portable spirometry

There have been various studies conducted comparing differences in data obtained between in-lab spirometry and portable spirometry device measurements supervised by a technician or respiratory scientist. There have only been a few done with the CF population, and all of these were in paediatric populations. A summary of these studies can be found in table 3.

A Canadian paediatric CF clinic compared a turbine home spirometer with an in-lab spirometer. Both tests were observed by a technician on the same day with coaching provided, and the order of the first device used was randomised (Avdimiretz et al., 2020). Results from 73 patients [mean age of 13 (range 6 to 17 years), volumes ranging between 830-4680 mL for FEV_1 ($ppFEV_1$ 30-119%), and 1170-6080 mL for FVC], found overall limits of agreement (LOA) for FEV_1 were -319 to 189 mL and $ppFEV_1$ were -13.9 to 9%, with a FEV_1 bias (mean difference between devices, portable – in-lab) of -65 ± 127 mL. Those with higher FEV_1 volumes of 2L or more showed a wider LOA between the two devices of -314 to 250 mL compared to those with FEV_1 values of less than 2L with -260 to 90 mL. These larger differences found at higher volumes corresponds with turbine spirometers being less accurate at higher volumes (Robert L. Maynard, 2020). FVC produced wider limits of -421 to 192 mL and a bias of -115 ± 153 mL. Because 15% of participants had a difference in $ppFEV_1$ of greater than 10 percentage points, this study concluded that portable turbine spirometers were not as accurate compared to in-lab spirometers because a 10% or more drop in $ppFEV_1$ could be used in defining an exacerbation. The wide limits of agreement for FEV_1 of up to 319 mL less on the portable spirometer, are over twice the accepted amount of difference based on ATS/ERS repeatability standards of 150 mL.

Doumit et al compared in-lab spirometry to an ultrasonic portable spirometer in 59 paediatric patients (mean age 12.3 years) with CF, asthma, or bronchiectasis over an 8-month period in 2020. The two devices were used in randomised order. LOA for FEV_1 were -220 to +240 mL, $ppFEV_1$ were -8.6 to 9.4%, and FVC were -300 to +330 mL. Although there was excellent reliability between measurements obtained on both devices, there were unacceptable differences in FEV_1 and/or FVC measurements in 22% of participants, defined as greater than 150 mL difference between devices. In 7% of participants this equated to the portable device being 10% or more lower in $ppFEV_1$ than the in-lab spirometer, which would ordinarily indicate a significant clinical change. Intraclass correlation coefficient (ICC) was high (0.991 for FEV_1, 0.989 for FVC and 0.972 for $ppFEV_1$) and the mean between devices were low ranging from -0.1 to 0.01 across the measures. The LOA were wide and differences between measurements were beyond acceptable limits in some participants, indicating that the portable devices are not always interchangeable with in-lab spirometers. Up to 89% were able to meet ATS/ERS standards with supervision from a respiratory scientist, indicating suitability for home use when supervision is provided (Doumit et al., 2022).

Another study with 48 adolescent participants (median age 13, range 12-18 years) with asthma performed in-lab spirometry followed by spirometry on a portable turbine device, with coaching from the technician on both devices. This was repeated 6-8 weeks later. LOA for FEV_1 were -706 to +721 mL and FVC was -1100 to +1100 mL. The bias (in-lab – portable) was 7.64 mL (SD 364mL) for FEV_1 and 2.61 mL (SD 505mL) for FVC. This study concluded that the portable device measures accurately when compared to the in-lab spirometer (Ring et al., 2021), however the LOA were wide for both measurements and would not meet ATS/ERS repeatability criteria. This study was conducted on asthma patients, and it is unclear as to whether the wide LOA's would have a practical impact on treatment.

As part of a larger study in children with CF and asthma looking at unobserved portable spirometry, 58 children (mean age 10, range 6-15 years) performed spirometry on both an in-lab and a portable turbine spirometer in any order, in the same visit. A 10-minute training and practice session was provided. The average bias for FEV_1 was 40 mL and for FVC was 3 mL. FEV_1 had a LOA of -270 to +352 mL, and FVC was -403 to 397 mL, and an absolute difference of $ppFEV_1$ 6.35% (SD 5%) and ppFVC 6.7% (SD 5.75). Approximately 36% of FEV_1 and 39% of FVC measurements did not achieve acceptable grades of A, B or C, and the LOA were smaller in the subgroup of children who did achieve these grades. The authors concluded that the portable spirometer gave reliable results when effort was made to ensure correct technique (Kruizinga et al., 2020), however LOA remained outside ATS/ERS repeatability criteria.

Finally, an adult study with 200 COPD, asthma and ILD participants as well as a control group of healthy participants used a portable turbine spirometer and an in-lab spirometer, with randomisation of the spirometer used first. Both tests were observed by trained personnel. ICC for the 2 spirometers was 0.976 for FEV_1 and 0.962 for FVC. When all four groups were analysed separately ICC remained about the same except for the COPD group which had an ICC of 0.914 for FVC. The mean difference between in-lab and portable spirometry was 70 mL for FEV_1 and 120 mL for FVC. LOA ranges were not quoted in this study, but Bland-Altman plots showed that while the majority of measurements would meet ATS/ERS repeatability criteria, there were some individual data points that were well beyond the LOA. This study concluded that portable spirometry results were reliable (Exarchos et al., 2020).

In summary, although the portable device produced lower results in these studies, the bias between devices was within 150 mL. LOAs were wide and repeatability criteria was not met in all cases, possibly explained by the fact that four of the five studies were in paediatric patients. The importance of supervised testing was highlighted within the paediatric cohort.

Table 3: Observed in-lab compared to observed portable spirometry

Paper name	Author/ Year of publication	Disease	N= Median age	Methods	Results	Conclusion
Comparison of a handheld turbine spirometer to conventional spirometry in children with cystic fibrosis	Avdimiretz et al 2020	CF	N=76 Median age 13	-Spirometry performed on both devices on the same day -Observed by a respiratory scientist -The order of the device used first was randomised	LOA: FEV_1 -319 to +189 mL ppFEV_1 -13.9 to +9% FVC -412 to +192 mL Bias (portable – in-lab): FEV_1 -65 ± 127 mL FVC -115 ± 153 mL	15% of participants had a decrease of more than 10% ppFEV_1 on the portable spirometer which would likely affect clinical decision making. Portable device may not be interchangeable with in-lab spirometer.
Telehealth application of an ultrasonic home spirometer	Doumit et al 2021	CF, asthma, BE	N=59 Mean age 12.3	-Spirometry performed on both devices on the same day -Observed by a respiratory scientist -The order of the device used first was randomised	LOA: FEV_1 -220 to 240 mL ppFEV_1 -8.6 to 9.4% FVC -300 to 330 mL Bias (in-lab – portable): FEV_1 10 mL FVC 20 mL ICC: FEV_1 0.991 (0.985 to 0.995) FVC 0.989 (0.981 to 0.993)	7% of participants had a decrease of more than 10% ppFEV_1 on the portable spirometer which would likely affect clinical decision making. Caution given about comparing results from the portable device with in-lab results. 89% met criteria with supervision
Validation of an app-based spirometer in adolescents with asthma	Ring et al 2021	Asthma	N=48 Mean age 13	-Spirometry performed on both devices on the same day, and on 2 separate occasions 6-8 weeks apart -Observed by a respiratory scientist -Spirometry on in-lab device performed first	LOA: FEV_1 -706 to +721 mL FVC -1100 to +1100 mL Bias (in-lab – portable): FEV_1 7.64 mL (SD 364 mL) FVC 2.61 mL (SD 505 mL)	The portable device produced lower results, with differences of greater than 150 mL not meeting ATS/ERS repeatability criteria
Technical validity and usability of a novel smartphone - connected spirometry device for pediatric patients with asthma and cystic fibrosis	Kruizinga et al 2020	Asthma, CF	N=60 Mean age 10	-Spirometry performed on both devices on the same day -Order of device used first was participants preference	LOA: FEV_1 -270 to +352 mL FVC -403 to 397 mL Bias (in-lab – portable): FEV_1 40 mL FVC 3 mL ppFEV_1 6.35 (SD 5%) ppFVC 6.7% (SD 5.75)	The average difference is within 150 mL however LOA for both measurements are wide and would not meet ATS/ERS repeatability criteria
Validation of the portable Bluetooth Air Next spirometer	Exarchos et al 2020	COPD, asthma, ILD	n=200 Age 18+	-Spirometry performed on both devices	ICC: FEV_1 0.976 FVC 0.962	The mean difference is within 150 mL

in patients with different respiratory diseases				on the same day -Observed by a respiratory scientist -The order of the device used first was randomised	Bias (in-lab – portable): FEV_1 70 mL FVC 120 mL	

BE: Bronchiectasis; CF: Cystic Fibrosis; COPD: chronic obstructive pulmonary disease; FEV_1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; ICC: Intraclass correlation coefficient; ILD: Interstitial lung disease; LOA: Limits of agreement; $ppFEV_1$: Forced expiratory volume in 1 second, percent predicted; SD: Standard deviation

Observed in-lab compared to unobserved portable spirometry

Several studies have also been undertaken with unobserved spirometry performed at home on a portable device as part of a trial or as part of a continuous monitoring program (Table 4).

From 2011 to 2014 a CF population from 14 sites was studied to determine if home monitoring could help in the early detection of exacerbations. 133 participants over the age of 14 years (mean age 26.5 years, S.D 11.5) were asked to use a turbine portable spirometer unsupervised at home twice a week for 12 months. A demonstration and written instructions on how to use the portable spirometer was given at enrolment, and baseline spirometry on the portable device was recorded. No further instruction on home spirometry technique was provided throughout the study. In-lab spirometry was performed every three months alongside the standard CF appointment. (Lechtzin et al., 2013). Spirometry analysis was performed by Paynter et al in 2022 who compared in-lab results to the closest portable spirometry session performed at home within seven days. Of the 44 participants who completed spirometry at all five time points, the average difference in $ppFEV_1$ (portable – in-lab) was -2.01% (95% CI -3.5, -0.3). A Bland-Altman plot compared the difference of $ppFEV_1$ (portable – in-lab) to the mean of portable and in-lab paired tests and found a mean difference of -2.13 (SD 11.91) with some outliers exceeding 30 $ppFEV_1$ on the portable spirometer. These larger differences mostly occurred in adolescents and young adults with $ppFEV_1$ above 80%. LOA's were not provided in this paper. Results were to be transmitted to the sites twice a week and an algorithm would flag any absolute changes in FEV_1 of greater than 10% from baseline. Results do not appear to be individually examined for correct technique. This study concludes that assumptions should not be made about home and in-lab spirometry being interchangeable as overall lower results were obtained on the portable device. Real-time quality control could reduce the outliers (Paynter et al., 2022).

Another study within the CF population (mean age 23 years) used two different brands of turbine portable spirometer, with 20 participants using each spirometer and another 10 using first one then repeating the process with the other. Home spirometer training was given at baseline via a virtual session and participants were asked to perform spirometry daily for 14 days, followed by an optional 8 weeks of weekly spirometry. In-lab spirometry was done within 90 days of enrolment and compared to the closest portable spirometry effort. Whilst there was good adherence to daily spirometry (80%), a lower percentage achieved acceptable attempts (63% on one device and 47% on the other) compared to 77% who had acceptable spirometry at training. Acceptability was defined by ATS/ERS criteria as receiving a grade A, B or C result. A Bland-Altman plot showed a bias towards lower values produced by the portable spirometer compared to in-lab testing. On one device the average measurements for ppFEV1 and ppFVC were lower by 5.1 ± 6.9% (170 ± 230 mL) and 6.2 ± 11% (250 ± 440 mL) respectively. The second device showed similarly lower average values with $ppFEV_1$ of 8.5 ± 14% (330 ± 350 mL) and ppFVC was 11 ± 13% (250 ± 440 mL). This study cautions the use of unsupervised spirometry due to suboptimal technique limiting the amount of usable sessions (Davis et al., 2022). The lower average results on both portable devices were outside the ATS/ERS criteria of 150 mL.

A study performed in a children's CF clinic compared in-lab spirometry to unobserved spirometry performed on a portable device. Training was provided face to face at the beginning of the trial and participants were to perform spirometry on their portable device twice a week for 6 months. Of the 144 participants who were recruited, 67 (mean age 10.7 years (IQR 7.6-13.9)) provided results within one day of their in-lab testing. Lower results were recorded on the portable device in 76.2% of participants, with a bias for ppFEV$_1$ of 6.5% (±8.2%) with LOA of -9.6 to 22.7%. There was a greater than 10% difference in 28% of participants, which was more commonly seen in the younger cohort. It was concluded that an abnormal result from the portable device should be repeated, and that trends should only be interpreted when performed on the same device (Edmondson et al., 2023).

A small study of 10 participants (mean age 71 years) with IPF performed spirometry on a turbine portable spirometer daily for 4 weeks. Participants were considered trained when they could perform spirometry to ATS/ERS standards. In-lab spirometry was done at baseline and at 4 weeks. A Bland-Altman plot showed FVC LOA of -610 to 900 mL. The portable spirometer produced overall lower readings with a median FVC difference of 220 mL (100 to 690 mL). The study concluded that home spirometry was highly feasible in this cohort (Moor et al., 2018). The median FVC result however was outside the ATS/ERS criteria of 150 mL and LOA were wide.

Another small study of 10 participants with systemic sclerosis-associated ILD (SSc-ILD) (mean age 60.3 years, S.D. 9.9) also used a turbine spirometer. Participants were given 20 minutes of training on the baseline visit and were considered trained if their spirometry met ATS/ERS criteria. Half the group did one spirometry measure daily for 6 weeks, followed by 3 spirometry measures once a week. The other half performed spirometry in the reverse order. In-lab spirometry was performed at baseline and after 3 months. Overall, the median FVC on the portable spirometer was 230 mL (IQR 160-370 mL) or 6% (IQR 4.5-9%) lower compared to the in-lab spirometer. This study found that variability was lower when participants did 3 spirometry measures in one session compared to just one single measure, and that overall portable spirometry monitoring is feasible in patients with SSc-ILD (Moor et al., 2021). Similarly to the above Moore et al., 2018 study, the portable device measured lower than the in-lab device and outside the ATS/ERS criteria of 150 mL.

10 patients with ILD (mean age of 61.9 years) used an ultrasonic portable device, with a 30-minute training session given at baseline. Participants were deemed to be suitably trained when they could obtain spirometry that met ATS/ERS criteria. Home spirometry was performed daily for 24 weeks, with in-lab spirometry performed at baseline and at the end of the study. The average FVC values of the portable spirometer were found to be lower than the average in-lab values, however differences were not statistically significant. Comparisons were made between the in-lab and portable spirometry performed at the beginning and end of the study. At the beginning, the difference of ppFVC was 6.8% (in-lab = 81.60±54.02%, portable = 74.80 ±22.67%) and at the end there was a difference of 18.6% (in-lab = 89.50±24.02%, portable = 70.90±21.44%). The portable spirometer measurements produced a statistically significant downward slope for the whole cohort, representing a 14.83% FVC average drop from beginning to end of the trial. This could have been due to a decrease in motivation as time went on or a lack of medical supervision. This study concluded that portable spirometry is a reliable tool for lung function

monitoring (Ilić et al., 2023) however the fact that the measurements on the portable device produced a decrease over time in ppFVC, whereas the final in-lab spirometry showed an increase suggests that device measurements as well as patient effort need to be considered.

46 participants with graft-versus-host disease (GVHD) were enrolled in a year-long study of which 36 completed. A turbine portable spirometer was used, with training provided at enrolment. Spirometry sessions of at least 3 efforts were required once a week for 52 weeks, with in-lab spirometry performed every 3 months as per standard care. Portable and in-lab spirometry performed within 14 days of each other were compared, resulting in a total of 106 pairs for analysis. The mean bias of FEV_1 on the portable device was 123 mL lower than the in-lab spirometer (LOA -294 to 541 mL) but still within ATS/ERS acceptability, however the bias for FVC was 369 mL lower (LOA -252 to 989 mL) which is outside the repeatability limits of 150 mL. If the participant had a decline in FEV_1 of ≥10% in absolute value (compared to baseline) over 3 consecutive measurements on the portable device, the primary care provider was informed. This study concluded that portable spirometry is feasible for this cohort of patients as changes in FEV_1 were detectable (Turner et al., 2021).

A study in allogenic hematopoietic cell transplant recipients compared a turbine spirometer with in-lab spirometry. 51 participants with a median age of 55 years received training immediately after performing in-lab spirometry. They were instructed to use their portable spirometer up to 3 times a week for 9 months, with at least 3 efforts per session, with in-lab spirometry done at enrolment, 3 and 9 months. A Bland-Altman analysis found that measurements for both FEV_1 and FVC on the portable spirometer were lower than in-lab spirometry, by 330 mL (CI -450 to -220 mL) and 290 mL (CI -420 to -170 mL) respectively. Their study demonstrated that although the portable spirometer measurements were slightly underestimated, they were still acceptable (Sheshadri et al., 2020). Differences between the devices for both FEV_1 and FVC were also outside ATS/ERS repeatability criteria of 150 mL.

Another study done within the same disease cohort had 571 participants with a median age of 51.4 years (IQR 38.8-60.5). Instructions on how to use the portable spirometer were given at enrolment. Portable spirometry was performed weekly with 3 efforts required per session, with in-lab spirometry done 3 times during the year. Comparisons were made between the in-lab spirometry and the portable spirometry session performed closest to this date. 437 participants had spirometry available for analysis with only 178 completing in-lab spirometry at all 3 time points. Comparisons between both devices at the 3 time points showed a bias (portable – in-lab) of FEV_1 of −240 mL (95% CI, −320, −170) at baseline, −190 mL (-023, −150) at 80 days, and −80 mL (−190, 30) at 1 year. In this study FVC_6 was measured on the portable device so results have not been included in this review. This study concluded that portable spirometry was a valid method of long-term monitoring in this cohort (Cheng et al., 2016). Differences in the devices were outside ATS/ERS criteria at baseline and 80 days but criteria were met at the 1-year timepoint.

In summary, unobserved portable spirometry performed in participants with a variety of obstructive and restrictively lung diseases raised the fact that although it is a valid and acceptable test, several limitations exist including the importance of adequate patient effort, wide LOA and many devices not meeting the ATS/ERS 150 mL requirements. While it is unclear from these publications whether any group of participants were more experienced than others in performing spirometry, all participants generally received training prior to testing. It is not possible to confirm if more experience in spirometry use ultimately leads to improved agreement between in-lab and home spirometry results.

Table 4: Observed in-lab compared to unobserved portable spirometry

Paper name	Author/ Year of publication	Disease	N= Median age	Methods	Results	Conclusion
A comparison of clinic and home spirometry as longitudinal outcomes in cystic fibrosis	Paynter et al 2022	CF	n=133 Mean age 26.5	-In person demonstration given -In-lab spirometry done at 0,3,6,9,12 months -Home spirometry done 2x a week for 12 months	Bias (in-lab – portable): ppFEV$_1$ -2.01% (95% CI -3.5, -0.3)	Overall results were lower on the portable device despite some large increases on the portable spirometer in participants with higher ppFEV$_1$ however no follow up training given.
Real-world feasibility of short-term, unsupervised home spirometry in CF	Davis et al 2022	CF	N=50 Mean age 23	-Virtual training session given -In-lab spirometry within 90 days -Home spirometry done daily for 14 days -2 different portable devices used	Bias (portable – In-lab): Device 1: ppFEV$_1$ -5.1 ± 6.9% (170 ± 230 mL) ppFVC -6.2 ± 11% (250 ± 440 mL) Device 2: ppFEV$_1$ -8.5 ± 14% (330 ± 350 mL) ppFVC -11 ± 13% (250 ± 440 mL)	Portable spirometer has a bias for lower results and average differences are outside ATS/ERS repeatability criteria
Unsupervised home spirometry is not equivalent to supervised clinic spirometry in children and young people with cystic fibrosis: Results from the CLIMB‐CF study	Edmondson et al 2023	CF	N=144 Median age 10.7	-Training provided at baseline -In-lab spirometry as per usual standard of care -Unsupervised spirometry x2 weekly for 6 months	Bias (in-lab – portable): ppFEV$_1$ 6.5% (±8.2%) LOA: -9.6 to 22.7%	Larger differences were found in younger children. This study concludes that the portable device should not be used interchangeably with an in-lab spirometer.
A home monitoring program including real-time wireless home spirometry in idiopathic pulmonary fibrosis: a pilot study on experiences and barriers	Moore et al 2018	IPF	N=10 Mean age 71	-Standardised instructions given -In-lab spirometry done at 0 and 4 weeks -Home spirometry done daily for 4 weeks	Bias (In-lab – portable): FVC (median) 220 mL (100-690 mL) LOA: -610 to 900 mL	This study concluded that portable spirometry is highly feasible in this cohort however LOA were wide and do not meet ATS/ERS criteria
Feasibility of online home spirometry in systemic sclerosis-associated interstitial lung disease: a pilot study	Moore et al 2020	SSc-ILD	N=10 Mean age 60.3	-Training at baseline -In-lab spirometry done at 0 and 3 months -Home spirometry done 1. 6 weeks x1 spiro daily 2. 6 weeks x3 spiro per week	Median difference (In-lab – portable): FVC 230 mL	This study concluded that portable spirometry in feasible in patients with SSc-ILD, however the median differences are greater than 150 mL so does not meet ATS/ERS repeatability criteria
Home-based spirometry in patients with interstitial lung disease: A real-	Ilić et al 2023	ILD	N=10 Mean age 61.9	-Training at baseline -In-lab spirometry done at 0 and end of trial (24 weeks)	Difference (in-lab – portable): Baseline ppFVC 6.8%	This study concluded that portable spirometry is a reliable tool for lung function

life pilot "FACT" study from Serbia				-Home spirometry done daily for 24 weeks	(in-lab = 81.60±54.02%, portable = 74.80 ±22.67%) End of trial ppFVC 18.6% (in-lab = 89.50±24.02%, portable = 70.90±21.44%)	monitoring however there was a much larger difference in ppFVC at the end of the trial
Home spirometry telemonitoring for early detection of bronchiolitis obliterans syndrome in patients with chronic graft versus host disease	Turner et al 2021	Graft versus host disease	N=46 Mean age 58.8	-Training at baseline -In-lab spirometry done at 0,3,6,9,12 months -Home spirometry done once a week for 52 weeks	Bias (in-lab – portable): FEV_1 123 mL FVC 369 mL LOA: FEV_1 -294 mL to 541 mL FVC -252 to 989 mL	Differences for FEV_1 between devices met ATS/ERS repeatability criteria
Feasibility and reliability of home-based spirometry telemonitoring in allogenic hematopoietic cell transplant recipients	Sheshadri at al 2020	Allogenic hematopoietic cell transplant recipients	N=51 Mean age 55	-Training at enrolment -In-lab spirometry done at 0,3,9 months -Home spirometry done x3 a week for 9 months	Bias (in-lab – portable): FEV_1 330 mL (-450 to -220 mL) FVC 290 mL (-420 to -170 mL)	The portable device measurements were lower than the in-lab spirometer and differences do not meet ATS/ERS repeatability criteria
Correlation and agreement of handheld spirometry with laboratory spirometry in allogenic hematopoietic cell transplant recipients	Cheng et al 2017	Allogenic hematopoietic cell transplant recipients	N=437 Mean age 51.4	-Training at enrolment -In-lab spirometry done at 0,2.5,12 months -Home spirometry done weekly for 1 year	Bias (portable – in-lab): FEV_1 at baseline (95% CI) -240 mL (-320 to -170) FEV_1 at 80 days -190 mL (-023 to -150) FEV_1 at 1-year -80 mL (-190 to 30)	ATS/ERS repeatability criteria were met at the 1-year time point but not at earlier timepoints

CF: Cystic Fibrosis; CI: Confidence interval; FEV_1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; ICC: intraclass correlation coefficient; ILD: Interstitial lung disease; IPF: Idiopathic pulmonary fibrosis; LOA: Limits of agreement; $ppFEV_1$: Forced expiratory volume in 1 second, percent predicted; SD: Standard deviation; SSc-ILD: Systemic sclerosis-associated interstitial lung disease

Observed portable compared to unobserved portable spirometry

The following study compared observed to unobserved spirometry performed on a portable spirometer (Table 5).

A group of 61 children with CF (mean age 11 years, range 6-17) performed spirometry on a portable turbine spirometer. All patients had an initial appointment with the lung function laboratory either face to face or via video link, where the portable spirometer and app were set up and training was given. At the end of this session patients were randomised into either a supervised or unsupervised group. Both groups were required to do spirometry on their portable device every 2 weeks for 12 weeks (6 measurements). Supervised spirometry was performed over video call, with similar instruction provided when a participant is in a face-to-face setting. For the unsupervised group, spirometry was performed at home without observation. 166 supervised measurements were obtained, and 153 unsupervised. At the initial visit 85% of participants achieved an A grade, with 98% of participants receiving a grade of A-C. Results showed the supervised group achieved 15% more A grades than the unsupervised group, however there was only a 3.6% difference if grades A to C were taken into account. In the unsupervised group, 13 participants required further coaching sessions to improve their technique which subsequently improved to acceptable levels. When a drop in FEV_1 of 10% or more from baseline occurred, further investigations were scheduled to assess for exacerbation. The authors concluded that supervised spirometry on a portable device was the best approach in children, although unsupervised testing can provide reportable results if ATS/ERS criteria is adhered to (Fettes et al., 2022).

Table 5: Observed portable compared to unobserved portable spirometry

Paper name	Author/ Year of publication	Disease	N= Median age	Methods	Results	Summary
"You're on mute!" Does pediatric CF home spirometry require physiologist supervision?	Fettes et al 2021	CF	N=61 Mean age 11	-Training at initial visit (face to face or video conferencing) -Supervised home spirometry done fortnightly for 12 weeks -Unsupervised home spirometry frequency not specified	Initial visit: A grade 85% A-C grade 98% Supervised: A grade 89% A-C grade 99% Unsupervised: A grade 73.9% A-C grade 95.4%	Supervised spirometry on a portable device is the best approach in children, although unsupervised testing can provide reportable results

CF: Cystic fibrosis

Observed in-lab compared to observed and unobserved portable spirometry

There has also been a study done in the CF community which compared in-lab spirometry with both observed and unobserved home spirometry performed on a portable spirometer (Table 6).

A paediatric CF Centre at a children's hospital recruited 52 children (mean age 12.7 ± 4 years) who were provided portable turbine spirometers. The initial appointment with spirometry was either face to face or done virtually over video conferencing. Unobserved portable spirometry was performed every day for five days after the initial session. Observed portable spirometry compared to in-lab spirometry (12 subjects performed on the same day) produced a median (IQR) difference of $ppFEV_1$ -6% (-10, -2%) and FEV_1 of -155 mL (-275, -88 mL). 42% had a greater than 10% difference of $ppFEV_1$. Comparison between observed and unobserved spirometry performed on the portable device produced a median difference for $ppFEV_1$ of-2% (-4, 3%) and FEV_1 of -25 mL (-93,93 mL). In this group 15% had a difference in $ppFEV_1$ of more than 10%. Unsupervised portable spirometry compared to in-lab spirometry (17 subjects, performed within a week of each other) gave a median difference of -4% (-10, 5%) $ppFEV_1$ and –110 mL (-280, 9 mL) FEV1, with 24% having a more than 10% difference. This study found the portable spirometer produced lower FEV_1 values than the in-lab sessions, and a significant number from all groups had a difference of 10% or greater which can be clinically relevant. This study demonstrated that spirometry performed at home on a portable spirometer in a paediatric cohort should be supervised (Berlinski et al., 2023).

Table 6: Observed in-lab compared to observed and unobserved portable spirometry

Paper name	Author/ Year of publication	Disease	N= Median age	Methods	Results	Summary
Home spirometry in children with cystic fibrosis	Berlinski et al 2023	CF	N=52 Mean age 12.7	-Training at initiation visit (face to face or video conferencing) -In-lab or supervised portable spirometry done at initiation -Unsupervised portable spirometry daily for 5 days following initiation visit	Median difference (IQR): Observed – in-lab: $ppFEV_1$ -6% (-10, -2%) Observed – unobserved: $ppFEV_1$ -2% (-4, 3%) Unobserved – in-lab: $ppFEV_1$ -4% (-10, 5%)	A significant number from all groups had between device differences larger than 10%, and the portable spirometer produced lower FEV_1 values

CF: Cystic fibrosis; FEV_1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; IQR: Interquartile range; $ppFEV_1$: Forced expiratory volume in 1 second, percent predicted

Much of the literature has demonstrated differences between home spirometry and lab-based equipment and showed a wide LOA. Some of these differences were due to the equipment but also patient technique and whether a trained scientist was present. The presence of the latter may reduce the difference between measurements on portable home devices and in-lab equipment. This study will investigate whether supervision by a respiratory scientist will affect patient technique and measurements obtained with home versus in-lab spirometry in adults. Based on this literature review, my aims and hypothesis as are follows:

Aims and hypothesis

Aims

Compare home spirometer results (including technique) when performed by adult patients in a CF clinic, with and without supervision by a qualified lung function scientist.

Hypothesis

There will be no significant difference between home spirometer results (including technique) when performed with and without supervision by a qualified lung function scientist.

Chapter 2 Masters Project

Quality of home spirometry performance amongst adults with cystic fibrosis

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Bell J, Sivam S, Dentice R, Dwyer T, Jo H, Lau E, Munoz P, Nolan S, Taylor N, Visser S, Yozghatlian V, Wong K. Quality of home spirometry performance amongst adults with Cystic Fibrosis. *J Cyst Fibros*. doi:10.1016/j.jcf.2021.10.012

This paper compares supervised and unsupervised spirometry performed on a home portable spirometer. This will address the aim to compare home spirometer results (technique) when performed by patients in a CF clinic, with and without supervision by a qualified lung function staff member.

Published paper

Quality of home spirometry performance amongst adults with Cystic Fibrosis

Running title: Quality of home spirometry in CF adults

Authors: Jody Bell[1*], Sheila Sivam[1-2*], Ruth Dentice[1-2], Tiffany Dwyer[1-2], Helen Jo[1-2], Edmund Lau[1-2], Phillip Munoz[1-2], Samantha Nolan[1-2], Nicole Taylor[1-2], Simone Visser[1-2], Veronica Yozghatlian[1-2], Keith Wong[1-2].

*Co-first authors

Affiliations:

1. Department of Respiratory and Sleep Medicine, Royal Prince Alfred Hospital, Sydney, NSW, Australia

2. Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia

Corresponding author: Jody Bell**,** Royal Prince Alfred Hospital**,** Missenden Road, Camperdown, NSW, 2050, Australia.

Email: jody.bell@health.nsw.gov.au

Abstract

Spirometry is usually performed under the supervision of a trained respiratory scientist to ensure acceptability and repeatability of results. To evaluate the quality of spirometry performance by adult cystic fibrosis (CF) patients with and without observation by a trained respiratory scientist, an observational, single centre study was conducted between February to December 2020. 74 adults were recruited and instructed to perform spirometry without supervision within 24 hours of their remote CF clinic consultation. Spirometry was repeated at their consultation, supervised by a respiratory scientist using video conferencing. The majority of patients achieved grade A (excellent) or B (very good) spirometry quality with (95%) and without supervision (93%) independent of lung function severity. Similarly, forced expiratory volume in 1 second demonstrated no significant differences with paired spirometry performed within a 24 hour period. For a large proportion of adult CF patients, unsupervised portable spirometry produces acceptable and repeatable results.

Keywords: telehealth, spirometry, cystic fibrosis

Introduction

In pulmonary function laboratories, spirometry is usually performed under the supervision of a trained respiratory scientist to optimise quality and ensure acceptability and repeatability of results as outlined by the 2019 American Thoracic Society (ATS) and European Respiratory Society (ERS) Statement (Graham et al., 2019). Prior studies have raised concerns regarding the usefulness of spirometry in the community without greater attention to quality assurance and training, including in primary care practices (Hegewald et al., 2016). With increased telehealth consultations during the COVID-19 pandemic, remote monitoring of lung function is encouraged at Cystic Fibrosis (CF) centres. When CF adolescents and adults were encouraged to self-monitor their lung function using unsupervised portable home spirometry, more exacerbations than usual were detected but challenges to home monitoring equipment use was a barrier to some participants (Lechtzin et al., 2017). The use of supervised and unsupervised home-based spirometry was shown to be feasible in highly selected CF children aged 7-11 years with previous experience with spirometry use and in adults with idiopathic pulmonary fibrosis (IPF) respectively (Logie et al., 2020; Russell et al., 2016). Other studies however have demonstrated a steady reduction in valid data with wide individual differences in patients with asthma over time even in ideal circumstances, resulting in incomplete and a potentially biased picture of longer term changes in lung function (Wensley & Silverman, 2001).

In this study, we compare the quality of unsupervised home spirometry performed by adults with CF with a wide range of lung function and age, with portable spirometry supervised by a respiratory scientist via telehealth over a 6-month period.

Methods

An observational, prospective, single-centre study was conducted between February and December 2020. Patients were recruited from the Cystic Fibrosis Clinic at Royal Prince Alfred Hospital, Sydney, Australia and instructed to perform spirometry without supervision in the 24 hours prior to their remote CF clinic consultation. This is a secondary aim of an observational study comparing telehealth with in person clinic-based care (ACTRN12620000084987). Coaching on spirometry use and written instructions outlining steps to connect the portable spirometer to their smartphone were provided at recruitment by the respiratory scientist (JB). Spirometry was repeated at their consultation, supervised by a respiratory scientist using video conferencing. This paired exercise was performed at baseline and at additional time-points within 6 months, coinciding with their telehealth CF clinic appointments using video conferencing. For each participant, the same validated portable spirometer (Air-Next™, NuvoAir, Stockholm, Sweden or Spirohome™, Inofab, Turkey) was used during all encounters. Spirometry grading as recommended by the ATS/ERS was recorded from their portable devices with review of flow volume loops, and severity of lung function was obtained from their supervised measurement (Graham et al., 2019). Demographic information was obtained from the medical record. Patients were divided into mild (>80%), moderate (50-80%) and severe (<50%) percent predicted forced expiratory volume in 1 second (FEV1). For this study, grade A or B (at least 2 or 3 acceptable manoeuvres within 150mls) was categorised as acceptable whereas grades C to F were not acceptable (Graham et al., 2019).

To take into account the possibility of multiple measurements per patient, mixed effects logistic regression models were used to look for an association between spirometry quality and severity of obstruction by FEV1 category, stratified by whether the measurement was supervised or unsupervised. Linear mixed-effects models were used to compare supervised and unsupervised FEV1, forced vital capacity (FVC) and spirometric ratios from the participants most recent paired encounter. Statistical significance was set at $p < 0.05$ (two-tailed). Data was analysed with the statistical software package R Core Team (2019, URL https://www.R-project.org/). The study protocol was approved by the Human Research Ethics Committee of the Sydney Local Health District (X19-0339 & 2019/ETH12749). This trial was registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12620000084987).

Results

A total of 74 adults were recruited. 15, 30 and 29 participants with mild, moderate and severe lung function respectively participated in the study (cohort mean age 37±11 years, 50% male, mean FEV1 59% (21-108%), mean number of patients who completed secondary school, 84%; Table 1). No participants required carer assistance to partake in clinic appointments using video conferencing or to perform home spirometry. The majority of patients achieved grade A or B spirometry quality with (n=213, 95%) and without supervision (n=159, 93%) independent of lung function severity (Table 2). Table 2 included all recorded spirometric encounters from the 74 recruited adults (between 3 - 6 encounters per patient). For those with acceptable spirometry quality, 75% (n=160) and 72% (n=114) of the supervised and unsupervised groups demonstrated an A spirometry grade respectively. Patients with poorer grades (C-F) experienced suboptimal spirometric manoeuvres including non-repeatable forced vital capacity, reduced time to peak volume, recurrent coughing or early termination of exhalation (n=22, 96%). One patient had a device malfunction. Patients who were unwell or reported worsening respiratory symptoms did not demonstrate poorer spirometry grade. Unsupervised spirometry quality did not significantly change between their baseline and most recent visit (Figure 1, n=53). Two patients misplaced or lost their home spirometers while 19 others did not submit their unsupervised spirometry results prior to their most recent clinic visit (n=21, 28%). No differences were observed between FEV1, FVC and spirometric ratios from the participants most recent paired supervised and unsupervised encounters ($p>0.05$). The mean difference between the participants most recent paired supervised and unsupervised FEV1 was 0.7ml, with limits of agreement of ± 220ml

(Figure 2). Remote spirometry was performed at home (n=60, 84.5%), work (n=2, 2.8%), or the local general practitioner's clinic (n=1, 1.4%).

Discussion

In this single centre study with 74 participants, we found the quality of unsupervised spirometry performed by trained adult CF patients to be comparable to that performed under the supervision of a respiratory scientist, independent of lung function severity. This was consistent across repeated encounters. Those with poorer spirometry grades failed to meet the ATS/ERS criteria for acceptability or repeatability due to suboptimal spirometric manouvres. Unsupervised spirometric variables, including FEV1, were also comparable with supervised encounters. A quarter of the cohort experienced challenges submitting unsupervised home spirometry results in a timely manner prior to their scheduled telehealth clinic appointment using video conferencing. Overall, these results suggest that while most patients are able to perform spirometry well on their own, many will still require reminders to submit their results prior to their clinic encounters, particularly as patients return to their usual work environment instead of working from home. Further research however is needed to confirm these findings.

In 22 children with CF (median age 10 years), supervised home spirometry was successful in 55 of 59 (93%) attempted sessions (Logie et al., 2020). Only patients with prior spirometry experience were recruited into the study. Unsupervised spirometry was not performed. Our study demonstrated similar supervised results although all adult patients were invited to participate in the study without formal assessment of technical abilities at recruitment. It is possible that the quality of unsupervised spirometry was equally good in our study as spirometer platforms provided feedback to patients who performed poorly, encouraging them to repeat their manoeuvres. This instant feedback may have resulted in higher repeatability for FEV1 data. In addition, adult participants would have had greater experience with spirometry.

In the early intervention in cystic fibrosis exacerbation study, adolescents and adults with CF were encouraged to complete twice weekly home spirometry over 52 weeks to identify and trigger the treatment of pulmonary exacerbations (Lechtzin et al., 2017). Adherence with once and twice weekly data transmission was 50% and 19% respectively. In patients with IPF, only 26% of study participants performed regular daily spirometry for the 70 week duration of the study (Russell et al., 2016). While only 28% of patients experienced challenges with submission of unobserved home spirometry results in a timely manner in our study, this is still a large proportion of patients who would not have spirometry data prior to their clinic visit, had a formal respiratory scientist assessment not also been organised. Participants were also only instructed to provide unobserved home spirometry results prior to their routine virtual clinic visit, rather than daily or weekly.

We acknowledge that this study is limited in that it was performed at a single site however we included a large number of patients compared to prior studies and included all adult patients independent of lung function or age, improving the generalizability of the results. In addition, patients were not instructed to perform home spirometry at a standard time of the day, or specifically before or after airway clearance. Despite this however, no significant differences in spirometric values were observed with paired encounters in our adult cohort. Acceptable variability between paired spirometry sessions was demonstrated (Herpel et al., 2006) . Lastly, spirometric manoeuvres performed at home using the home spirometer were not compared with in-person, clinic-grade spirometry.

In summary, the quality of unsupervised spirometry and spirometric values in adults with CF appears comparable to supervised spirometry performed virtually with a respiratory scientist, independent of lung function severity. Regular quality control measures by respiratory scientists and opportunities for additional coaching for patients who experience difficulty performing acceptable spirometric manoeuvres will likely still be necessary until longer multi-site studies evaluating patient adherence and quality of remote spirometry are available. Further multi-site research is needed to confirm our findings. Future studies in other cohorts with airways disease will also be helpful.

Summary of conflicts of interest statement: There are no conflicts of interests for all authors in regards to this study.

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Table 1: Patient demographics and characteristics

	Severe (FEV1 <50%) n=29	Moderate (FEV1 50-80%) n=30	Mild (FEV1>80%) n=15
Age, *mean (S.D)*	39 (11)	34 (11)	37 (11)
Male, *n (%)*	12 (41%)	15 (50%)	10 (66.7%)
Caucasian *n (%)*	29 (100%)	26 (87%)	14 (93%)
Completed secondary school, *n (%)*	25 (86%)	25 (83%)	12 (80%)

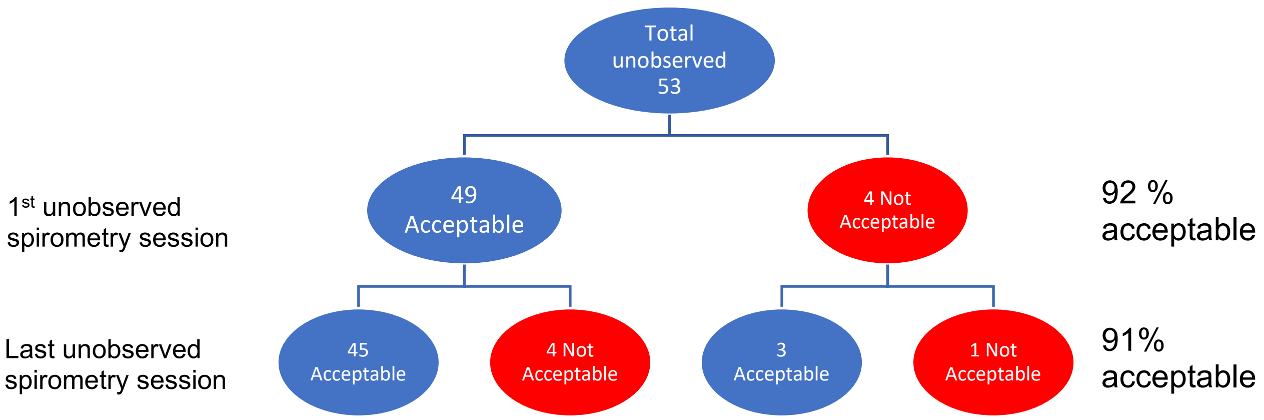
FEV1: Forced expiratory volume in 1 second

Table 2: Spirometry grade in CF patients with and without supervision by a lung function scientist

	Severe (FEV1 <50%)	**Moderate (FEV1 50-80%)**	**Mild (FEV1>80%)**
With scientist (n, %)			
Grade A+B	102 (98%)	76 (90%)	35 (100%)
Grade C-F	2 (2%)	9 (10%)	0
			p = 0.87
Without scientist (n, %)			
Grade A+B	70 (91%)	61 (94%)	28 (97%)
Grade C-F	7 (9%)	4 (6%)	1 (3%)
			p = 0.43

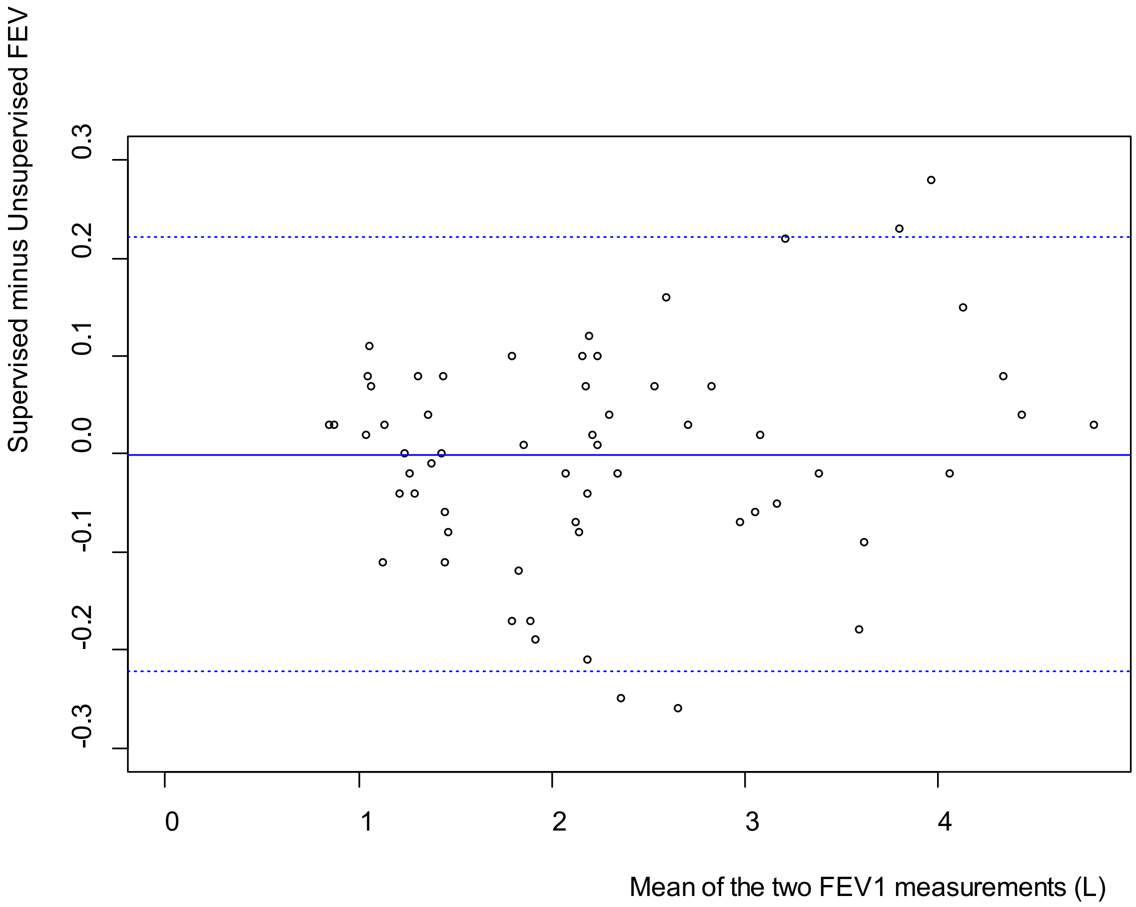
FEV1: Forced expiratory volume in 1 second; Note: p=values provided reflect differences in spirometry grade by lung function severity.

Figure 1: Quality of unobserved spirometry at baseline and at their most recent encounter



Acceptable ATS/ERS grade: A + B

Figure 2: Bland-Altman plot of supervised versus unsupervised forced expiratory volume (L)



*Addition to methods section

As participants in this cohort had many years of experience performing spirometry, coaching involved explaining how to meet ATS/ERS criteria rather than coaching on spirometry technique. They were instructed to do at least 3 blows and to make sure there were no errors which the device would flag. They were to aim for a session grade of A.

Instruction was given on how to use their portable spirometer. For the NuvoAir™ portable spirometer, no tidal breathing was need before the blow out, which differed from the in-lab spirometer. For the Spirohome™ device, there is the option to turn tidal breathing on or off, so participants needed to be aware of which option they were using and how to change it.

Chapter 3
Summary and Conclusion

Summary of findings

The aim of this thesis was to compare the spirometry technique of pwCF using a portable spirometer, with and without supervision from a respiratory scientist. It was hypothesized that there would be no difference between the supervised and unsupervised results. The result of this study confirms the hypothesis with 93% of participants achieving an A or B grade when performing unsupervised spirometry compared to 95% when supervised.

In 2019 when this study was conceptualised, there had been no other studies published comparing supervised and unsupervised spirometry performed on a portable spirometer. Since that time there was a publication in 2021 of a similar design but in a paediatric cohort. This study by Fettes et al. reported lower successful sessions (A and B graded spirometry) than this study for both supervised spirometry (92% compared to 96%) and unsupervised (82% compared to 94%).

Many of the reviewed studies found the accuracy of the portable spirometers differed from the in-lab spirometers, with the portable devices predominately producing lower measurements. Some studies concluded that measurements made on the portable device were reliable despite some large differences with the in-lab spirometer readings that did not meet ATS/ERS reproducibility criteria. Other studies reported that while the portable spirometers reported lower measurements and caution should be taken when comparing the results to spirometry performed on an in-lab spirometer, they were a useful tool to monitor lung function when comparisons were only made with measurements from the same device.

Not all studies reviewed were done within the CF cohort, thus different criteria would be used to assess if a change in measurement needed further investigation. Within the CF cohort, spirometry is important for monitoring change, and a decline in FEV_1 of 10% or more can be an indicator of an exacerbation. As a result, having accurate portable spirometry devices is important in this cohort. For those with CF and other lung diseases, the ability to monitor trends in lung function on a regular basis without the burden of having to attend a respiratory laboratory is important. This may allow early detection of an acute exacerbation or acute on chronic deterioration.

Patients who were supervised by a respiratory scientist either face to face or via video conferencing calls in all cohorts were more likely to produce results that met ATS/ERS standards as coaching can be given in real time and correct spirometry technique can be ensured. Adult pwCF have often been performing spirometry since they were young children. As a result, they are very familiar with the correct technique and are also conscious of how important it is to put in maximum effort every time. It is possible this cohort could produce high standard spirometry unsupervised, whereas the younger cohort of adolescents would benefit from more frequent supervised sessions until they become familiar with the acceptable technique. It is also possible that a case-by-case approach needs to be taken.

In 2023, a review and meta-analysis was published on unsupervised home spirometry compared to supervised in-lab spirometry, in which this study was included (Bell et al., 2022). 28 studies were compared, and results demonstrated an overall mean difference of FEV1 of 106ml between supervised and unsupervised spirometry, with the unsupervised spirometry group having lower values. FVC data was analysed, and the mean difference was 184 mL lower for unsupervised spirometry compared to supervised group. This study demonstrated that unsupervised spirometry performed on a portable device underestimated lung function measurements compared to supervised spirometry. It also recommended that unsupervised home spirometry should not be used for diagnostic purposes (Anand et al., 2023)

Future studies replicating this study design in other adult CF centres as well as in different disease cohorts and age groups would be useful to determine if our results can be reproduced and thus generalizable to the wider adult population with chronic lung disease.

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Appendix

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Quality of home spirometry performance amongst adults with cystic fibrosis

Jody M Bell[a,b,#,*], Sheila Sivam[a,b,#], Ruth L Dentice[a,b], Tiffany J Dwyer[a,b], Helen E Jo[a,b], Edmund M Lau[a,b], Phillip A Munoz[a,b], Samantha A Nolan[a,b], Nicole A Taylor[a,b], Simone K Visser[a,b], Veronica A Yozghatlian[a,b], Keith KH Wong[a,b]

[a] Department of Respiratory and Sleep Medicine, Royal Prince Alfred Hospital, Sydney, NSW, Australia
[b] Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia

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ABSTRACT

Spirometry is usually performed under the supervision of a trained respiratory scientist to ensure acceptability and repeatability of results. To evaluate the quality of spirometry performance by adult cystic fibrosis (CF) patients with and without observation by a trained respiratory scientist, an observational, single centre study was conducted between February to December 2020. 74 adults were recruited and instructed to perform spirometry without supervision within 24 h of their remote CF clinic consultation. Spirometry was repeated at their consultation, supervised by a respiratory scientist using video conferencing. The majority of patients achieved grade A (excellent) or B (very good) spirometry quality with (95%) and without supervision (93%) independent of lung function severity. Similarly, forced expiratory volume in 1 second demonstrated no significant differences with paired spirometry performed within a 24 hour period. For a large proportion of adult CF patients, unsupervised portable spirometry produces acceptable and repeatable results.

1. Introduction

In pulmonary function laboratories, spirometry is usually performed under the supervision of a trained respiratory scientist to optimise quality and ensure acceptability and repeatability of results as outlined by the 2019 American Thoracic Society (ATS) and European Respiratory Society (ERS) Statement [1]. Prior studies have raised concerns regarding the usefulness of spirometry in the community without greater attention to quality assurance and training, including in primary care practices [2]. With increased telehealth consultations during the COVID-19 pandemic, remote monitoring of lung function is encouraged at cystic fibrosis (CF) centres. When CF adolescents and adults were encouraged to self-monitor their lung function using unsupervised portable home spirometry, more exacerbations than usual were detected but challenges to home monitoring equipment use was a barrier to some participants [3]. The use of supervised and unsupervised home-based spirometry was shown to be feasible in highly selected CF children aged 7–11 years with previous experience with spirometry use and in adults with idiopathic pulmonary fibrosis (IPF) respectively [4,5]. Other studies however have demonstrated a steady reduction in valid data with wide individual differences in patients with asthma over time even in ideal circumstances, resulting in incomplete and a potentially biased picture of longer term changes in lung function [6].

In this study, we compare the quality of unsupervised home spirometry performed by adults with CF with a wide range of lung function and age, with portable spirometry supervised by a respiratory scientist via telehealth over a 6-month period.

2. Methods

An observational, prospective, single-centre study was conducted between February and December 2020. Patients were recruited from the Cystic Fibrosis Clinic at Royal Prince Alfred Hospital, Sydney, Australia and instructed to perform spirometry without supervision in the 24 h prior to their remote CF clinic consultation. This is a secondary aim of an observational study comparing telehealth with in person clinic-based care (ACTRN12620000084987). Coaching on spirometry use and written instructions outlining steps to connect the portable spirometer to their smartphone were provided at recruitment by the respiratory scientist (JB). Spirometry was repeated at their consultation, supervised by a respira-

* Corresponding author at: Royal Prince Alfred Hospital, Missenden Road, Camperdown, NSW, 2050, Australia.
E-mail address: jody.bell@health.nsw.gov.au (J.M. Bell).
Co-first authors.

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Table 1
Patient demographics and characteristics.

	Severe(FEV1 <50%) $n = 29$	Moderate(FEV1 50–80%) $n = 30$	Mild (FEV1>80%) $n = 15$
Age, *mean (S.D)*	39 (11)	34 (11)	37 (11)
Male, *n (%)*	12 (41%)	15 (50%)	10 (66.7%)
Caucasian *n (%)*	29 (100%)	26 (87%)	14 (93%)
Completed secondary school, *n (%)*	25 (86%)	25 (83%)	12 (80%)

FEV1: Forced expiratory volume in 1 second.

tory scientist using video conferencing. This paired exercise was performed at baseline and at additional time-points within 6 months, coinciding with their telehealth CF clinic appointments using video conferencing. For each participant, the same validated portable spirometer (Air-Next**TM**, NuvoAir, Stockholm, Sweden or Spirohome**TM**, Inofab, Turkey) was used during all encounters. Spirometry grading as recommended by the ATS/ERS was recorded from their portable devices with review of flow volume loops, and severity of lung function was obtained from their supervised measurement [1]. Demographic information was obtained from the medical record. Patients were divided into mild (>80%), moderate (50–80%) and severe (<50%) percent predicted forced expiratory volume in 1 second (FEV1). For this study, grade A or B (at least 2 or 3 acceptable manoeuvres within 150mls) was categorised as acceptable whereas grades C to F were not acceptable [1].

To take into account the possibility of multiple measurements per patient, mixed effects logistic regression models were used to look for an association between spirometry quality and severity of obstruction by FEV1 category, stratified by whether the measurement was supervised or unsupervised. Linear mixed-effects models were used to compare supervised and unsupervised FEV1, forced vital capacity (FVC) and spirometric ratios from the participants most recent paired encounter. Statistical significance was set at $p < 0.05$ (two-tailed). Data was analysed with the statistical software package R Core Team (2019, URL https://www.R-project.org/). The study protocol was approved by the Human Research Ethics Committee of the Sydney Local Health District (X19–0339 & 2019/ETH12749). This trial was registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12620000084987).

3. Results

A total of 74 adults were recruited. 15, 30 and 29 participants with mild, moderate and severe lung function respectively participated in the study (cohort mean age 37±11 years, 50% male, mean FEV1 59% (21–108%), mean number of patients who completed secondary school, 84%; Table 1). No participants required carer assistance to partake in clinic appointments using video conferencing or to perform home spirometry. The majority of patients achieved grade A or B spirometry quality with ($n = 213$, 95%) and without supervision ($n = 159$, 93%) independent of lung function severity (Table 2). Table 2 included all recorded spirometric encounters from the 74 recruited adults (between 3 - 6 encounters per patient). For those with acceptable spirometry quality, 75% ($n = 160$) and 72% ($n = 114$) of the supervised and unsupervised groups demonstrated an A spirometry grade respectively. Patients with poorer grades (C-F) experienced suboptimal spirometric manoeuvres including non-repeatable forced vital capacity, reduced time to peak volume, recurrent coughing or early termination of exhalation ($n = 22$, 96%). One patient had a device malfunction. Patients who were unwell or reported worsening respiratory symptoms did not demonstrate poorer spirometry grade. Unsupervised spirometry quality did not significantly change between their baseline and most recent visit (Fig. 1, $n = 53$). Two patients misplaced or lost their home spirometers while 19 others did not submit their unsupervised spirometry results prior to their most recent clinic visit ($n = 21$, 28%). No differences were observed between FEV1, FVC and spirometric ratios from the participants most recent paired supervised and unsupervised encounters ($p>0.05$). The mean difference between the participants most recent paired supervised and unsupervised FEV1 was 0.7 ml, with limits of agreement of ± 220 ml (Fig. 2). Remote spirometry was performed at home ($n = 60$, 84.5%), work ($n = 2$, 2.8%), or the local general practitioner's clinic ($n = 1$, 1.4%).

4. Discussion

In this single centre study with 74 participants, we found the quality of unsupervised spirometry performed by trained adult CF patients to be comparable to that performed under the supervision of a respiratory scientist, independent of lung function severity. This was consistent across repeated encounters. Those with poorer spirometry grades failed to meet the ATS/ERS criteria for acceptability or repeatability due to suboptimal spirometric manouvres. Unsupervised spirometric variables, including FEV1, were also comparable with supervised encounters. A quarter of the cohort experienced challenges submitting unsupervised home spirometry results in a timely manner prior to their scheduled telehealth clinic appointment using video conferencing. Overall, these results suggest that while most patients are able to perform spirometry well on their own, many will still require reminders to submit their results prior to their clinic encounters, particularly as patients return to their usual work environment instead of working from home. Further research however is needed to confirm these findings.

In 22 children with CF (median age 10 years), supervised home spirometry was successful in 55 of 59 (93%) attempted sessions [4]. Only patients with prior spirometry experience were recruited into the study. Unsupervised spirometry was not performed. Our study demonstrated similar supervised results although all adult patients were invited to participate in the study without formal assessment of technical abilities at recruitment. It is possible that the quality of unsupervised spirometry was equally good in our study as spirometer platforms provided feedback to patients who performed poorly, encouraging them to repeat their manoeuvres. This instant feedback may have resulted in higher repeatability for FEV1 data. In addition, adult participants would have had greater experience with spirometry.

In the early intervention in cystic fibrosis exacerbation study, adolescents and adults with CF were encouraged to complete twice weekly home spirometry over 52 weeks to identify and trigger the treatment of pulmonary exacerbations [3]. Adherence with once and twice weekly data transmission was 50% and 19% respectively. In patients with IPF, only 26% of study participants performed reg-

Table 2
Spirometry grade in CF patients with and without supervision by a lung function scientist [1].

	Severe(FEV1 <50%)	Moderate(FEV1 50–80%)	Mild(FEV1>80%)
With scientist			
(n,%)			
Grade *A* + *B*	102 (98%)	76 (90%)	35 (100%)
Grade C-F	2 (2%)	9 (10%)	0
			***p* = 0.87**
Without scientist			
(n,%)			
Grade *A* + *B*	70 (91%)	61 (94)%	28 (97%)
Grade C-F	7 (9%)	4 (6%)	1 (3%)
			***p* = 0.43**

FEV1: Forced expiratory volume in 1 second; Note: *p*=values provided reflect differences in spirometry grade by lung function severity.

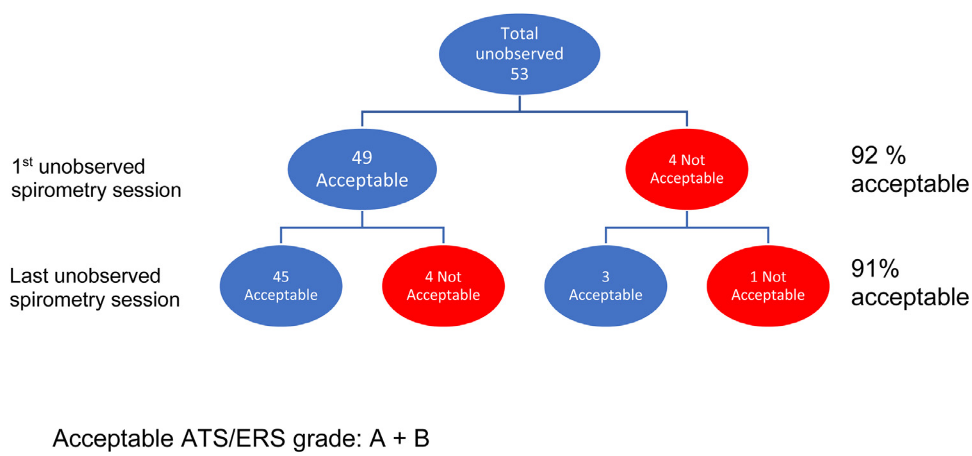

Fig. 1. Quality of unobserved spirometry at baseline and at their most recent encounter. Acceptable ATS/ERS grade: *A* + B.

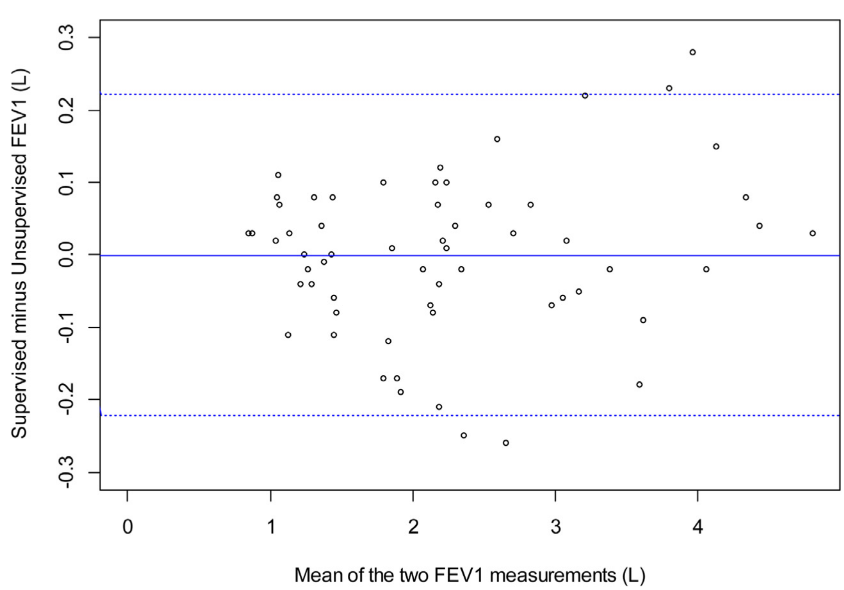

Fig. 2. Bland-Altman plot of supervised versus unsupervised forced expiratory volume (L).

ular daily spirometry for the 70 week duration of the study [5]. While only 28% of patients experienced challenges with submission of unobserved home spirometry results in a timely manner in our study, this is still a large proportion of patients who would not have spirometry data prior to their clinic visit, had a formal respiratory scientist assessment not also been organised. Participants were also only instructed to provide unobserved home spirometry results prior to their routine virtual clinic visit, rather than daily or weekly.

We acknowledge that this study is limited in that it was performed at a single site however we included a large number of patients compared to prior studies and included all adult patients independent of lung function or age, improving the generalizability of the results. In addition, patients were not instructed to perform home spirometry at a standard time of the day, or specifically before or after airway clearance. Despite this however, no significant differences in spirometric values were observed with paired encounters in our adult cohort. Acceptable variability between paired spirometry sessions was demonstrated [7] . Lastly, spirometric manoeuvres performed at home using the home spirometer were not compared with in-person, clinic-grade spirometry.

In summary, the quality of unsupervised spirometry and spirometric values in adults with CF appears comparable to supervised spirometry performed virtually with a respiratory scientist, independent of lung function severity. Regular quality control measures by respiratory scientists and opportunities for additional coaching for patients who experience difficulty performing acceptable spirometric manoeuvres will likely still be necessary until longer multisite studies evaluating patient adherence and quality of remote spirometry are available. Further multi-site research is needed to confirm our findings. Future studies in other cohorts with airways disease will also be helpful.

Declaration of Competing Interest

There are no conflicts of interests for all authors in regards to this study.

CRediT authorship contribution statement

Jody M Bell: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Project administration. **Sheila Sivam:** Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Funding acquisition, Supervision. **Ruth L Dentice:** Funding acquisition, Writing – review & editing. **Tiffany J Dwyer:** Writing – review & editing. **Helen E Jo:** Writing – review & editing. **Edmund M Lau:** Writing – review & editing. **Phillip A Munoz:** Writing – review & editing. **Samantha A Nolan:** Writing – review & editing. **Nicole A Taylor:** Writing – review & editing. **Simone K Visser:** Writing – review & editing. **Veronica A Yozghatlian:** Writing – review & editing. **Keith KH Wong:** Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Supervision.

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