

Adherence of Subjects With Cystic Fibrosis to Their Home Program: A Systematic Review

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BACKGROUND: The management of cystic fibrosis (CF) includes adherence to a home management program (airway clearance, medication, nutritional advice, and exercise). This has led to an increase in life expectancy, although the benefits depend greatly on a patient's level of adherence to daily treatments at home. To date, no systematic review has established adherence rates to all World Health Organization guidelines in the home setting; hence, this review was undertaken. **METHODS:** The review comprised 3 phases. A methodological assessment of databases (Embase, CINAHL, PsychINFO, PEDro, PubMed, Cochrane Central Register of Controlled Trials) identified potentially relevant papers. These papers were screened for inclusion criteria by 2 independent reviewers, data were extracted, and the internal validity was rated using a valid and reliable scale. Results were categorized into 4 themes: medication, nutrition, airway clearance techniques, and exercise. **RESULTS:** The search generated a total of 26 papers, 24 of which were rated as being poor quality. Adherence to a treatment program for CF patients is generally low (from 22% for nutritional guidelines to 130% for oral antibiotics), and it varies greatly depending on the type of treatment and the method of assessment employed (objective tool vs self-reported questionnaires). **CONCLUSIONS:** Consensus on how to measure adherence is lacking, and the quality of studies addressing adherence in this population is generally poor. Overall, studies using self-reported measures yielded higher adherence scores than those that used objective measures, suggesting that current efforts to improve methods of adherence are appropriate. The prevalence of non-adherence remains unclear due to these limitations. *Key words:* cystic fibrosis; adherence; home treatment program; systematic review. [Respir Care 2014;59(11):1731–1746. © 2014 Daedalus Enterprises]

Introduction

The World Health Organization (WHO) guidelines for the management of cystic fibrosis (CF) include airway clearance, medication (antibiotics, pancreatic enzyme replacement therapy), nutrition (high-calorie diet, nutritional supplements), and exercise.¹ These strategies have led to an increased life expectancy, which has increased from 28

to 37 y in the past 2 decades in the United States.² However, the benefits of these new treatments depend greatly on the patients' level of adherence to daily treatments at home. Treatments can be burdensome, time-consuming, and costly, and given the long-term and arduous nature of the regimes, poor adherence is commonly reported.³ The daily regimen can include ingesting as many as 40–50 pills, inhalation treatments requiring up to 2 h, and 2–3 airway clearance sessions lasting 30 min each. In addition, patients are encouraged to exercise and eat several high-calorie, high-fat meals each day.⁴ The average number of treatments per day has been calculated as 7, taking an average of 108 min.⁵ In addition, the maintenance of equipment and preparation of medications (and overcoming administrative barriers to maintaining access to medications) add to the time burden.⁶ Individual studies have reported mainly on adherence rates to some of the recommended treatments, for example, medication and chest physical therapy. Adherence rates have been reported to be 67% for

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oral antibiotics, 31–53% for inhaled antibiotics,⁷ 33% for dornase alfa, and 40–70% for chest physical therapy.^{3,8-12}

Although adherence levels for subcategories of 2 of the 4 WHO recommendations have been the subject of systematic reviews (adherence to antibiotics only,¹³ airway clearance techniques¹⁴), the inclusion of randomized controlled trials may not reflect participants' level of adherence to their independent home treatment regimes due to the nature of frequent monitoring as part of being involved in a trial. Hence, this review was undertaken to include all 4 WHO recommendations (nutrition, medication, exercise, pancreatic enzyme replacement therapy) in non-interventional studies.

Poor adherence to treatment results in increased morbidity and mortality, a reduction in quality of life, and increased health-care utilization.¹⁵⁻¹⁷ Briesacher et al¹⁸ demonstrated both a 60% decrease in the risk of hospitalization for people who were adherent to their treatment regimen and a relationship between low usage of chronic medications and increased exacerbations requiring intravenous therapy. Improving patient outcomes rests, in part, on increasing adherence to chronic therapies, and identifying reasons for non-adherence to treatment is important.

Thus, due to the multiple facets of CF treatment (exercise, nutritional advice, airway clearance techniques, and medication) as recommended by the WHO¹⁹ and the importance of determining adherence in observational rather than formal research settings, this review was undertaken.

Methods

Overview

The review comprised 3 phases. Phase 1 involved a systematic search of the literature using devised criteria and a search strategy of key words. Phase 2 involved the initial screening of appropriate abstracts and subsequently entire papers by 2 independent reviewers (RO'D and Ms Anastasia Kitova [School of Public Health, Physiotherapy and Population Science, University College Dublin, Dublin, Ireland]). Phase 3 involved classifying the internal validity of the included papers and grading the strength of the evidence using the Effective Public Health Practice Project quality assessment tool for quantitative studies.²⁰

Phase 1: Search Strategy

Electronic searches of PubMed, CINAHL, Embase, PEDro, and the Cochrane Central Register of Controlled Trials were carried out from January 1992 to October 2012 on October 30, 2012. A battery of key words was developed using the WHO guidelines for the diagnosis and management of cystic fibrosis¹⁹ to identify the various

QUICK LOOK

Current knowledge

Successful treatment of cystic fibrosis requires home management, including nutrition, airway clearance, exercise, and pharmacotherapy. Good adherence to home management is associated with improved quality of life.

What this paper contributes to our knowledge

A systematic review of the literature suggests that adherence is quite variable and that studies are commonly of poor quality. Self-reported adherence rates are routinely higher than adherence rates measured by objective measures. These data suggest that continued efforts to improve adherence are warranted.

treatment strategies used for CF. Key terms included cystic fibrosis AND adherence AND treatment plan AND exercise OR airway clearance techniques OR diet OR medication. Appropriate synonyms of each search term were used in each search string, along with suitable MeSH terms found in the PubMed database. The complete search strategy is summarized in Table 1. The same search strategy was used for PubMed (Medline), CINAHL (EBSCOhost), Embase (Elsevier), and Cochrane. The search terms used in PEDro included cystic fibrosis AND adherence.

The inclusion criteria were studies involving patients with CF, studies relating to patients' home treatment, studies focusing on adherence as the primary or secondary measure, and studies published from 1992 to 2012. Exclusion criteria were studies published before 1992, intervention studies, review papers, studies conducted in a hospital setting, studies related to exacerbations, and studies that appeared only as abstracts in supplements or poster sessions. Hand searches were also conducted on the bibliographies of identified articles for relevant papers.

Phase 2: Screening Process and Data Extraction

Potentially relevant articles were identified from the titles, abstracts, and key words of the references retrieved by the literature search, and they were scrutinized by 2 researchers (RO'D and AK) for inclusion/exclusion criteria. Duplicates were removed, and the entire papers of accepted abstracts were retrieved and independently scrutinized by the 2 researchers using a detailed pro forma developed to capture and subsequently categorize relevant information from the included papers (participants' demographic data, study methodology, results). Accepted papers were re-categorized into themes: medication, airway clearance techniques, nutrition, and exercise.

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Table 1. Database Search Strategy

Date of Search	October 28, 2012
Years	No restriction
Search Strings	
(1) Patient group	Cystic fibrosis [MeSH] OR cystic fibrosis OR CF OR mucoviscidosis
(2) Focus of study	Medication adherence [MeSH] OR guideline adherence [MeSH] OR patient compliance [MeSH] OR adherence OR compliance OR conformability OR obedience OR accordance
(3) Airway clearance strategies	Chest physiotherapy OR CPT OR conventional chest physiotherapy OR CCPT OR postural drainage OR percussion [MeSH] OR chest percussion OR clapping OR vibration OR high frequency chest wall oscillations OR chest wall oscillation [MeSH] OR HFCWO OR coughing exercises OR coughing OR cough [MeSH] OR ACBT OR active cycle of breathing technique OR breathing control OR BC OR thoracic expansion exercises OR thoracic expansion OR TEE OR forced expiratory technique OR FET OR AD OR autogenic drainage OR oscillating positive pressure device OR flutter OR PEP OR PEP mask OR PEP device OR positive expiratory pressure device OR positive expiratory pressure mask OR positive-pressure respiration [MeSH] OR high pressure positive expiratory pressure OR high pressure PEP OR HPEP
(4) Exercise	Exercise OR exercise [MeSH] OR exercise therapy [MeSH] OR exercise movement techniques OR resistance training [MeSH] OR muscle stretching exercises [MeSH] OR breathing exercises [MeSH] OR train OR training OR work out OR working out OR activity OR physical activity OR motor activity [MeSH] OR PA OR strengthening OR stretching OR sport OR sports [MeSH] OR aerobic OR anaerobic
(5) Medication therapy	Inhalation therapy OR inhaler OR nebulizers and vaporizers [MeSH] OR metered dose inhalers [MeSH] OR dry powder inhalers [MeSH] OR steroids [MeSH] OR steroids OR bronchodilator agents [Pharmacological Action] OR bronchodilator agents [MeSH] OR bronchodilator OR anti-bacterial agent [MeSH] OR anti-bacterial agents [Pharmacological Action] OR antibiotic prophylaxis [MeSH] OR saline solution, hypertonic [MeSH] OR hypertonic saline OR expectorants [MeSH] OR expectorants [Pharmacological Action] OR mucolytic OR DNase OR amiloride OR UTP OR uridine triphosphate OR pancreatic enzymes
(6) Dietary recommendations	Nutrition OR diet [MeSH] OR diet therapy [MeSH] OR diet therapy [Subheading] OR diet OR vitamins [MeSH] OR vitamins [Pharmacological Action] OR supplements OR dietary supplements [MeSH] OR vitamin A OR vitamin K OR vitamin D OR vitamin E
(7) General treatment	Therapeutics [MeSH] OR therapy [Subheading] OR clinical protocols [MeSH] OR therapies, investigational [MeSH] OR placebos [MeSH] OR treatment OR care OR medical care OR nondirective therapy [MeSH] OR drug therapy, computer-assisted [MeSH] OR enzyme therapy [MeSH] OR physical therapy modalities [MeSH] OR recreation therapy [MeSH] OR gene therapy [MeSH] OR respiratory therapy [MeSH] OR enzyme replacement therapy [MeSH] OR medication therapy management [MeSH] OR drug therapy, combination [MeSH] OR oxygen inhalation therapy [MeSH] OR nutrition therapy [MeSH] OR exercise therapy [MeSH] OR drug therapy [MeSH] OR relaxation therapy [MeSH] OR drug therapy [Subheading] OR individualized medicine [MeSH] OR diet therapy [Subheading] OR medicine [MeSH] OR evidence-based medicine [MeSH] OR pulmonary medicine [MeSH] OR infectious disease medicine [MeSH] OR preventive medicine [MeSH] OR physical medicine [MeSH] OR medication therapy management [MeSH] OR medication OR management
(8) Regime	Health plan implementation [MeSH] OR plan OR program OR programme OR scheme OR regimen OR regime OR strategy OR method OR procedure OR early intervention (education) [MeSH] OR clinical protocols [MeSH] OR methods [MeSH] OR methods [Subheading]
Combination of terms	9 = 1 AND 2 (CF and adherence) 10 = 3 OR 4 OR 5 OR 6 (all specific treatment types) 11 = 7 AND 8 (treatment plan) 12 = 10 AND 11 (all treatments encompassed)
Final search	13 = 9 AND 12
Limitations	CF AND adherence AND all treatments
	Humans only, English only

Phase 3: Internal Validity

An assessment of quality was carried out on each remaining paper using the Effective Public Health Practice Project quality assessment tool for quantitative studies.²⁰ It comprises 8 components (selection bias, study design, confounders, blinding, data collection methods, withdrawal and dropouts, intervention integrity, analyses) that are individually scored, and an overall rating of the internal validity is assigned: strong, moderate, or weak. This tool has been deemed appropriate for assessing the quality of non-randomized trials as well as randomized controlled trials.²¹

Results

In total, 26 papers of various methodologies were included in the review: cross-sectional studies ($n = 13$) and longitudinal design ($n = 13$). The search strategy is reported in Table 1, and included studies, study designs, results, and internal validity ratings are summarized in Tables 2–5 and Figure 1.

Characteristics of Included Studies

Two of the 26 papers were classified as being of moderate methodological quality, 24 were of low quality, and no studies were classified as being of high quality. The review included 2,967 participants. The age range varied from 3 to 28 y, and study duration ranged from 3 d to 1 y. Different methods were used to determine adherence rates (eg, electronic diaries, pharmacy refills, and health insurance patient, parent caregiver, and doctor questionnaires, interviews, and telephone surveys). Questionnaires included disease-specific questionnaires (Manchester cystic fibrosis questionnaire, treatment adherence rating scale) and adherence questionnaires (disease management interview-cystic fibrosis, medical and nonmedical compliance questionnaire, confidential cystic fibrosis management profile). The inconsistency in the measurement of adherence across studies makes comparison difficult, although overall objective measures of adherence scored lower than the self-reported questionnaires. The treatment themes are discussed in detail below.

Medication

Twenty papers assessed participants' adherence to medication (male, $n = 916$; female, $n = 855$; unspecified, $n = 69$).^{3,10,11,20,22-25,27-29,31-39} Eighteen papers were of low quality, and 2 were of moderate quality. The categories of medications are summarized below (Table 3).

Nebulized Antibiotics. Seven papers assessed adherence with nebulized antibiotics in 1,093 participants (male, $n = 565$; female, $n = 528$). All papers were of low quality. Some studies used multiple methods of assessment. Two studies used electronic monitoring via an adaptive aerosol delivery device,^{33,34} 3 used participant questionnaires,^{3,25,31} 2 used parent questionnaires,^{3,23} one used daily telephone diaries,³ one used pharmacy refill data,³⁵ and one used data from a research database of health-care claims²⁰ to assess adherence. Mean overall percentage of adherence ranged from $36.1 \pm 35.6\%$ by daily telephone diary³ to $85.0 \pm 33.7\%$ by patient questionnaire.³

Antibiotics. Two studies assessed adherence to antibiotics (not focusing on specific medication/delivery) in 127 participants (male, $n = 68$; female, $n = 59$). Both studies were of low quality. One study used a participant questionnaire²⁷; the other used a parent questionnaire.²⁹ Mean adherence ranged from $76 \pm 28.8\%$ ³⁷ to $87.5 \pm 19.5\%$.¹⁰

Two studies assessed adherence to oral antibiotics in 148 participants (male, $n = 68$; female, $n = 80$). Both studies were of low quality. One used pharmacy refill data,³⁵ whereas the other used both participant and parent questionnaires.²⁷ The mean adherence ranged from 76% by pharmacy refill³⁵ to 130% by patient questionnaire.³¹

Bronchodilators. One low-quality study assessed adherence to nebulized bronchodilators in 53 participants (male, $n = 22$; female, $n = 31$) using parent and participant questionnaires. Adherence was recorded at 60% and 61%, respectively.³¹

Undifferentiated Inhalational Therapy. Five studies assessed adherence to nebulizer therapy (not focusing on specific medication) in 192 participants (male, $n = 93$; female, $n = 72$; unspecified, $n = 27$). All studies were of low quality. Four studies used participant questionnaires,^{3,23,27,32} 2 used clinician questionnaires,^{27,32} 2 used parent questionnaires,^{3,27} one used electronic monitoring,³² and one used pharmacy refill data and daily telephone diaries.³ Adherence ranged from a median (interquartile range) of 36% (5–85.5%) by electronic measurement³² to 93.5% by parent report.²⁸

Hypertonic Saline. One low-quality study assessed adherence to hypertonic saline nebulizers in 95 participants (male, $n = 46$; female, $n = 49$) using pharmacy refill data. Median (interquartile range) adherence was 49% (0–85%).³⁵

One low-quality study reported a combined result for airway clearance techniques and nebulizers in 95 participants (male, $n = 50$; female, $n = 46$) using mother, father, and participant questionnaires. Mean adherence scores were

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Table 2. Adherence to Airway Clearance Techniques

Authors	Participants	Treatment Category	Study Duration	Measurement of Adherence	Results	Q
Eddy et al ²²	<i>n</i> = 41 (20 males, 21 females) Age 6.7 ± 2.67 y Range 3–11 y	CPT (not specified)	C/S General adherence	Questionnaire: (1) Parent-reported adherence to recommendations (2) Clinician-reported: Likert scale, 1 (≥ 95% of time) to 5 (≤ 5% of time)	<i>n</i> , mean ± SD, % of total <i>n</i> who scored 1 (1) Parent-reported: <i>n</i> = 39, 2.0 ± 1.3, 51% Clinician-reported: <i>n</i> = 41, 1.9 ± 0.9, 35%	W
Myers and Myers ²³	<i>n</i> = 31 (18 males, 13 females) Age 28.1 ± 6.7 y	ACT (not specified)	C/S General adherence	Cystic fibrosis adherence patient questionnaire: Likert scale, 1–7 (< 4 = poor, 4 = average, > 4 = high)	Mean ± SD 3.00 ± 2.59	W
Ward et al ²⁴	<i>n</i> = 117 (64 males, 53 females) Age 36.3 ± 19.8 mo	CPT (not specified)	C/S General adherence	Care giver questionnaire: Likert scale, 1–7 (≥ 4 = adherence is a problem males, < 4 = not a problem) (1) <i>n</i> (%) with adherence problems	(1) 50.4%	W
Dalcin et al ²⁵	<i>n</i> = 38 (18 males, 20 females) Age 23.8 ± 6.5 y	Respiratory therapy (not specified)	C/S General adherence	Patient-reported questionnaire: (1) <i>n</i> (%) with ≥ 70% overall adherence (2) Median overall adherence (3) Each treatment: <i>n</i> (%) with high adherence (≥ 5 d/wk = high) Clinician-reported: (4) Overall % median adherence	Patient-reported (1) <i>n</i> = 31 (81.6%) (2) 79% (3) 84.2% (4) Median 71	W
Myers & Horn ²⁶	<i>n</i> = 563 (253 males, 310 females) Mean age 27.85 y Range 18–66 y Median 26 y	CPT (not specified)	C/S General adherence	Patient questionnaire: Likert scale, 1 (never) to 5 (always) (1) <i>n</i> (%) who reported being prescribed daily CPT (2) <i>n</i> (%) with high adherence (≥ 4 on scale)	(1) <i>n</i> = 522 (92.7%) (2) 44%	W
Arias Llorente et al ²⁷	<i>n</i> = 34 (13 males, 21 females) Age 14.5 y Range 1.6–40.6 y	CPT (not specified)	C/S General adherence	(1) Self-reported questionnaire (patient-reported if > 12 y, parent-reported if < 12 y) (2) Clinician opinion of patient's compliance, scored out of 8 (compliant if score was ≥ 4)	(1) Questionnaire: mean adherence 41.2% (2) Clinician: mean adherence 35.3%	W
Hobbs et al ²⁸	<i>n</i> = 27 (mothers) Childs' age range 2–18 y	CPT (not specified)	C/S General adherence	Parent-reported MNCQ: Treatments completed/prescribed) × 100	Overall adherence: 90.1% Individual treatment CPT: 91.2%	W
Abbott et al ²⁹	<i>n</i> = 60 (35 males, 25 females) Mean age 20.98 y Range 16–44 y	CPT (not specified)	C/S General adherence	Interview, patient-reported questionnaire: Degree of adherence on 6-point scale (adherence = ≥ 4)	<i>n</i> (%) of patients who were adherent/ <i>n</i> who participated in treatment: 32 (53%)	M
White et al ³⁰	<i>n</i> = 57 (34 males, 23 females) Age 25.8 ± 6.8 y	PEP therapy, coughing, ACBT, huffing, autogenic drainage, percussion, PD, flutter therapy, vibrations	6 mo	Patient questionnaire (based on MCFQ)	<i>n</i> (%) of patients classed as adherent: <i>n</i> = 40 (72%)	W

(continued)

Table 2. Continued

Authors	Participants	Treatment Category	Study Duration	Measurement of Adherence	Results	Q
White et al ³¹	<i>n</i> = 53 (22 males, 31 females) Age 12.4 ± 2.57 y	(1) CPT (2) PEP mask/flutter coughing, ACBT, chest wall percussion, chest wall vibrations	3 d	CCFMP questionnaire: (1) Patient-reported adherence to prescription (2) Parent-reported adherence to prescription	Reported adherence to prescriptions: (1) Patient %, 66, 57 (2) Parent %, 55, 61	W
DeLambo et al ¹⁰	<i>n</i> = 96 (50 males, 46 females) Age 13.12 ± 1.69 y	ACT (not specified)	2 wk	TARS questionnaire on following one's treatment regime: Likert scale, 1 (never) to 5 (always) (1) Mother-reported (2) Patient-reported (3) Father-reported	Mean ± SD (1) 3.84 ± 0.98 (2) 4.14 ± 0.9 (3) 4.12 ± 0.81	W
Modi et al ³	<i>n</i> = 37 (19 males, 18 females) Age 10.1 ± 2.5 y	ACT (not specified)	2 wk	Multimethod assessment: (1) DMI-CF patient-reported questionnaire (2) DMI-CF parent-reported questionnaire (3) 2 × daily phone diaries by primary caretaker	Mean ± SD % adherence (1) 66.9 ± 30.2 (2) 74.4 ± 35.3 (3) 51.1 ± 40.2	W

Q=quality
W=weak
M=moderate
CPT = chest physical therapy
ACT = airway clearance techniques
PEP = positive expiratory pressure
ACBT = airway cycle of breathing technique
PD = postural drainage
C/S = cross-sectional
MNCQ = medical and nonmedical compliance questionnaire
CCFMP = confidential cystic fibrosis management profile
MCFQ = Manchester cystic fibrosis questionnaire
TARS = treatment adherence rating scale
DMI-CF = disease management interview-cystic fibrosis

measured as 71 ± 24.5%, 78.5 ± 22.5%, and 78 ± 20.25%, respectively.¹⁰

Deoxyribonuclease. Six studies assessed 298 participants (male, *n* = 113; female, *n* = 143; unspecified, *n* = 42). All studies were of low quality. A number of strategies were used to determine adherence. Two studies used pharmacy refill data,^{35,36} 3 used participant questionnaires,^{3,25,31} 2 used parent questionnaires,^{3,31} one used participant interviews,³⁶ one used a collection of empty medication vials,¹¹ and one used daily telephone diaries.³ Mean adherence ranged from 54% by participant interview³⁶ to 77.8 ± 44.1% by patient questionnaire.³

Pancreatic Enzyme Replacement Therapy

Nine studies assessed 518 participants (male, *n* = 262; female, *n* = 256). Seven studies were of low quality, and 2 were of moderate quality. Six studies used participant questionnaires^{3,25,27,29,31,37}; 3 used parent questionnaires^{3,22,31}; one used participant interviews³⁸; one used

7-d recordings²²; and one used pharmacy refill records, daily telephone diaries, and electronic monitoring via the Medication Event Monitoring System (MEMS SmartCap, AARDEX, Richmond, Virginia).³ Mean adherence ranged from 27.4 ± 22.9% by daily telephone diary³ to 96.5% by patient report.³⁵

Two studies reported a combined result for pancreatic enzyme replacement therapy, electrolytes, and supplements in 151 participants (male, *n* = 77; female, *n* = 74). Both studies were of low quality. One study used caregiver questionnaires,²⁴ and the other used participant and clinician questionnaires.²⁷ Adherence ranged from 70.4% to 88.2%.³⁰ In the study by Ward et al,²⁴ problematic behavior regarding adherence was reported in 6% of participants.

One low-quality study reported a combined result for antibiotics and pancreatic enzyme replacement therapy in 41 participants (male, *n* = 20; female, *n* = 21) by parent and clinician questionnaires. Mean adherence ranged from 87.5 ± 17.5% by clinician report to 95 ± 15% by participant report.⁴¹

Table 3. Adherence to Medication

Authors	Participants	Treatment Category	Study Duration	Measurement of Adherence	Results	Q
Latchford et al ³³	n = 38 (20 males, 18 females) Age 24.6 ± 5.3 y	Nebulized antibiotics	3 mo	Electronically monitored (prodose AAD): (1) Overall % adherence (times used/prescribed) (2) Consistency (% of days fully adhered to) (3) Minimum (% of days used at least once)	Mean ± SD %, median (range) (1) 50 ± 29.7, 45.3 (1.1–155.6) (2) 31.6 ± 29.4, 25.5 (0–97.2) (3) 57.1 ± 34.2, 74.5 (3.3–100)	W
Eddy et al ²²	n = 41, 20 males, 21 females Age: 6.7 ± 2.7 y Range 3–11 y	Antibiotics/PERT	C/S General adherence	Questionnaire (adherence to recommendations): (1) Parent-reported: (2) Clinician-reported: Likert scale, 1 (≥ 95% of time) to 5 (≤ 5% of time)	n, mean ± SD, % of total n who scored 1 (1) Parent-reported: 39, 1.2 ± 0.6, 82 (2) Clinician-reported: 41, 1.5 ± 0.7, 59	W
Schall et al ³⁹	n = 75 (39 males, 36 females) Age 9.3 ± 1.0 y	PERT	1 wk	(1) % of n with good adherence (≥ 80%) (2) Overall adherence	(1) n = 29% (2) Mean ± SD %, 75 ± 14	W
Eakin et al ³⁵	n = 95 (46 males, 49 females) Age 20.9 ± 1.9 y	(a) DNase (b) TIS (antibiotics) (c) Azithromycin (oral antibiotics) (d) Hypertonic saline	12 mo	Pharmacy refill data: (1) n (%) taking each medication (2) median % MPR (IQR) (3) Median % CMPR (IQR)	(1) (a) n = 90 (95), (b) n = 65 (68), (c) n = 76 (80), (d) n = 25 (26) (2) (a) 70% (28–97),* (b) 66% (29–91),* (c) 76% (49–90), (d) 49% (0–85) (3) 63% (39–80)	W
Myers and Myers ²³	n = 31 (18 males, 13 females) Age 28.1 ± 6.7 y	(a) PERT (b) Antibiotics (c) Medication (d) Nebulizer	C/S General adherence	Cystic fibrosis adherence patient questionnaire: Likert scale, 1–7 (< 4 = poor, 4 = average, > 4 = high)	Mean ± SD (a) 6.34 ± 1.82, (b) 5.61 ± 1.73, (c) 4.91 ± 2.10, (d) 5.10 ± 2.44	W
Burrows et al ³⁶	n = 42 Age 20.7 ± 4.7 y	DNase	Recall (30 d) Dispensing records (1 y)	Interview, patient recall: (1) % of n who took treatment > 20 d/mo Pharmacy dispensing records: (2) n (%) with good adherence (collecting > 9-mo supply) (3) Overall % adherence for 1 y	(1) 80% (2) 10 (24) (only 3 patients collected a 12-mo supply) (3) 54%	W
Dalcin et al ²⁵	n = 38 (18 males, 20 females) Age 23.8 ± 6.5 y	(a) PERT (b) Nebulized antibiotics (c) DNase	C/S General adherence	Patient-reported questionnaire: (1) n (%) with ≥ 70% overall adherence (2) Overall median % adherence (3) Each treatment, % of n with > 70% adherence (≥ 5 d/wk = high) (4) Overall median % adherence	Patient-reported: (1) 31 (81.6) (2) 79 (3) (a) 96.3, (b) 76.7, (c) 79.4 Clinician-reported: (4) Median 71	W

(continued)

Table 3. Continued

Authors	Participants	Treatment Category	Study Duration	Measurement of Adherence	Results	Q
Ward et al ²⁴	n = 117 (64 males, 53 females) Age 36.3 ± 19.8 mo	PERT/electrolytes	C/S General adherence	Caregiver questionnaire: Likert scale, 1–7 (≥ 4 = adherence is a problem) % of n with problem with adherence Multimethod assessment (mean ± SD % adherence): (1) DMI-CF patient-reported questionnaire (2) DMI-CF parent-reported questionnaire (3) Twice daily phone diaries by primary caretaker (4) Pharmacy refill data (no. received/prescribed] × 100) (5) Electronic recording: MEMS SmartCap ([no. received/prescribed] × 100)	6 Mean ± SD PERT: (1) 90 ± 25.5, (2) 89.5 ± 21.7, (3) 27.4 ± 22.9, (4) 46.4 ± 32.5, (5) 42.5 ± 32.4 Nebulizer: (1) 80 ± 36.9, (2) 82.4 ± 31.6, (3) 47.6 ± 41.0, (4) 68.3 ± 40.7 DNase: (1) 77.8 ± 44.1, (2) 90.4 ± 25.9, (3) 56.7 ± 45.8, (4) 71.7 ± 41.7 TIS: (1) 83.3 ± 25.8, (2) 85.0 ± 33.7, (3) 36.1 ± 35.6 (1) Mean ± SD %, 67 ± 31; n = 12 with > 80% adherence (2) Mean ± SD, 3.8 ± 2.1; median (range) = 3 (2–11)	W
Modi et al ³	n = 37 (19 males, 18 females) Age 10.1 ± 2.5 y	(a) PERT (b) Nebulizer (general, DNase + TIS + albuterol) (c) DNase (d) TIS (antibiotics)	2 wk 3 mo for antibiotics			
McNamara et al ³⁴	n = 28 (16 males, 12 females) Median age 9.1 y Range 2.8–14.9 y	Nebulized antibiotics	12 mo	Electronic monitoring (I-neb AAD): (1) Overall % adherence (recorded/prescribed doses) (2) Treatment time (min; standard treatment = 2 times/dW Adherence to prescription		W
Simon et al ³⁸	n = 54 (25 males, 29 females) Age 13.6 ± 2.3 y Range 9–17 y	PERT	C/S General adherence		Mean ± SD, 77.1 ± 31.0	M
Arias Llorente et al ²⁷	n = 34 (13 males, 21 females) Mean age 14.5 y Range 1.6–40.6 y	Nebulizer (general; eg, DNase, nebulized antibiotics, nebulized corticosteroids) Digestive medication (PERT, vitamins, antacids, deoxycholic acids)	C/S General adherence	(1) Self-reported questionnaire (patient-reported if > 12 y, parent-reported if < 12 y) (2) Clinician opinion of patient compliance (0–8, ≥ 4 = compliant)	(1) Patient/parent-reported mean % adherence: 61.8, 88.2 (2) Clinician-reported mean % adherence: 59, 70.4	W
Adde et al ³⁷	n = 74 (36 males, 38 females) Age 6 mo to 8.4 y	PERT	C/S General adherence	Interview: PERT and supplement use	% of n taking treatment regularly: 80	W
DeLambo et al ¹⁰	n = 96 (50 males, 46 females) Age 13.1 ± 1.7 y	(a) Antibiotics (b) PERT	2 wk 6 mo for antibiotics	TARS questionnaire on compliance with treatment regime: (1) Likert scale, 1 (no) to 5 (always) (2) Mother-reported	Mean ± SD (a) 4.49 ± 0.78, (b) 3.85 ± 0.8	W
Gayer and Ganong ⁴⁰	n = 318 (mothers) Age not specified	Not specified	C/S General adherence	Parent questionnaire: (1) No. of treatments prescribed (2) No. of treatments ordered/d (3) % of treatments done	Mean ± SD (1) 5.7 ± 2.1 (2) 12.4 ± 5.2 (3) 94 ± 13	W

(continued)

Table 3. Continued

Authors	Participants	Treatment Category	Study Duration	Measurement of Adherence	Results	Q
Briesacher et al ¹⁸	n = 804 (424 males, 380 females) Age > 18 y, n = 347; < 18 y, n = 457	Tobramycin-inhaled solution (antibiotics)	1 y	Health-care claims database: One cycle = d dispensed ÷ 56 ≥ 4 cycles/y = high adherence n (%) with high adherence	54 (7)	W
Zindani et al ¹¹	n = 33 (8 males, 25 females) Age < 12 y (group 1), > 12 y (group 2)	DNase	3 mo prospective	Empty vials	Mean ± SD % Group 1: 62.9 ± 35.4 Group 2: 70 ± 27 Mean = 66.5 ± 31.2	W
Abbott et al ²⁹	n = 60 (35 males, 25 females) Mean age 21.0 y Range 16–44 y	PERT	C/S General adherence	Interview, patient-reported questionnaire Degree of adherence on 0–4-point scale (adherence = ≥ 3)	n (%) of adherent patients/n who participated in treatment 58 (97)	M
Daniels et al ²²	n = 63 (43 males, 20 females) Median age 26 y IQR 21–31 y	Nebulizer	3 mo	Overall % adherence (1) Patient questionnaire (2) Clinician questionnaire (3) Electronic measurement	Median % (IQR) (1) 80 (57.5–95) (2) 58 (estimated from graph) (3) 36 (5–84.5)	W
Hobbs et al ²⁸	n = 27 (mothers) Childs' age range 2–18 y	(a) Nebulizer therapy (b) Medication	C/S General adherence	Parent-reported MNCQ (treatments completed/prescribed) × 100	Overall adherence 90.1% Individual treatments: (a) Nebulizer = 93.5% (b) Medication = 97.2%	W
White et al ³¹	n = 53 (22 males, 31 females) Age 12.4 ± 2.6 y	(a) PERT (b) DNase (c) Nebulize Bronchodilators (d) Nebulized antibiotic (e) Oral antibiotics	1 w	CCFMP questionnaire Adherence to prescriptions: (1) Patient-reported (2) Parent-reported	Adherence to prescriptions (1) Patient %: (a) 96.5, (b) 56, (c) 61, (d) 67, (e) 130 (2) Parent %: (a) 93, (b) 55, (c) 60, (d) 58, (e) 104	W

Age is expressed as mean ± SD.
 * Values for deoxyribonuclease (DNase) and tobramycin-inhaled solution (TIS) are approximate values taken from the graph.
 Q = quality
 W = week
 M = moderate
 PERT = pancreatic enzyme replacement therapy
 C/S = cross-sectional
 AAD = adaptive aerosolized delivery
 MPR = medication possession ratio
 IQR = interquartile range
 CMPR = composite medication possession ratio
 DMI-CF = disease management interview-cystic fibrosis
 TARCS = treatment adherence rating scale
 CCFMP = confidential cystic fibrosis management profile

ADHERENCE TO CYSTIC FIBROSIS PROGRAMS

Table 4. Adherence to Nutritional Recommendations

Authors	Participants	Treatment Category	Study Duration	Measurement of Adherence	Results	Q
Schall et al ³⁹	<i>n</i> = 75 (39 males, 36 females) Age 9.3 ± 1.0 y	(a) High-calorie diet (b) Calories from fat	7 d	7-d food record (a) (1) % of <i>n</i> getting ≥ 120% EER (2) Median % EER achieved (b) (3) % of <i>n</i> getting ≥ 40% of total calories from fat sources (4) Median % of EER from fat	(a) (1) <i>n</i> = 39% (2) 115% EER (b) (3) 28% (4) 37% EER	W
Adde et al ³⁷	<i>n</i> = 74 (36 males, 38 females) Age 6 mo to 8.4 y	(a) Use of supplements (b) High-calorie diet	C/S General adherence	24-h diet recall (mean ± SD % RDA intake)	(a) 33 (b) 124 (42)	W
Eddy et al ²²	<i>n</i> = 41 (20 males, 21 females) Age 6.7 ± 2.67 y Range 3–11 y	(a) Eating/avoiding food determined by dietician (b) Vitamins	C/S General adherence	Questionnaire: Likert scale, 1 (≥ 95% of time) to 5 (≤ 5% of time) (1) Parent-reported adherence: (2) Clinician-reported:	<i>n</i> , mean ± SD, % of total <i>n</i> who scored a 1 (1) Parent-reported: (a) 17, 2.2 ± 1.1, 12 (b) 41, 1.1 ± 0.3, 93 (2) Clinician-reported: (a) 41, 1.8 ± 0.8, 41 (b) 41, 1.5 ± 0.8, 66	W
Myers and Myers ²³	<i>n</i> = 31 (18 males, 13 females) Age 28.05 ± 6.7 y	(a) High-calorie diet (b) Vitamins	C/S General adherence	Cystic fibrosis adherence patient questionnaire: Likert scale, 1–7 (< 4 = poor, > 4 = high)	Mean ± SD (a) 4.06 ± 2.00 (b) 6.13 ± 1.74	W
Dalcin et al ²⁵	<i>n</i> = 38 (18 males, 20 females) Age 23.8 ± 6.5 y	(a) High-calorie diet (b) Vitamins A, D, E, K	C/S General adherence	Questionnaire: Patient-reported: (1) High (≥ 70%) overall adherence (2) Overall % median adherence (3) Each treatment, % of <i>n</i> with high adherence (≥ 5 d/wk=high) Clinician-reported: (4) Overall % median adherence	Patient-reported: (1) <i>n</i> = 31 (81.6%) (2) 79 (3) (a) 65.8, (b) 79.4 Clinician-reported: (4) Median 71	W
Hollander et al ⁴²	<i>n</i> = 79 (44 males, 35 females; with PI) Median age 25 y Range 18–50 y	Vitamins A, D, E, K	C/S General adherence	Telephone survey of patients Intake vs recommendations (1) % of <i>n</i> taking vitamins (2) % of <i>n</i> using specific vitamins (3) % of <i>n</i> reaching recommended amounts	(1) 84% Vitamins A, D, E, K (%) (2) 71, 72, 77, 33 (3) 9, 32, 59, 81	W
Hobbs et al ²⁸	<i>n</i> = 27 (mothers) Childs' age range 2–18 y	High-calorie diet	C/S General adherence	Parent-reported MNCQ: Adherence ([treatments completed/prescribed] × 100)	Nutrition 81%	W
Anthony et al ⁴³	<i>n</i> = 25 (14 males, 11 females) Mean age 9.1 y Range 7–12 y	High-calorie diet	7 d	7-d food weighed records % of <i>n</i> achieving > 120% DRI	16%	W
Abbott et al ²⁹	<i>n</i> = 60 (35 males, 25 females) Mean age 20.98 y Range 16–44 y	Vitamins	C/S General adherence	Interview, patient-reported questionnaire: Degree of adherence on 0–4-point scale (adherence = ≥ 3)	<i>n</i> (%) patients adherent/ <i>n</i> who participated in treatment 37 (83)	M

(continued)

ADHERENCE TO CYSTIC FIBROSIS PROGRAMS

Table 4. Continued

Authors	Participants	Treatment Category	Study Duration	Measurement of Adherence	Results	Q
Modi et al ³	<i>n</i> = 37 (19 males, 18 females) Age 10.1 ± 2.5 y Age 3 m to 56 y	Vitamins	2 wk	Multimethod assessment: Mean ± SD % adherence (1) DMI-CF patient-reported questionnaire (2) DMI-CF parent-reported questionnaire (3) Twice daily phone diaries by primary care taker (4) Pharmacy refill data (no. received/prescribed] × 100)	Mean ± SD % Vitamin (1) 93.8 ± 17.1 (2) 88.4 ± 27.6 (3) 22.2 ± 34.2 (4) 33.7 ± 45.6	W
Borowitz et al ⁴¹	<i>n</i> = 80 (38 males, 42 females; with PI)	Multivitamins	C/S	Questionnaire, phone interview	<i>n</i> = 47%	W
Simon et al ³⁸	<i>n</i> = 54 (25 males, 29 females) Age 13.61 ± 2.32 y Range = 9–17 y	(a) High-calorie diet (b) Calories from fat	C/S General adherence	Interview (24-h diet recall) (1) (a) Reported caloric intake Adherence = ≥ 120% DRI (2) (b) % of <i>n</i> adherent (≥ 35% of total calories from fat)	(mean ± SD) (1) (a) 3,951 ± 1,747 Range 1,172–9,812; % of <i>n</i> adherent = 76 (2) (b) 59.3	M
Arias Llorente et al ²⁷	<i>n</i> = 34 (13 males, 21 females) Mean age 14.5 Range 1.6–40.6 y	High-calorie supplements	C/S General adherence	(1) Self-reported questionnaire (patient-reported if > 12 y, parent-reported if < 12 y) (2) Clinician opinion of patient compliance (score 0–8, compliant if ≥ 4)	(1) Parent/patient-reported mean adherence of 59% (2) Clinician-reported mean adherence of 56%	W
DeLambo et al ¹⁰	<i>n</i> = 96 (50 males, 46 females) Age 13.12 ± 1.69 y	Nutrition	2 wk	TARS questionnaire on following treatment regime: Likert scale, 1 (never) to 5 (always) (1) Mother-reported (2) Patient-reported (3) Father-reported	Mean ± SD (1) 2.63 ± 1.27 (2) 2.82 ± 1.41 (3) 2.59 ± 1.27	W
White et al ³¹	<i>n</i> = 53 (22 males, 31 females) Age 12.4 ± 2.57 y	Tube feeding	1 wk	CCFMP questionnaire: (1) Patient-reported adherence (2) Parent-reported adherence	Adherence to prescriptions. (1) Patient 95% (2) Parent 53%	W
Zindani et al ¹¹	<i>n</i> = 33 (8 males, 25 females) Age < 12 y (group 1), > 12 y (group 2)	Vitamins A, D, E, K	3 mo prospective	Electronic recording, MEMS SmartCap	Group 1: 70.5 ± 27.3% Group 2: 56.7 ± 20.6% Mean 63.6 ± 24	W

Age is expressed as mean ± SD.

Q=quality

W=weak

M=moderate

C/S=cross-sectional

EER = estimated energy requirement

RDA = recommended daily allowance

MNCQ = Medical and Nonmedical Compliance Questionnaire

DRI = daily recommended intake

DMI-CF = disease management interview-cystic fibrosis

TARS = treatment adherence rating scale

CCFMP = confidential cystic fibrosis management profile

MEMS = medication event-monitoring system

Table 5. Adherence to Exercise Recommendations

Authors	Participants	Treatment Category	Study Duration	Measurement of Adherence	Results	Q
Myers and Myers ²³	<i>n</i> = 31 (18 males, 13 females) Age 28.1 ± 6.7 y*	Regular exercise	C/S General adherence	Cystic fibrosis adherence patient questionnaire: Likert scale, 1–7 (< 4 = poor, 4 = average, > 4 = high)	4.41 ± 1.87*	W
White et al ³⁰	<i>n</i> = 57 (34 males, 23 females) Age 25.8 ± 6.8 y*	Exercise (walking, gym)	6 mo	Patient questionnaire (based on MCFQ)	<i>n</i> (%) of subjects classed as adherent <i>n</i> = 24 (42.1%)	W
Hobbs et al ²⁸	<i>n</i> = 27 (mothers) Childs' age range 2–18 y	Exercise (not specified)	C/S General adherence	Parent-reported MNCQ: Adherence (treatments completed/prescribed] × 100)	Exercise = 88%	W
Abbott et al ²⁹	<i>n</i> = 60 (35 males, 25 females) Median age 20.98 y (range 16–44 y)	Exercise (not specified)	C/S General adherence	Interview, patient-reported questionnaire: Degree of adherence (3 questions assessed by physiotherapist)	<i>n</i> (%) of subjects who were adherent/ <i>n</i> who participated in the treatment 41 (75%)	M
Dalcin et al ²⁵	<i>n</i> = 38 (18 males, 20 females) Age 23.8 ± 6.5 y*	Exercise (physical activity)	C/S General adherence	Patient-reported questionnaire: (1) N (%) with high (≥ 70%) overall adherence (2) Median overall adherence (3) Each treatment (% of <i>n</i> with high adherence, ≥ 5 d/wk) Clinician-reported: (4) Overall median adherence	Patient-reported: (1) <i>n</i> = 31 (81.6%) (2) 79% (3) 21.1% Clinician-reported: (4) Median = 71%	W

* Values are expressed as mean ± SD.

Q=quality

W=weak

M=moderate

C/S = cross-sectional

MCFQ = Manchester cystic fibrosis questionnaire

MNCQ = medical and nonmedical compliance questionnaire

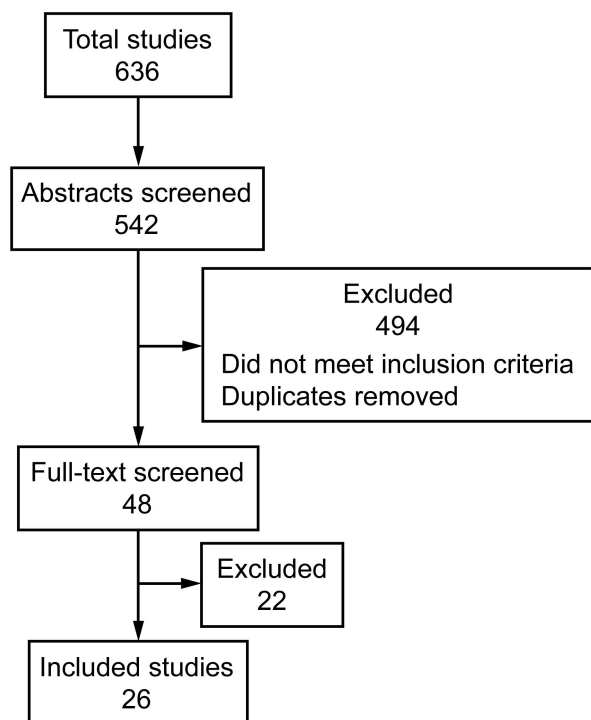


Fig. 1. Flow chart of study selection process.

Two studies assessed adherence rates for medications in general in 58 participants (male, *n* = 18; female, *n* = 13; unspecified, *n* = 27). One used participant questionnaires,²⁶ and the other used parent questionnaires.²⁸ Mean adherence ranged from 70.1 ± 30%²⁶ to 97.2%.²⁸

Nutrition

Sixteen papers assessed 837 participants' adherence to various nutritional recommendations (male, *n* = 399; female, *n* = 411; unspecified, *n* = 27). Fourteen of the studies were of low quality, and 2 were of high quality (Table 4).

Adherence to calorie intake was assessed in 10 studies with 507 participants (male, *n* = 235; female, *n* = 245; unspecified, *n* = 27). All but one study was of low quality. Five studies used participant questionnaires,^{3,25,27,31} 3 used parent questionnaires,^{10,28,31} one used clinician questionnaires,²⁸ 2 used 24-h recall,^{37,38} and 2 used 7-d food records.^{39,43} Reported adherence to guidelines ranged from 40.8 ± 31.75%¹⁰ to 81%.²⁸

Adherence to vitamin intake was assessed in 8 studies with 399 participants (male, *n* = 200; female, *n* = 199).

All but one study was of low quality. Four studies used participant questionnaires,^{3,23,25,29} 2 used parent questionnaires,^{3,22} one used clinician questionnaires,²² 3 used interviews via telephone,^{3,41,42} and one used pharmacy refill data and electronic recordings via MEMS SmartCap.³ Mean adherence ranged from $22.2 \pm 34.2\%$ by daily telephone diary³ to $97.5 \pm 7.5\%$ by parent questionnaire.²² In another study, the percentages of the sample group who reached the recommended doses for vitamins A, D, E, and K were 9, 32, 59, and 81%, respectively.⁴²

One low-quality study assessed compliance with a dietitian's food guidelines. Forty-one participants (male, $n = 20$; female, $n = 21$) were included. Mean adherence ranged from $70 \pm 27.5\%$ by clinician questionnaire to $80 \pm 20\%$ by parent questionnaire.²²

Airway Clearance Techniques

Eleven papers assessed 1058 participants (male, $n = 496$; female, $n = 535$; unspecified, $n = 27$). All but one study was of low quality. Eight studies used participant questionnaires,^{3,4,23,25-27,30,31} 4 used parent questionnaires,^{3,22,28,30} 2 used clinician questionnaires,^{22,27} one used caregiver questionnaires,²⁴ and one used daily telephone diaries.³ Only 2 papers of low quality^{30,31} specified the individual aspects of chest physical therapy involved (positive expiratory pressure, coughing, active cycle of breathing technique, chest wall percussion, chest wall vibrations). All other papers ($n = 10$) simply summarized treatment as airway clearance techniques or chest physical therapy. Adherence rates ranged from $33.3 \pm 43.15\%$ ²³ to 91.2% ²⁸ by patient questionnaire.

Exercise

Five papers assessed 321 participants (male, $n = 213$; female, $n = 81$; unspecified, $n = 27$). All papers were of low quality. Four studies used participant questionnaires,^{23,25,29,30} and one study used parent questionnaires.²⁸ Only 2 papers described the exercise undertaken: one paper described exercise as walking or attending a gym,²⁸ whereas the second reported exercise as physical activity.²⁵ Details of exercise prescriptions were not included. All other papers simply reported the category as exercise, and limited details to reporting compliance rates to regular exercise, number of times prescribed exercises were undertaken, or whether exercises were undertaken every day or almost every day (Table 5).

Discussion

This systematic review examined levels of adherence to home treatment programs for people with CF. Twenty-six studies were included and categorized into one of four

main themes: exercise, medication, airway clearance, and nutrition. Results showed that adherence levels were generally low and wide ranging (nutrition, 22.2–97.5%; airway clearance techniques, 33.3–91.2%; exercise, 56.8–88%; pancreatic enzyme replacement therapy, 27.4–96.5%; medication [inhaled therapy], 31.6–85%), varying greatly depending on the type of treatment being assessed and the mode of assessment being employed.

The present study included home-based observational studies only to establish subjects' own level of adherence, which is an integral part of the long-term management of CF. Intervention studies were excluded due to the effect of participating in a formal research trial, in which greater monitoring/measurement of patients would take place. Indeed, compared with a previous review of randomized controlled trials examining adherence rates for airway clearance techniques (88–96%),¹⁴ rates for compliance in observational studies reported in the present study are lower (33.3–91.2%). The previous review of adherence to antibiotics (mixed methodologies) reported similar adherence rates (35–87%)¹³ compared with the present review (36–85%).

Multiple issues concerning the design of studies investigating adherence were found: study duration, participant recall, and use of multiple measures and questionnaires.

The time frame over which the studies were conducted varied greatly from 2 weeks³⁷ to 6 months,³¹ which could influence recall bias. Given that CF is a chronic disease, one would argue that studies of longer duration are more clinically relevant. Shorter intervals have been used previously because of the assumption that recall would be better for shorter periods⁴⁴; however, it has been reported that patients do not recall more recent pill-taking events any more accurately.^{44,45}

Some studies utilized multiple modes of assessment,^{3,30,37} which may, in some cases, prove challenging for participants when multiple outcome scales are used (eg, Likert scale, percentage rates, etc). Issues with health literacy and numeracy may impact on patients' ability to complete adherence forms when different scoring scales are utilized (eg, percentages) and need to be considered.⁴⁶

A large range of tools (electronic technologies, self-reported questionnaires) were also utilized to determine levels of adherence. Daily telephone diaries have been thought to allow for a greater precision of recalled information,⁴⁷ and electronic recording via MEMS SmartCap allows for precise recording of usage.⁴⁸

Disparities between self-reported and objective measures of medication adherence were found; both adherence to nebulized antibiotics by parent and self-reported adherence were higher compared with electronic monitoring, consistent with previous research.^{3,10} However, one must be cautious when interpreting results given the low-quality rating of the majority of studies. The improvement in pa-

tient-reported adherence to treatments and the availability of objective recordings in clinical practice (eg, measuring changes in sweat chloride in those taking ivacaftor⁴⁹) should allow for open and honest discussion between patient and clinician.³² Similar disparities have been found in other chronic conditions in which self-reported measures are higher than objective measures (eg, functional ability of patients with low back pain⁵⁰ and adherence to medication for patients with HIV⁵¹⁻⁵³).

Mismatches were also found regarding adherence rates depending on who completed the questionnaire. When comparing people with CF and their health-care professionals (physiotherapist or doctor), health-care professionals' opinion/impression of adherence was lower than that of the people with CF, similar to levels reported for adults with hypertension.⁵⁴ Multiple factors have been reported as reasons for this (eg, impact of a patient's previous medical history⁵⁵ or a patient's expectations of the consultation⁵⁶). Self-reported adherence levels were also found to be generally greater than those reported by parents.^{3,22,25,32} White et al³¹ found a 30% disparity between CF teams' recommendations for oral antibiotics and CF patients' reports, compared with a 4% disparity for parents. Similarly with regard to adherence with tube feeding, patients with CF reported 95% adherence compared with the parents' report of 53% despite both groups being aware of the CF teams' recommendations.³¹ Along with issues regarding recall, patients with CF and respondents may provide answers that conform to their perceived expectations of their interviewer, as seen in patients with HIV.^{57,58}

The challenge for researchers in measuring adherence rates is first to define adherence. The WHO defines adherence as the extent to which a person's behavior (in terms of taking medication, following diets, or executing lifestyle changes) coincides with medical or health advice.⁵⁹ However, adherence to a treatment plan has many levels, such as overall adherence (defined as times treatment is used compared with times prescribed), adherence to the full-length treatment, and the number of days the treatment is used.³³ These multiple factors relating to adherence again make it difficult to establish, and measuring it is an inexact science.⁶

Reasons for non-adherence to CF have also been explored. As survival rates improve, people with CF are faced with new challenges relating to age, such as the transition between adolescence to adulthood and coming to terms with their independence with regard to adherence.²⁸ It is therefore not surprising that they are non-adherent to aspects of their treatment regimen at different times throughout their lives. This behavior can be acknowledged as a normal adaptation to the physical and emotional intrusion of illness.⁶ For a person growing up with CF, treatment demands become repetitive, often with no immediate perceived benefit.³⁰ These young adults are de-

termined to live as normal a life as possible and acknowledge that sometimes they are making an informed decision not to carry out their treatment. Older children and adults report poor adherence to treatment regimens, describing them as boring, different from the normal lives of their peers, and a waste of time.²⁷

However, it cannot be assumed that reduction in administration time alone will solve the adherence dilemma. For example, asthma medications take only a few seconds to administer via a metered-dose inhaler or powder inhaler, yet adherence rates are low. Treatment programs should perhaps be planned around individual patient's requirements, modifying treatment ideals when necessary according to the exigency and pattern of that patient's lifestyle.⁶⁰

Innovative approaches to increase patients' adherence to recommendations are required. The use of mobile health technologies and telecommunication has rapidly been integrated into the health-care delivery system for the management of chronic illnesses (eg, hypertension,⁶¹ weight loss,⁶² and diabetes⁶³) and may prove useful for improving adherence in patients with CF by allowing adolescents to directly call their CF health-care team and by promoting safe social interactions and peer support.⁴

The results of this systematic review should be considered in light of the following limitations. Only papers written in English and published in the last 20 y were included to reflect the development of guidelines and best practice for the management of patients with CF.

Conclusion

Overall adherence to home treatments was assessed with a variety of adherence tools in low-quality studies. There were wide disparities in adherence rates, with studies utilizing self-reported tools consistently higher than those utilizing objective measures. The lower objective measures of adherence suggest current efforts to improve adherence are appropriate.

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