Adherence in Cystic Fibrosis

Objectives

- Overview
- Measuring Adherence
- Barriers to Adherence
- Strategies to Improve Adherence
- Summary

Overview

Adherence -- the degree to which a patient actively participates in their prescribed treatment regimen[1]

- Includes oral and inhaled medication regimens, dietary recommendations, airway clearance, and lifestyle changes[2]

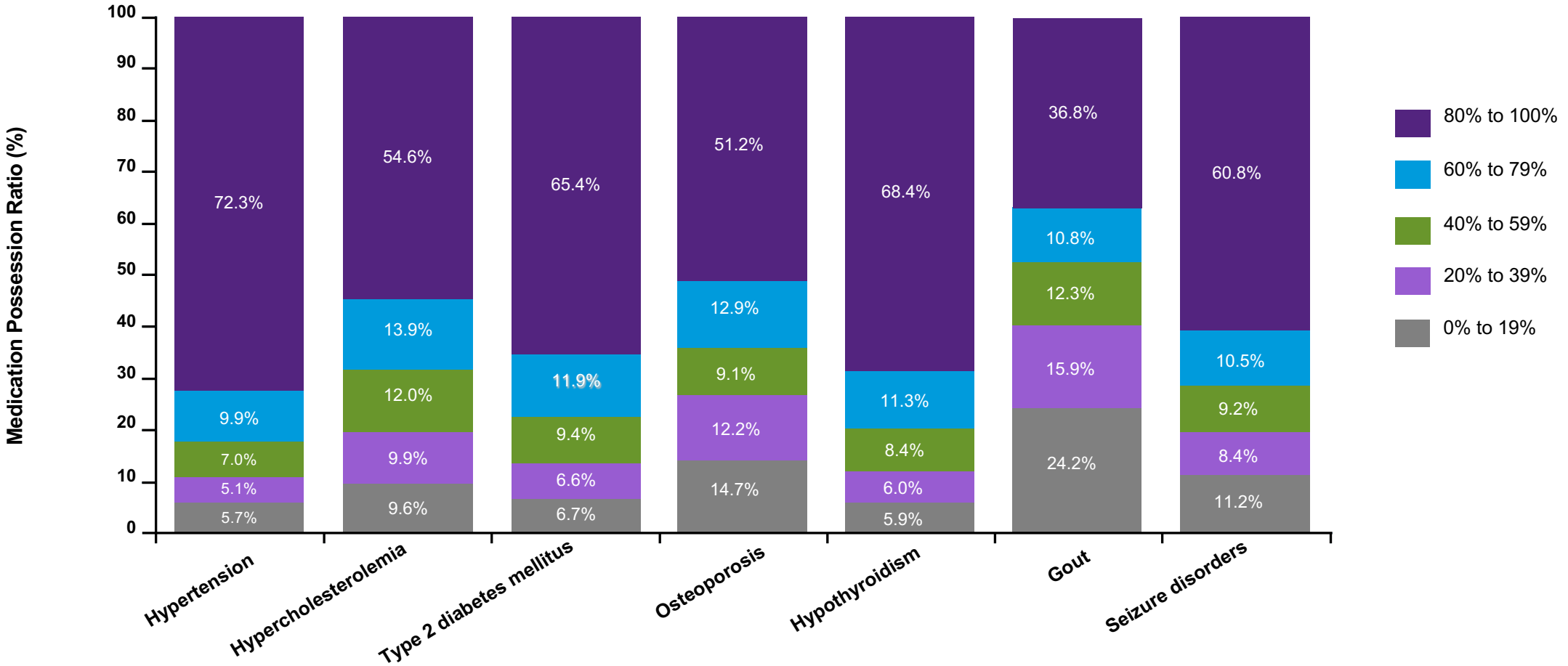
Adherence issues impact all age groups[1] and clinicians[3]

- Young children: parents are responsible for treatment management[1]
- Adolescence: greater independence and autonomy[1], lung function decline accelerates[3]
- Teens: typically worsening health, more frequent hospitalizations and increased responsibility to manage their care[1]
- Adults: balancing family, work, education and increased comorbidities with age[3]
- Clinicians: selecting appropriate therapeutic interventions[3]

Adherence is positively impacted by family and social support, perception of control over one's life and physician empathy[1]

1. Quittner AL, Alpern AN, Balckwell LS, et al. *Healthcare issues and challenges in adolescents with cystic fibrosis.* Eds. European Cystic Fibrosis Society 2012; Ch 6:77-92.
2. Quittner AL, Modi AC, Lemanek KL, et al. Evidence-based assessment of adherence to medical treatments in pediatric psychology. *J Pediatr Psychol*. 2008;33(9):916–936.
3. Sawicki GS, Tiddens H. Managing treatment complexity in cystic fibrosis: challenges and opportunities. *Pediatr Pulmonol*. 2012;47:523-33

Adherence Rates in Certain Chronic Diseases[1]



Adherence rate of ≥80% is considered "highest" adherence to a particular treatment regimen

US health care claims data from 2001 to 2004 covering a total of 706,032 adults aged ≥18 years. Medication Possession Ratio was used to measure adherence (i.e., the days' supply of the drug dispensed during the follow-up year divided by the number of days in the year).

1. Briesacher BA, Andrade SE, Fouayzi H, et.al. Comparison of drug adherence rates among patients with seven different medical conditions. *Pharmacotherapy.* 2008; (4): 437–443.

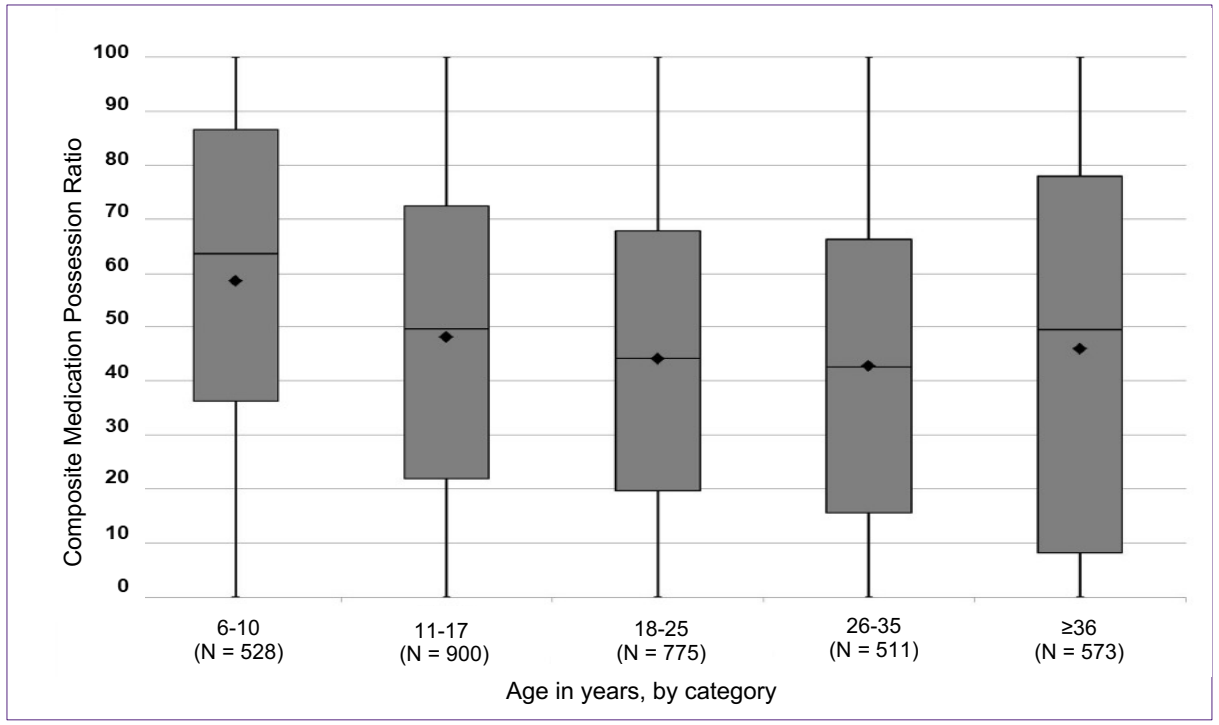
Factors Influencing CF Medication Adherence[1]

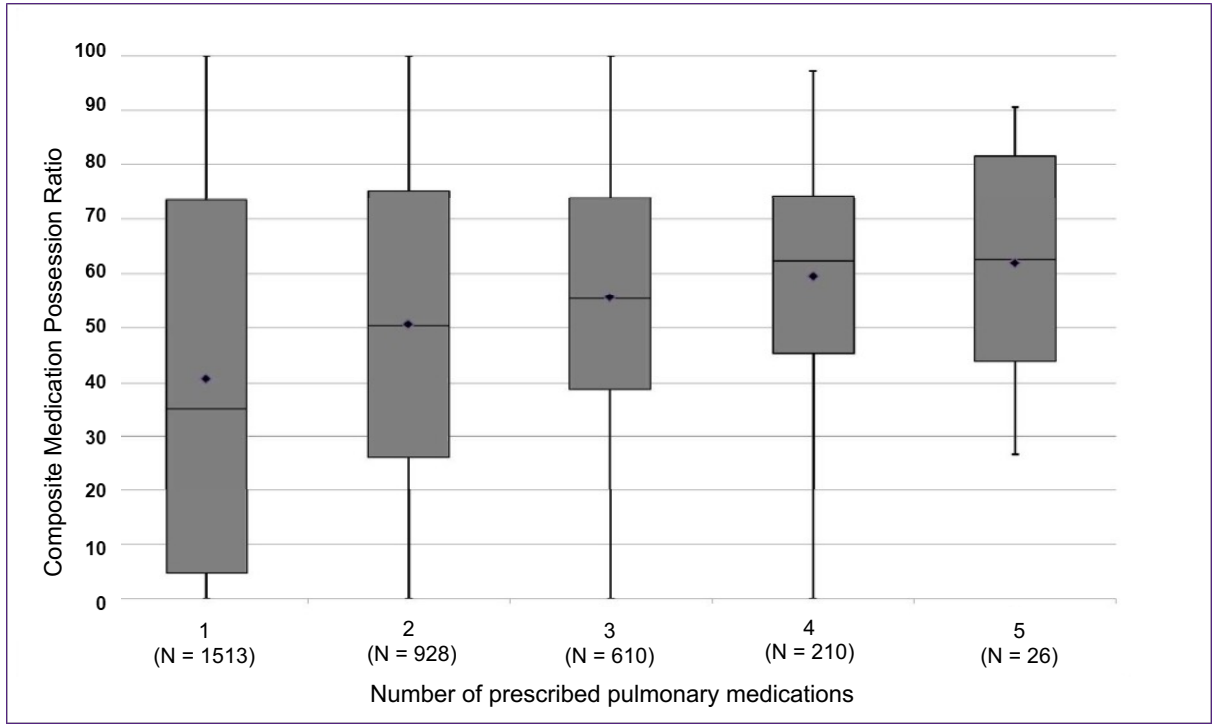
Patient/family factors	Disease-related factors	Regimen-oriented factors
Demographics • Age • Sex • Socioeconomic status • Knowledge Developmental • Transition to independence • Cognitive limitations • Inadequate supervision Psychiatric co-morbidity • Depression and anxiety • Attention deficit hyperactive disorder • Patient and family adjustment and coping • Parent-child conflict	• Disease progression • Genotype-phenotype relationships • Course of treatment • Disease Severity • Daily Symptoms	• Regimen complexity • Patient treatment burden • Under- or overdosing • Inadequate follow-up with CF team • Perceived efficacy • Treatment side-effects • Duration and frequency of device use

1. Quittner AL, Alpern AN, Balckwell LS, et.al. *Healthcare issues and challenges in adolescents with cystic fibrosis.* Eds. European Cystic Fibrosis Society 2012; Ch 6:77-92.

Pulmonary Medication Adherence in CF

US National 12-month retrospective study (3,287 CF patients ≥6 years old)[1]





Medication possession ratio varies by age[1]

Medication possession ratio varies by number of pulmonary medications[1]

The bottom, mid-line and top of each box represent the lower quartile, median and upper quartile, respectively
The endpoints of the vertical lines represent the minimum and maximum values
♦ = Mean value. The composite Medication Possession Ratio (MPR) is the average of the individual drug MPRs

1. Quittner AL, Zhang J, Marynchenko M, et al. Pulmonary medication adherence and healthcare use in cystic fibrosis. *Chest.* 2014;146 (1):142–151

Potential Consequences of Poor Adherence in Cystic Fibrosis

- Drug resistance[1,3]
- Increased morbidity, earlier mortality[1,3]
- Decreased quality of life[1,3]
- Treatment failure[1]
  - Potentially increase dosages or discontinue medications thought to be ineffective

Clinically may result in[2]:

↑ Pulmonary exacerbations
↓ Lung function
↑ Hospitalizations

→ ↑ Healthcare costs

1. Quittner AL, Modi AC, Lemanek KL, et. al. Evidence-based assessment of adherence to medical treatments in pediatric psychology. *J Pediatr Psychol*. 2008;33(9):916–936.
2. Quittner AL, Eakin MN, Alpern AN, et.al. Clustered randomized controlled trial of a clinic-based problem-solving to improve adherence in adolescents with cystic fibrosis. *J Cyst Fibros*. 2019;18(6):879-885.
3. Quittner et al. *Healthcare issues and challenges in adolescents with cystic fibrosis.* Eds. Castellani et al. European Cystic Fibrosis Society 2012; Ch 6:77-92

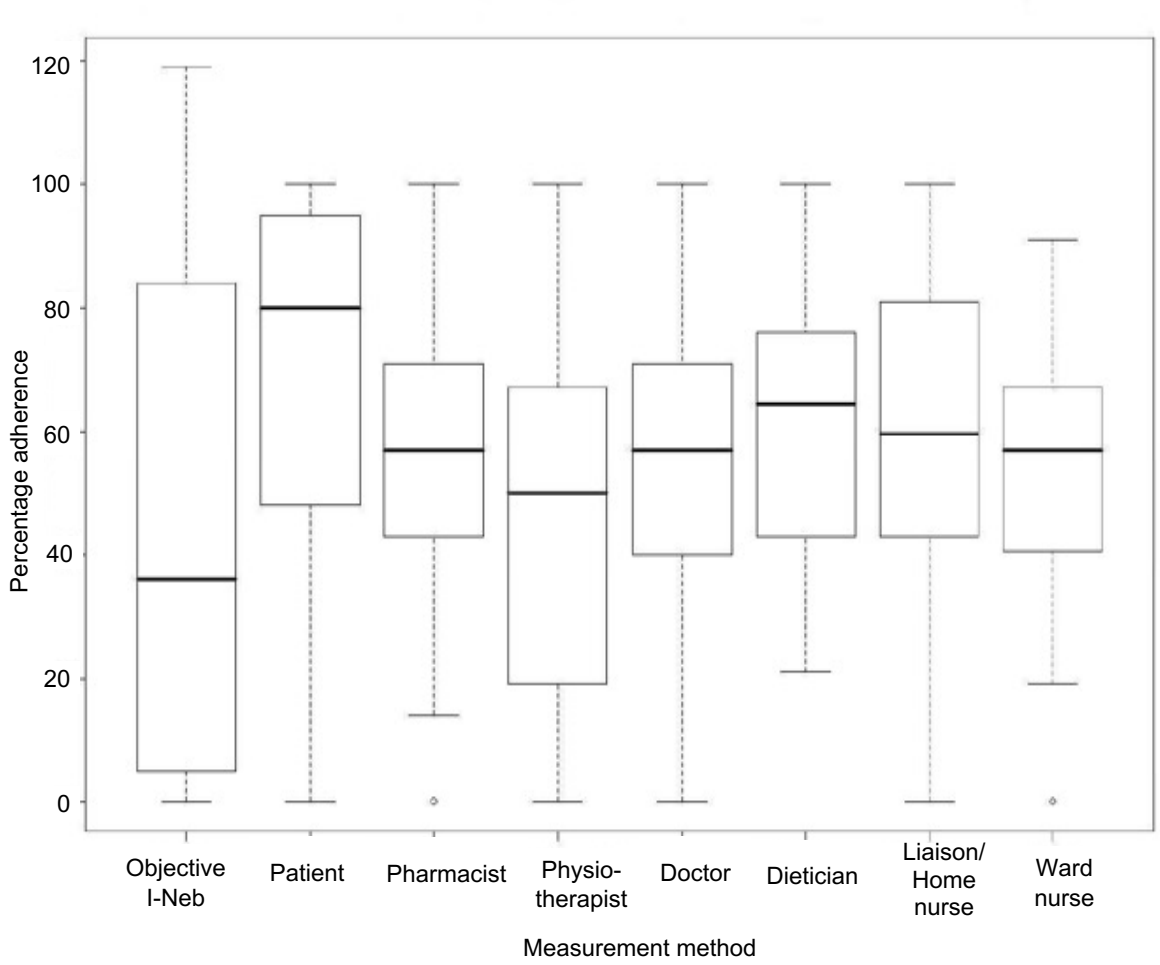
Measuring Adherence

Adherence Rates Vary Based on Reporting Method

UK study of 78 adults with CF assessing adherence to prescribed nebulizers over 3 months[1]

- Median adherence of 36% objectively reported by I-Neb electronic monitoring downloaded data[1]
- Median adherence of 80% reported by patients with CF[1]
  - 9 patients reported 100% adherence with downloaded data rates of 105-119%; overmedicated although a tendency to underestimate[1]
- Median adherence of 50-60% reported by clinicians[1]

Subjective reports (self and clinician) overestimate adherence and are not as accurate as objective reports (device electronic monitoring)[1]



The median prescription was three nebs/day (ranging from 1-7) including Colistin, Tobramycin, Dornase Alpha, Salbutamol, Ipratropium bromide and hypertonic saline.

1. Daniels T, Goodacre L, Sutton C, et al. Accurate assessment of adherence: Self and clinician report versus electronic monitoring of nebulizers. *Chest.* 2011;140(2):425-432.

Measures of Adherence: Pros and Cons

Measure	Pros	Cons
Self-report[1] (patient completes)	Quick, inexpensive, comprehensive	Recall bias, overestimates, wanting to please provider[1,2, 5]
Clinician report[2] (clinician estimates patient adherence)	Quick, inexpensive, comprehensive	Biased by patient's report, relationship, perceptions
Daily phone diary[2] (24-hour recall on phone [EMA])	Good reliability, validity; matches electronic data	Time-consuming (15-minute call), trained interviewer
Apps for phones[4] (reminders, alarms on phone)	Novel initially; can provide rewards (points, sound effects)	Missing data; users often lose interest
Medication Possession Ratios[2,3] (pharmacy refill data)	Objectively counts refills; can calculate what % has been picked up; data across time	Medication picked up, but is it taken? Stockpiling medications is common (enzymes); multiple pharmacies
Electronic monitors[1]	Microchipped; collects on frequency and duration of treatments; objective therefore more accurate; can provide patient feedback	Not available for all treatments, expensive, often malfunction[1,2]

EMA, European Medicines Agency

1. Quittner AL, Modi AC, Lemanek KL, et. al. Evidence-based assessment of adherence to medical treatments in pediatric psychology. *J Pediatr Psychol*. 2008;33(9):916–936.
2. Quittner AL, Alpern AN, Balckwell LS, et.al. *Healthcare issues and challenges in adolescents with cystic fibrosis.* Eds. European Cystic Fibrosis Society 2012; Ch 6:77-92.
3. Quittner AL, Li-Rosi AM. Cystic fibrosis. *Adherence and Self-Management in Pediatric Populations*. Elsevier Academic Press 2020; Ch 5:107-132.
4. Quittner AL, Eakin MN, Alpern AN, et.al. Clustered randomized controlled trial of a clinic-based problem-solving to improve adherence in adolescents with cystic fibrosis. *J Cyst Fibros*. 2019;18(6):879-885.
5. Bishay LC, Sawicki GS. Strategies to optimize treatment adherence in adolescent patients with cystic fibrosis. *Adolesc Health Med Ther*. 2016;(7):117-124.

Major Barriers to Adherence

CF Treatment Regimens are Complex and High Treatment Burden[1]

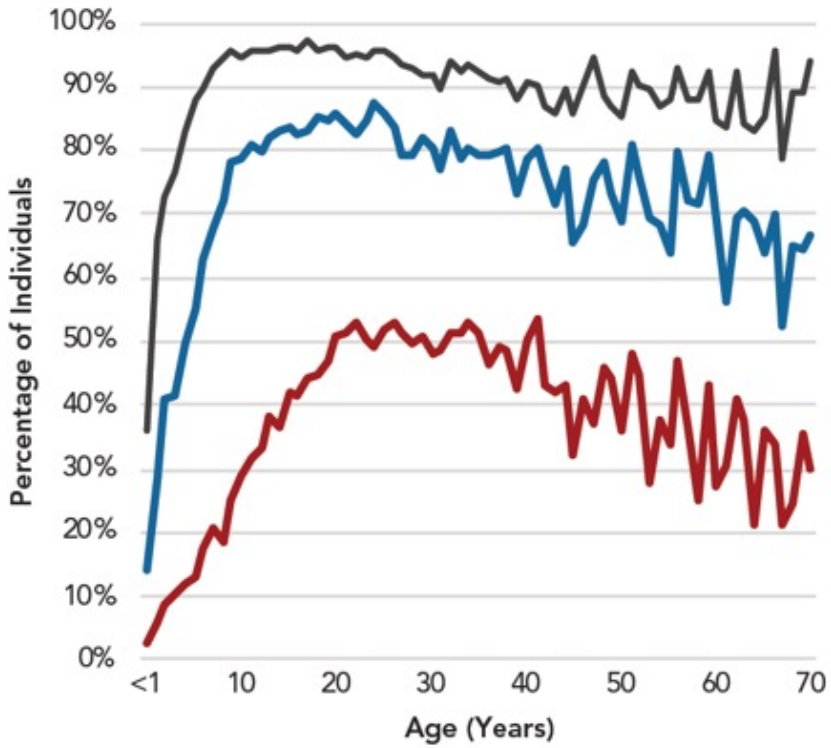
Individuals with CF take an average of 7+ therapies a day, requiring >100 minutes a day[1]

Approximately 80% of individuals aged 15-40 years are prescribed two or more inhaled medications[2]

- Inhaled medications require time to prepare, administer and clean equipment after treatment[2]

Overall burden on individuals and caregivers increase with multiple, complex pulmonary therapies[2]

Inhaled Medication* Prescription by Age[2]



≥ 1 medications; ≥ 2 medications; All 3 medications

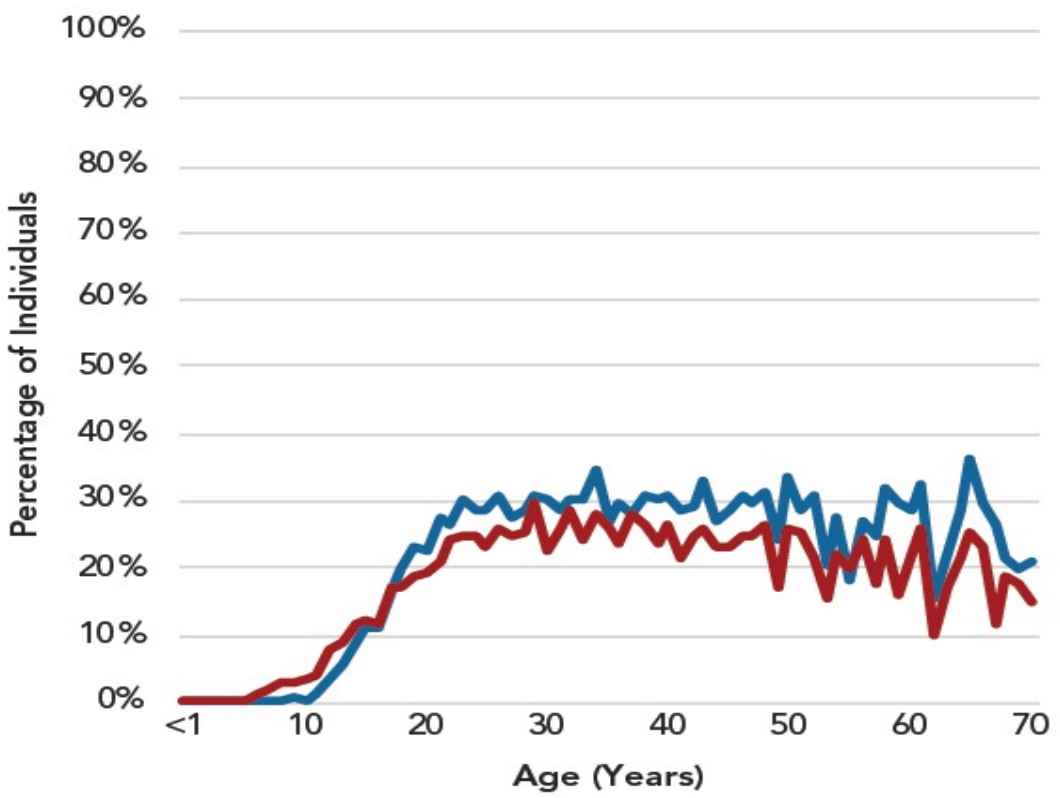
*Inhaled medication includes dornase alfa, hypertonic saline and inhaled antibiotics (tobramycin/aminoglycoside, aztreonam or colistin)

1. Quittner AL, Eakin MN, Alpern AN, et.al. Clustered randomized controlled trial of a clinic-based problem-solving to improve adherence in adolescents with cystic fibrosis. *J Cyst Fibros*. 2019;18(6):879-885.
2. CFF Patient Registry 2019 Annual Data Report Bethesda, MD ©2020 Cystic Fibrosis Foundation

Anxiety and Depression Impact on Adherence[1]

- Anxiety and depression increase during adolescence and remains high with substantial overlap[2]
  - Higher prevalence in older patients and those with greater impairment in lung function[2]
- Depression contributes to missed clinical appointments, worse quality of life and reduced adherence[1]
- Early diagnosis and treatment of depression and mental health conditions may ultimately improve CF outcomes[1]

Depression and Anxiety by Age[2]



1. Sawicki GS, Tiddens H. Managing treatment complexity in cystic fibrosis: challenges and opportunities. *Pediatr Pulmonol*. 2012;47:523-33
2. CFF Patient Registry 2019 Annual Data Report Bethesda, MD ©2020 Cystic Fibrosis Foundation

Strategies To Improve Adherence

Strategies to Improve Adherence

- Recognize that 100% compliance is unrealistic[1]
- Encourage openness with self-reporting by adopting a non-judgmental approach[1]
- Simplify treatments[1]
- Provide individualized treatment-specific education[1]
- Address barriers to non-compliance through careful and effective communication[1]
- Accept compromise[1]
- Agree on treatment planning and decisions; provide written treatment plan[1,2]
- Tailor treatments to daily lifestyle[1]
- Encourage self-management and self-efficacy[1]
- Give support and praise efforts[1]

Good relationship and clear communication with patient, caregiver, and healthcare team[3]

1. Dodd ME, Webb AK. Understanding non-compliance with treatment in adults with cystic fibrosis. *J R Soc Med*. 2000;93(Suppl 38):2–8.
2. Quittner AL, Modi AC, Lemanek KL, et. Al. Evidence-based assessment of adherence to medical treatments in pediatric psychology. *J Pediatr Psychol*. 2008;33(9):916–936.
3. Sawicki GS, Tiddens H. Managing treatment complexity in cystic fibrosis: challenges and opportunities.*Pediatr Pulmonol*. 2012;47:523-33

Summary

- Adherence is a significant challenge
- The CF regimen is very complex, long-term, and time-intensive
- Poor adherence significantly limits treatment efficacy, leading to substantial morbidity earlier mortality and higher healthcare costs[1]
- Generating collaborative solutions between the patient and healthcare providers may be the key to overcome adherence barriers due to the developed patient-provider relationship

Quittner et al. *Healthcare issues and challenges in adolescents with cystic fibrosis.* Eds. Castellani et al. European Cystic Fibrosis Society 2012; Ch 6:77-92