Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Clinical practice guidelines from the Cystic Fibrosis Foundation for preschoolers with cystic fibrosis.

Bibliographic Source(s)

Lahiri T, Hempstead SE, Brady C, Cannon CL, Clark K, Condren ME, Guill MF, Guillerman RP, Leone CG, Maguiness K, Monchil L, Powers SW, Rosenfeld M, Schwarzenberg SJ, Tompkins CL, Zemanick ET, Davis SD. Clinical practice guidelines from the Cystic Fibrosis Foundation for preschoolers with cystic fibrosis. Pediatrics. 2016 Apr;137(4):1-26. [157 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions of recommendation and certainty of benefit (low) are provided at the end of the "Major Recommendations" field.

Health Maintenance

1. For children with cystic fibrosis (CF), ages 2 through 5 years, the Cystic Fibrosis (CF) Foundation recommends routine well-child care at primary care provider (PCP) following American Academy of Pediatrics (AAP) guidelines. (Consensus Recommendation)
2. The CF Foundation recommends that children with CF, ages 2 through 5 years, receive all routine immunizations, following the recommended vaccination schedule per the AAP. (Consensus Recommendation)
3. The CF Foundation recommends that children with CF, ages 2 through 5 years, family members, and caregivers should receive annual seasonal influenza vaccination. (Consensus Recommendation)
4. The CF Foundation recommends that children with CF, ages 2 through 5 years, receive the first dose of the pneumococcal polysaccharide vaccine (PPSV23), given at least 8 weeks after last pneumococcal conjugate (Prevnar) vaccine dose. (Consensus Recommendation)
5. For children with CF, ages 2 through 5 years, the CF Foundation recommends that a smoke-free environment be provided and that all caregivers are informed that cigarette smoke exposure harms children with CF. (Consensus Recommendation)

Caregiver Engagement

6. For children with CF, ages 2 through 5 years, the CF Foundation recommends that parents and a CF health care professional review treatment goals and individualized care plans quarterly to assess and address barriers to CF care (Consensus Recommendation)

Screening and Monitoring

Pulse Oximetry

7. For children with CF, ages 2 through 5 years, the CF Foundation concludes that there is insufficient evidence to recommend for or against the use of pulse oximetry routinely as an adjunctive tool to detect lung disease. (Grade I; Certainty: Low)

Spirometry

8. For children with CF, ages 2 through 5 years, the CF Foundation recommends that spirometry should be attempted as early as age 3, depending on the developmental stage of the individual child. (Consensus Recommendation)
9. For children with CF, ages 3 and older, the CF Foundation recommends the use of spirometry for identifying pulmonary exacerbations and monitoring response to therapy in those children able to perform acceptable and reproducible maneuvers. (Consensus Recommendation)

Bronchodilator

10. For children with CF, ages 2 through 5 years, the CF Foundation concludes that there is insufficient evidence to recommend for or against routine monitoring of bronchodilator responsiveness. (Grade: I; Certainty: Low)

Multiple Breath Washout

11. For children with CF, ages 2 through 5 years, the CF Foundation concludes that there is insufficient evidence to recommend for or against routine monitoring of multiple breath washout. (Grade: I; Certainty: Low)

Chest Imaging

12. For children with CF, ages 2 through 5 years, the CF Foundation recommends chest radiographs be obtained at a minimum every other year to monitor progression of lung disease. (Consensus Recommendation)
13. For children with CF, ages 2 through 5 years, the CF Foundation recommends consideration of chest CT as an alternative to chest radiograph to monitor progression of lung disease. If chest CT is performed, it should replace chest radiograph, be performed every 2 to 3 years, and use the lowest radiation dose possible. (Consensus Recommendation)

Microbiology

14. For children with CF, ages 2 through 5 years, the CF Foundation recommends routine monitoring of airway microbiology by oropharyngeal cultures at least quarterly. (Consensus Recommendation)
15. For children with CF, ages 2 through 5 years, the CF Foundation recommends against routine use of bronchoscopy to obtain lower airway cultures. (Grade: D; Certainty: Moderate; Benefit: Negative)

Therapeutics

Exacerbations

16. For children with CF, ages 2 through 5 years, the CF Foundation recommends the use of oral, inhaled, and/or intravenous antibiotics to treat pulmonary exacerbations. (Consensus Recommendation)

Airway Clearance

17. For children with CF, ages 2 through 5 years, the CF Foundation recommends the use of daily airway clearance to improve lung function and reduce exacerbations. (Consensus Recommendation)
18. For children with CF, ages 2 through 5 years, the CF Foundation recommends increasing frequency and/or duration of airway clearance treatments for children diagnosed with pulmonary exacerbations. (Consensus Recommendation)

Bronchodilators

19. For children with CF, ages 2 through 5 years, the CF Foundation concludes that the evidence is insufficient to recommend for or against the chronic use of inhaled bronchodilators to improve lung function and quality of life or reduce exacerbations. (Grade: I; Certainty: Low)

Hypertonic Saline

20. For children with CF, ages 2 through 5 years, the CF Foundations recommends that hypertonic saline be selectively offered to patients

based on individual circumstances. (Grade C; Certainty: Moderate; Benefit: Low)

Dornase alfa

21. For children with CF, ages 2 through 5 years, the CF Foundation recommends that dornase alfa be selectively offered to patients based on individual circumstances. (Grade C; Certainty: Moderate; Benefit: Low)

Inhaled Corticosteroids

22. For children with CF, ages 2 through 5 years, and without asthma or recurrent wheezing, the CF Foundation recommends against the routine use of inhaled corticosteroids to reduce exacerbations, airway inflammation, or improve lung function or quality of life. (Grade: D; Certainty: High; Benefit: Low)

Corticosteroids

23. For children with CF, ages 2 through 5 years, and without allergic bronchopulmonary aspergillosis, the CF Foundation recommends against the chronic use of systemic corticosteroids to reduce exacerbations, or improve lung function, or quality of life. (Grade: D; Certainty: High; Benefit: Low)

Ibuprofen

24. For children with CF, ages 2 through 5 years, the CF Foundation concludes that there is insufficient evidence to recommend for or against chronic high-dose ibuprofen use to slow rate of decline of forced expiratory volume in 1 second (FEV_1), reduce exacerbations and hospitalizations, or improve quality of life. (Grade: I; Certainty: Low)

Leukotriene Modifiers

25. For children with CF, ages 2 through 5 years, the CF Foundation concludes that the evidence is insufficient to recommend for or against the routine chronic use of leukotriene modifiers to improve lung function or quality of life or reduce exacerbations. (Grade: I; Certainty: Low)

Azithromycin

26. For children with CF, ages 2 through 5 years, the CF Foundation concludes that there is insufficient evidence to recommend for or against the chronic use of azithromycin. (Grade: I; Certainty: Low)

Chronic *Pseudomonas* Infection

27. For children with CF, ages 2 through 5 years, the CF Foundation recommends that children who remain persistently infected with *P. aeruginosa* be treated chronically with alternate-month inhaled antipseudomonal antibiotics. (Grade B; Certainty: Moderate; Benefit: Moderate)

Staphylococcus aureus

28. For children with CF, ages 2 through 5 years, the CF Foundation recommends against the prophylactic use of oral antistaphylococcal antibiotics. (Grade: D; Certainty: Moderate; Benefit: Negative)
29. For children with CF, ages 2 through 5 years, the CF Foundation concludes that there is insufficient evidence to recommend for or against active attempts to eradicate *Staphylococcus aureus*, including methicillin-resistant *S. aureus*, in asymptomatic patients. (Grade: I; Certainty: Low)
30. For children with CF, ages 2 through 5 years, and with *Staphylococcus aureus* persistently present in cultures of the airways, the CF Foundation concludes that the evidence is insufficient to recommend for or against the chronic use of oral antistaphylococcal antibiotics to improve lung function or quality of life or reduce exacerbations. (Grade: I; Certainty: Low)

Ivacaftor

31. For children with CF, ages 2 through 5 years, the Preschool Guidelines Committee recommends the routine use of ivacaftor in those with specific gating mutations* and a consideration for those with a confirmed diagnosis of CF and a R117H mutation. (Consensus Recommendation)

*The mutations are G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, and S549R.

Nutrition, Behavior, and Gastrointestinal

Nutrition

32. For children with CF, ages 2 through 5 years, the CF Foundation recommends that weight-for-age be maintained at ≥10th percentile. (Grade: A; Certainty: High; Benefit: Substantial)
33. For children with CF, ages 2 through 5 years, the CF Foundation recommends weight-for-stature assessments use the body mass index (BMI)% method on the Centers for Disease Control and Prevention growth charts and a BMI ≥50th percentile be maintained. (Grade: B; Certainty: High; Benefit: Moderate)
34. For children with CF, ages 2 through 5 years, who are meeting optimal nutritional thresholds, the CF Foundation recommends ≥90–110 kcal/kg per day and protein intake based on dietary reference intakes and dietary guidelines recommendations: ≥13 g protein/day 2–3-year-old, ≥19 g protein/day 4–5-year-old. (Grade: A; Certainty: High; Benefit: Substantial)

Nutritional Risk

35. For children with CF, ages 2 through 5 years, the CF Foundation recommends evaluation and more intensive management of children demonstrating any of these criteria of nutritional risk:
    - BMI <50th percentile, or rate of weight gain <50th percentile expected for age (≥6 g/d), or weight-for-age <10th percentile, or inappropriate weight loss (Grade: B; Certainty: High; Benefit: Moderate)
36. For children with CF, ages 2 through 5 years, and at nutritional risk, the CF Foundation recommends patients be seen in 8 weeks or sooner. These visits should include medical, behavioral, and nutritional assessment; education; and intervention. Nutritional intervention should aim at achieving the patient's target goal for both weight-for-age and BMI. (Consensus Recommendation)
37. For children with CF, ages 2 through 5 years, and at nutritional risk, the CF Foundation recommends energy intake 10% to 20% above baseline with continued incremental upward adjustments of 10% to 20% as needed up to 200% to achieve weight gain. (Grade: B; Certainty: Moderate; Benefit: Moderate)
38. For children with CF, ages 2 through 5 years, and at nutritional risk, the CF Foundation recommends the use of oral nutrition supplements, in addition to usual dietary intake, to improve rate of weight gain. (Grade: B; Certainty: Moderate; Benefit: Moderate)
39. For children with CF, ages 2 through 5 years, at nutritional risk who do not respond to previously described nutritional interventions, see Figure 2, the CF Foundation recommends an expanded evaluation to consider other causes of poor growth, including gastrointestinal, endocrine, behavioral, and social causes. Subspecialty consultation may be considered. (Consensus Recommendation)
40. For children with CF, ages 2 through 5 years, at nutritional risk who do not respond to standard nutritional intervention and who have not responded to the evaluation and management plan of the multidisciplinary team, the CF Foundation recommends the use of enteral nutritional supplements via a feeding tube to improve the rate of weight gain. The concept of enteral feedings should be introduced early as a component of CF care. (Grade: B; Certainty: Moderate; Benefit: Moderate)

Vitamins

41. For children with CF, ages 2 through 5 years, the CF Foundation recommends standard, age-appropriate non–fat-soluble vitamins and the recommended levels of vitamins A, D, E, and K by using a fat-soluble vitamin supplement formulated for children with CF and if indicated based on levels, additional supplementation of vitamins A, D, E, and K. (Consensus Recommendation)
42. For children with CF, ages 2 through 5 years, the CF Foundation recommends that blood levels of fat-soluble vitamins be measured annually. If values are abnormal, more frequent measurements after dose adjustment are recommended. (Consensus Recommendation)
43. For children with CF, ages 2 through 5 years, the CF Foundation recommends that management of vitamin D deficiency follow the treatment outlined in the CF Foundation Vitamin D guidelines: An Update on the Screening, Diagnosis, Management, and Treatment of Vitamin D Deficiency in Individuals with Cystic Fibrosis: Evidence-Based Recommendations from the Cystic Fibrosis Foundation, 2012. (Consensus Recommendation)

Salt

44. For children with CF, ages 2 through 5 years, the CF Foundation recommends adding additional salt to meals and snacks, especially during the summer months and for those who live in warm climates. (Consensus Recommendation)

Pancreatic Enzyme Replacement Therapy (PERT)

45. For children with CF and pancreatic insufficiency (PI), ages 2 through 5 years, the CF Foundation recommends that PERT be adjusted up to a dose of no greater than 2500 lipase units per kg per meal with a maximum daily dose of 10,000 lipase units/kg. (Consensus Recommendation)

Behavior

46. For children with CF, ages 2 through 5 years, the CF Foundation recommends that the CF team members, working in concert with the family, set energy-intake goals and assess progress on a regular basis. (Grade: B; Certainty: Moderate Benefit: Substantial)
47. For children with CF, ages 2 through 5 years, the CF Foundation recommends that all families are regularly assessed for the presence of mealtime behavior challenges and are provided with proactive behavioral assistance when needed. (Grade: A; Certainty: High; Benefit: Substantial)
48. For children with CF, ages 2 through 5 years, who are at nutritional risk, or exhibiting challenging mealtime behaviors, or not meeting energy intake goals, behavioral therapy provided by knowledgeable team members should accompany nutritional therapy. (Grade: A; Certainty: High; Benefit: Substantial)

Gastrointestinal

49. The CF Foundation recommends that all providers be aware of the presenting symptoms of the following gastrointestinal tract disorders: constipation, gastroesophageal reflux disease, small bowel overgrowth, distal intestinal obstruction syndrome, and celiac disease. (Consensus Recommendation)
50. For children with CF, ages 2 through 5 years, the CF Foundation recommends that children and their parents be questioned regarding abdominal pain at each visit, and that pain is investigated if persistent or recurrent. (Consensus Recommendation)
51. For children with CF, ages 2 through 5 years, and who are pancreatic sufficient (PS), the CF Foundation recommends that children are reevaluated annually for the conversion to PI with fecal elastase measurement, particularly if genetic testing reveals 2 mutations potentially associated with PI. (Consensus Recommendation)
52. For children with CF, ages 2 through 5 years, and who are PS with severe abdominal pain, particularly if associated with vomiting, the CF Foundation recommends measurement of lipase and amylase to determine if pancreatitis is present. (Consensus Recommendation)
53. For children with CF, ages 2 through 5 years, who had terminal ileal bowel resection, the CF Foundation recommends annual measurement of serum vitamin B12 concentration. (Consensus Recommendation)

Definitions

Strength of Recommendation

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

U.S. Preventive Services Task Force (USPSTF) Grade Definitions

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as:

Level of Certainty	Description
	• The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to routine primary care practice • Lack of coherence in the chain of evidence As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence • Findings not generalizable to routine primary care practice • A lack of information on important health outcomes More information may allow an estimation of effects on health outcomes.

Clinical Algorithm(s)

The following algorithms are provided in the original guideline document:

- Approach to preschool-aged children with increased respiratory symptoms
- Three tiered nutrition algorithm:
  - Tier one: initial evaluation
  - Tier two: consultation and in-depth diagnostic evaluation
  - Tier three consideration of G-tube

Scope

Disease/Condition(s)

Cystic fibrosis (CF)

Guideline Category

Management

Screening

Treatment

Clinical Specialty

Family Practice

Pediatrics

Pulmonary Medicine

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Respiratory Care Practitioners

Guideline Objective(s)

To provide comprehensive evidence-based and consensus recommendations for the care of preschool children, ages 2 to 5 years, with cystic fibrosis (CF)

Target Population

Preschool children between the ages of 2 and 5 years

Interventions and Practices Considered

1. Health maintenance
    - Routine well-child care with immunizations as indicated
    - Smoke-free environment
2. Caregiver engagement, including a review of treatment goals
3. Screening and monitoring
    - Spirometry
    - Routine monitoring by microbiology by oropharyngeal cultures
    - Chest radiographs or computed tomography (CT)
4. Therapeutics
    - Antibiotics, including antipseudomonal as indicated
    - Daily airway clearance
    - Hypertonic saline
    - Dornase alfa
    - Ivacaftor
5. Nutrition
    - Maintenance of weight-for-age
    - Weight-for-stature assessments using the body mass index (BMI) % method
    - Ensuring adequate energy intake
    - Protein intake based on dietary reference intakes and dietary guidelines
    - Evaluation and more intensive management in children with specified risk factors
    - Oral and enteral nutrition supplements
    - Subspecialty consultation
    - Vitamins
    - Additional salt
    - Pancreatic enzyme replacement therapy (PERT)
6. Behavior
    - Setting nutrition goals and assessing progress
    - Assessing mealtime behavior and therapy for mealtime challenges
7. Gastrointestinal

    Awareness of symptoms

    Evaluation for conversion to pancreatic insufficiency

    Measurement of lipase and amylase to assess for pancreatitis

    Annual measurement of serum B12 concentration in patients who had terminal ileal bowel resection

Note: The following were considered but no recommendation could be made for or against: routine use of pulse oximetry; routine monitoring of bronchodilator responsiveness; routine

monitoring of multiple breath washout; chronic use of bronchodilators to improve lung function and quality of life or reduce exacerbations; chronic high-dose ibuprofen use to slow rate of decline of forced expiratory volume in 1 second (FEV_1), reduce exacerbations and hospitalizations, or improve quality of life; routine chronic use of leukotriene modifiers to improve lung function or quality of life or reduce exacerbations; chronic use of azithromycin; active attempts to eradicate *Staphylococcus aureus*, including methicillin-resistant *S. aureus*, in asymptomatic patients; chronic use of oral antistaphylococcal antibiotics to improve lung function or quality of life or reduce exacerbations in children with *S. aureus* present in cultures.

Note: The following were considered but not recommended: routine use of bronchoscopy to obtain lower airway cultures; chronic use of systemic corticosteroids to reduce exacerbations, or improve lung function, or quality of life; routine use of inhaled corticosteroids to reduce exacerbations, airway inflammation, or improve lung function or quality of life; prophylactic use of oral antistaphylococcal antibiotics.

Major Outcomes Considered

- Lung function
- Optimal nutritional status
- Quality of life
- Adherence to therapy
- Behavioral challenges
- Rate of exacerbations or hospitalizations

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Evidence Synthesis and Review

At the initial meeting, the committee determined the scope of the document, developed Population, Intervention, Comparison, and Outcome (PICO) questions, and determined Medical Subject Headings (MeSH). The committee reviewed and approved each workgroup's PICO questions. An evidence synthesis was conducted at Dartmouth College from January to March 2014 in Ovid MEDLINE. The search included records from 2000 to 2013. Committee members also conducted their own searches.

Each workgroup reviewed the records found in the Dartmouth evidence synthesis. These records included the citation, abstract, and link to the Ovid Full Text or Citation. Abstracts that were not in English, did not address the PICO question, were not original research, did not involve humans, were not pertinent to the age group, reviews, case reports, letters and editorials were excluded. Abstract only citations were also excluded. Relevant guidelines were searched for through the American Academy of Pediatrics' (AAP) Web site.

If a committee member determined that the full text should be considered, it was pulled from either their institution or Dartmouth.

Number of Source Documents

In total, 10,427 articles were retrieved. Review articles, case reports, letters, nonhuman studies, and studies not related to the PICO questions were removed. A total of 344 articles were retained for review. 167 articles were included. Additional details on the review process can be found in the Supplemental Information (see the "Availability of Companion Documents" field).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

U.S. Preventive Services Task Force (USPSTF) Grade Definitions

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as: • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to routine primary care practice • Lack of coherence in the chain of evidence As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence • Findings not generalizable to routine primary care practice • A lack of information on important health outcomes More information may allow an estimation of effects on health outcomes.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Workgroups completed evidence tables for the records reviewed.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

In January 2014, the Cystic Fibrosis (CF) Foundation convened a committee of 16 CF pediatric experts and parents to develop clinical care guidelines for preschool-aged children with CF. Committee members participated in 1 of 3 workgroups. Each group developed population, intervention, comparison, and outcome (PICO) questions, which were reviewed and approved by the wider committee.

In May 2014 the committee convened to review draft recommendation statements and supporting evidence. Unfortunately, the evidence is lacking for most treatments and monitoring tools in the 2- to 5-year-old age group. Whenever possible, statements were developed and graded by using the U.S. Preventive Services Task Force grade definitions (see the "Rating Scheme for the Strength of the Evidence" field). The committee decided to make recommendations for CF care that would guide both CF clinicians and primary care providers (PCPs). Therefore, questions for which evidence was limited or absent were then presented and discussed by committee members. Use of existing evidence from older children and adults, as well as clinical experience, was then used as the basis for consensus recommendations. An 80% approval by the committee was agreed on a priori, and required for all statements.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

A draft manuscript was distributed by the Cystic Fibrosis (CF) Foundation to all accredited care centers for a 2-week public comment period. Feedback was collected by using an online survey and the guidelines were revised accordingly.

All recommendations were approved by the committee, and had a final consensus rate of at least 87.5%.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is specifically stated for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Behavioral and nutrition treatment can lead to improvements in attaining energy-intake goals.
- Routine use of dornase alfa is associated with reduced pulmonary exacerbations, improved lung function, and decreased rate of lung

function decline among older children and adults with cystic fibrosis (CF). Dornase alfa has been shown to have positive effects on computed tomography (CT) changes and lung clearance index (LCI) and improved health-related quality-of-life scores in children >6 years. Safety and tolerability of dornase alfa has been demonstrated in children ages 3 months to 5 years. Potential benefits include its effect on mucous plugging, air trapping, and lung health in CF that may result in delayed pulmonary disease progression.
- Ivacaftor has been shown to improve lung function, sweat chloride values, weight gain, and quality of life in people 6 years and older with at least 1 copy of the G551D mutation.

Potential Harms

Monitoring of liver function abnormalities in children treated with ivacaftor will be important.

Qualifying Statements

Qualifying Statements

The committee recognizes the limitations of these guidelines, which are the first step in standardization of preschool cystic fibrosis (CF) care.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Lahiri T, Hempstead SE, Brady C, Cannon CL, Clark K, Condren ME, Guill MF, Guillerman RP, Leone CG, Maguiness K, Monchil L, Powers SW, Rosenfeld M, Schwarzenberg SJ, Tompkins CL, Zemanick ET, Davis SD. Clinical practice guidelines from the Cystic Fibrosis Foundation for preschoolers with cystic fibrosis. Pediatrics. 2016 Apr;137(4):1-26. [157 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Apr

Guideline Developer(s)

Cystic Fibrosis Foundation - Disease Specific Society

Source(s) of Funding

Funding was provided by the Cystic Fibrosis Foundation.

Guideline Committee

Cystic Fibrosis Foundation Pulmonary Clinical Practice Guidelines Committee

Composition of Group That Authored the Guideline

Primary Authors: Thomas Lahiri, MD, Pediatric Pulmonology, University of Vermont Children's Hospital and Department of Pediatrics, University of Vermont College of Medicine, Burlington, Vermont; Sarah E. Hempstead, MS, The Dartmouth Institute for Health Policy and Clinical Practice, Lebanon, New Hampshire and Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire; Cynthia Brady, DNP, Children's Respiratory and Critical Care Specialists and Children's Hospitals and Clinics of Minnesota, Minneapolis, Minnesota; Carolyn L. Cannon, MD, PhD, Texas A&M Health Science Center, College Station, Texas; Kelli Clark, BS, Department of Pediatrics, University of North Carolina, Charlotte, North Carolina; Michelle E. Condren, PharmD, University of Oklahoma College of Pharmacy and School of Community Medicine, Tulsa, Oklahoma; Margaret F. Guill, MD, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire and Allergy and Pediatric Pulmonology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire; R. Paul Guillerman, MD, Department of Radiology, Baylor College of Medicine and Department of Pediatric Radiology, Texas Children's Hospital, Houston, Texas; Christina G. Leone, MSW, LCSW, Cystic Fibrosis Center, Children's Hospital Colorado, Aurora, Colorado; Karen Maguiness, MS, RD, CSP, Section of Pediatric Pulmonology, Allergy and Sleep Medicine, Department of Pediatrics, Riley Hospital for Children, Indiana University School of Medicine, Indianapolis, Indiana; Lisa Monchil, RRT-NPS, CCRC, AE-C, Armond V. Mascia, MD Cystic Fibrosis Center, Maria Fareri Children's Hospital at Westchester Medical Center, Valhalla, New York; Scott W. Powers, PhD, ABPP, Department of Pediatrics and Cincinnati Children's Research Foundation, University of Cincinnati College of Medicine and Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children's Hospital, Cincinnati, Ohio; Margaret Rosenfeld, MD, MPH, Division of Pulmonary Medicine, Seattle Children's Hospital and Department of Pediatrics, University of Washington School of Medicine, Seattle, Washington; Sarah Jane Schwarzenberg, MD, Pediatric Gastroenterology, Hepatology and Nutrition, University of Minnesota Masonic Children's Hospital, Minneapolis, Minnesota; Connie L. Tompkins, PhD, Department of Rehabilitation and Movement Sciences, University of Vermont College of Nursing and Health Sciences, Burlington, Vermont; Edith T. Zemanick, MD, Department of Pediatrics, University of Colorado School of Medicine, Aurora, Colorado; Stephanie D. Davis, MD, Section of Pediatric Pulmonology, Allergy and Sleep Medicine, Department of Pediatrics, Riley Hospital for Children, Indiana University School of Medicine, Indianapolis, Indiana

Financial Disclosures/Conflicts of Interest

Financial Disclosure

The authors have indicated they have no financial relationships relevant to this article to disclose.

Potential Conflict of Interest

Dr. Cannon's institution has received funding from Vertex Pharmaceuticals, Gilead Sciences, Insmed, and Novartis Pharmaceuticals for running the studies supported by Cystic Fibrosis Therapeutics funds. Dr. Cannon is an inventor on a patent for an antimicrobial licensed to Akron Research Commercialization Corporation, DBA Nebusil. Dr. Guillerman has consulted for PTC Therapeutics, Inc., received funding from the Cystic Fibrosis Foundation Therapeutics, Inc., and compensation from Vertex Pharmaceuticals. Dr. Rosenfeld has received grant funding from Vertex Pharmaceuticals. Dr. Davis has served as a board member for Vertex Pharmaceuticals and served as an unpaid consultant for Eli Lilly. The other authors have indicated they have no potential conflicts of interest to disclose.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available to subscribers from the American Academy of Pediatrics (AAP) Policy Web site.

Availability of Companion Documents

Supplemental information is available from the American Academy of Pediatrics (AAP) Policy Web site.

Patient Resources

A variety of information for parent and guardians is available from the Cystic Fibrosis Foundation Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on July 5, 2016. The information was verified by the guideline developer on August 8, 2016.

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