Cystic fibrosis (CF) clinical care guidelines exist for the care of infants up to age 2 years and for individuals ≥6 years of age. An important gap exists for preschool children between the ages of 2 and 5 years. This period marks a time of growth and development that is critical to achieve optimal nutritional status and maintain lung health. Given that disease often progresses in a clinically silent manner, objective and sensitive tools that detect and track early disease are important in this age group. Several challenges exist that may impede the delivery of care for these children, including adherence to therapies. A multidisciplinary committee was convened by the CF Foundation to develop comprehensive evidence-based and consensus recommendations for the care of preschool children, ages 2 to 5 years, with CF. This document includes recommendations in the following areas: routine surveillance for pulmonary disease, therapeutics, and nutritional and gastrointestinal care.

Early nutritional intervention and monitoring for respiratory and gastrointestinal disease in infants with cystic fibrosis (CF) is vital to improve long-term outcomes. Clinical care guidelines specific to infants with CF, and nutrition and pulmonary guidelines for children ≥6 years of age have been published by the CF Foundation. However, a gap exists in clinical care recommendations pertaining to preschoolers with CF, children ages 2 to 5 years.

In addition to typical developmental milestones, preschoolers with CF and their families face complex, time-consuming treatment regimens to maintain lung health and achieve optimal growth. It is well established that airway inflammation, infection, airway obstruction, and structural damage exist during preschool years in children with CF, often in the absence of overt respiratory symptoms. For families of preschoolers with CF, it can be challenging to institute appropriate mealtime behaviors, which can lead to poor nutritional outcomes and decreased survival at age 18 years when weight-for-age is ≤10th percentile for age and gender at age 4 years. Supporting preschoolers with CF and their families is critical to establish habits that promote normal growth and development and an active lifestyle (ie, exercise) to prevent pulmonary decline.

**METHODS**

In January 2014, the CF Foundation convened a committee of 16 CF pediatric experts and parents to develop clinical care guidelines for preschoolers with CF. The committee comprised members with expertise in CF care, including adherence to therapies. A multidisciplinary committee was convened by the CF Foundation to develop comprehensive evidence-based and consensus recommendations for the care of preschool children, ages 2 to 5 years, with CF. This document includes recommendations in the following areas: routine surveillance for pulmonary disease, therapeutics, and nutritional and gastrointestinal care.
preschool-aged children with CF. The treatment of this population has become increasingly important, as earlier diagnoses are made, primarily through newborn screening. 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. Dartmouth College investigators conducted a Medline literature search using PICO questions and additional medical search headings provided by the committee. Committee members conducted hand searches for additional literature and existing guidelines.

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 US Preventive Services Task Force grade definitions (Supplemental Table 1). 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. Revisions and voting were managed by using an online survey. All recommendations were approved by the committee, and had a final consensus rate of at least 87.5%.

A draft manuscript was distributed by the 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. The committee recognizes the limitations of these guidelines, which are the first step in standardization of preschool CF care. We fully expect these recommendations to evolve over time, as randomized controlled trials in these younger patients may provide evidence in favor of or against consensus recommendations.

RESULTS
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. Additional details on the review process can be found in the Supplemental Information. Guideline recommendations are summarized in Table 1.

DISCUSSION
Health Maintenance
Preschoolers with CF should receive routine well-child care from a PCP. Collaboration among the family, PCP, and a CF Foundation accredited care center is essential, and information about CF and the child’s CF care should be provided to the PCP. Children should receive age-appropriate immunizations and annual seasonal influenza vaccination along with family members and caregivers. They should receive the first dose of pneumococcal polysaccharide vaccine (PPSV23), given at least 8 weeks after the last pneumococcal conjugate vaccine (PCV13) dose. Environmental tobacco smoke exposure should be avoided; providers should routinely assess for environmental smoke exposure and offer caregivers information about smoking cessation and interventions to limit exposure.

Table 2 outlines routine monitoring care for preschoolers with CF including primary care visits. Table 1: Recommendations 1-5.

Caregiver Engagement
Parenting a preschooler with CF can be demanding and stressful. Families can face significant obstacles accessing CF care, including the high cost of insurance and prescription medications, and delays in, or denial of, coverage. Families may need guidance to model behaviors to handle refusals to take medications and to navigate mealtime struggles. To promote normal growth and development, it is essential to institute and maintain CF care routines in partnership with families, especially during preschool-age development. Parents and CF providers should collaborate to develop individualized treatment goals and plans that address barriers to care. Supplemental Table 2 lists some risk factors for poor adherence and Supplemental Table 3 outlines questions and topics to help caregiver engagement with treatment adherence. Table 1: Recommendation 6.

SURVEILLANCE FOR PULMONARY DISEASE
Pulse Oximetry
Few studies have evaluated oxygen saturation levels in CF. In older children and adolescents with CF, correlations between nocturnal O₂ saturation and lung function indices, chest computed tomography (CT), and chest radiograph scores have been reported. Hypoxia during sleep has been demonstrated to be associated with low forced expiratory volume in 1 second (FEV₁). In infants and preschoolers, no significant difference was observed in nocturnal O₂ saturation in those with CF versus controls. Given the paucity of data in preschoolers with CF, the committee concluded...
<table>
<thead>
<tr>
<th>Topic</th>
<th>Recommendation Statement</th>
<th>Grade or Consensus</th>
<th>Previous Guideline(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Maintenance 1</td>
<td>For children with CF, ages 2 through 5 y, the CF Foundation recommends routine well-child care at PCP following AAP guidelines.</td>
<td>Consensus Recommendation</td>
<td>AAP, Preventative Health Care (2014)</td>
</tr>
<tr>
<td>Health Maintenance 2</td>
<td>The CF Foundation recommends that children with CF, ages 2 through 5 y, receive all routine immunizations, following the recommended vaccination schedule per the AAP.</td>
<td>Consensus Recommendation</td>
<td>AAP, Immunization Schedule (2014)</td>
</tr>
<tr>
<td>Health Maintenance 3</td>
<td>The CF Foundation recommends that children with CF, ages 2 through 5 y, family members, and caregivers should receive annual seasonal influenza vaccination.</td>
<td>Consensus Recommendation</td>
<td>AAP, Recommendations for Prevention and Control of Influenza in Children, 2013–2014 (2013)</td>
</tr>
<tr>
<td>Health Maintenance 4</td>
<td>The CF Foundation recommends that children with CF, ages 2 through 5 y, receive the first dose of the pneumococcal polysaccharide vaccine (PPSV23), given at least 8 wk after last pneumococcal conjugate (Prevnar) vaccine dose.</td>
<td>Consensus Recommendation</td>
<td>AAP Immunization Schedule (2014)</td>
</tr>
<tr>
<td>Health Maintenance 5</td>
<td>For children with CF, ages 2 through 5 y, 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.</td>
<td>Consensus Recommendation</td>
<td>Cystic Fibrosis Foundation Evidence-Based Guidelines for Management of Infants with Cystic Fibrosis (2009) Consensus Recommendation</td>
</tr>
<tr>
<td>Caregiver Engagement 6</td>
<td>For children with CF ages, 2 through 5 y, the CF Foundation recommends that parents and CF health care professional review treatment goals and individualized care plans quarterly to assess and address barriers to CF care.</td>
<td>Consensus Recommendation</td>
<td>AAP-Tobacco Use: A Pediatric Disease (2009)</td>
</tr>
<tr>
<td>Screening and Monitoring: Pulse Oximetry 7</td>
<td>For children with CF, ages 2 through 5 y, 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.</td>
<td>Grade: I; Certainty: Low</td>
<td>Cystic Fibrosis Foundation Evidence-Based Guidelines for Management of Infants with Cystic Fibrosis (2009) Grade: I, Certainty: Low, Benefit: Small</td>
</tr>
<tr>
<td>Screening and Monitoring: Spirometry 8</td>
<td>For children with CF, ages 2 through 5 y, the CF Foundation recommends that spirometry be attempted as early as age 3, depending on the developmental stage of the individual child.</td>
<td>Consensus Recommendation</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health (2015) Grade: I Certainty: Low</td>
</tr>
<tr>
<td>Screening and Monitoring: Spirometry 9</td>
<td>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.</td>
<td>Consensus Recommendation</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Management of Infants with Cystic Fibrosis (2009)</td>
</tr>
<tr>
<td>Screening and Monitoring: Bronchodilator 10</td>
<td>For children with CF, ages 2 through 5 y, the CF Foundation concludes that there is insufficient evidence to recommend for or against routine monitoring of bronchodilator responsiveness.</td>
<td>Grade: I; Certainty: Low</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health (2015) Grade: I Certainty: Low</td>
</tr>
<tr>
<td>Screening and Monitoring: Multiple Breath Washout 11</td>
<td>For children with CF, ages 2 through 5 y, the CF Foundation concludes that there is insufficient evidence to recommend for or against routine monitoring of multiple breath washout.</td>
<td>Grade: I; Certainty: Low</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Management of Infants with Cystic Fibrosis (2009)</td>
</tr>
<tr>
<td>Screening and Monitoring: Chest Imaging 12</td>
<td>For children with CF, ages 2 through 5 y, the CF Foundation recommends chest radiographs be obtained at a minimum every other year to monitor progression of lung disease.</td>
<td>Consensus Recommendation</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Management of Infants with Cystic Fibrosis (2009)</td>
</tr>
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<td></td>
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</tbody>
</table>
### TABLE 1 Continued

<table>
<thead>
<tr>
<th>Topic</th>
<th>Recommendation Statement</th>
<th>Grade or Consensus</th>
<th>Previous Guideline(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening and Monitoring: Chest Imaging</td>
<td>13. For children with CF, ages 2 through 5 y, 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 2–3 y, and use the lowest radiation dose possible.</td>
<td>Consensus Recommendation</td>
<td>Cystic Fibrosis Adult Care (2004) Consensus Recommendation</td>
</tr>
<tr>
<td>Screening and Monitoring: Microbiology</td>
<td>14. For children with CF, ages 2 through 5 y, the CF Foundation recommends routine monitoring of airway microbiology by oropharyngeal cultures at least quarterly.</td>
<td>Consensus Recommendation</td>
<td>Cystic Fibrosis Foundation Evidence-Based Guidelines for Management of Infants with Cystic Fibrosis (2009) Consensus Recommendation</td>
</tr>
<tr>
<td>Screening and Monitoring: Microbiology</td>
<td>15. For children with CF, ages 2 through 5 y, the CF Foundation recommends against routine use of bronchoscopy to obtain lower airway cultures.</td>
<td>Grade: D; Certainty: Moderate; Benefit: Negative</td>
<td>Cystic Fibrosis Foundation Pulmonary Guideline: Pharmacologic Approaches to Prevention and Eradication of Initial Pseudomonas aeruginosa Infection (2014) Grade: D, Certainty: Moderate, Benefit: Zero</td>
</tr>
<tr>
<td>Therapeutics: Exacerbations</td>
<td>16. For children with CF, ages 2 through 5 y, the CF Foundation recommends the use of oral, inhaled, and/or intravenous antibiotics to treat pulmonary exacerbations.</td>
<td>Consensus Recommendation</td>
<td></td>
</tr>
<tr>
<td>Therapeutics: Airway Clearance</td>
<td>17. For children with CF, ages 2 through 5 y, the CF Foundation recommends the use of daily airway clearance to improve lung function and reduce exacerbations.</td>
<td>Consensus Recommendation</td>
<td>Cystic Fibrosis Foundation Evidence-Based Guidelines for Management of Infants with Cystic Fibrosis (2009) Consensus Recommendation</td>
</tr>
<tr>
<td>Therapeutics: Airway Clearance</td>
<td>18. For children with CF, ages 2 through 5 y, the CF Foundation recommends increasing frequency and/or duration of airway clearance treatments for children diagnosed with pulmonary exacerbations.</td>
<td>Consensus Recommendation</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Airway Clearance Therapies (2009) Grade B</td>
</tr>
<tr>
<td>Therapeutics: Bronchodilators</td>
<td>19. For children with CF, ages 2 through 5 y, 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.</td>
<td>Grade: I, Certainty: Low</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health (2015), Grade: I, Certainty: Low</td>
</tr>
<tr>
<td>Therapeutics: Hypertonic saline</td>
<td>20. For children with CF, ages 2 through 5 y, the CF Foundations recommends that hypertonic saline be selectively offered to patients based on individual circumstances.</td>
<td>Grade C, Certainty: Moderate; Benefit: Low</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health (2015) Grade: B, Certainty: Moderate, Benefit: Moderate</td>
</tr>
</tbody>
</table>

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### TABLE 1 Continued

<table>
<thead>
<tr>
<th>Topic</th>
<th>Recommendation Statement</th>
<th>Grade or Consensus</th>
<th>Previous Guideline(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Therapeutics: Inhaled Corticosteroids</strong></td>
<td>For children with CF, ages 2 through 5 y, 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.</td>
<td>Grade: D; Certainty: High; Benefit: Low</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health (2015) Grade: D, Certainty: High; Benefit: Zero. Cystic Fibrosis Foundation Evidence-Based Guidelines for Management of Infants with Cystic Fibrosis (2009) Consensus Recommendation, Certainty: Low; Benefit: Zero/Negative</td>
</tr>
<tr>
<td><strong>Therapeutics: Corticosteroids</strong></td>
<td>For children with CF, ages 2 through 5 y, 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.</td>
<td>Grade: D; Certainty: High; Benefit: Low</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health (2015) Grade: D, Certainty: High; Benefit: Negative</td>
</tr>
<tr>
<td><strong>Therapeutics: Ibuprofen</strong></td>
<td>For children with CF, ages 2 through 5 y, 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 FEV₁, reduce exacerbations and hospitalizations, or improve quality of life.</td>
<td>Grade: I; Certainty: Low</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health (2015), Grade: B, Certainty: Moderate, Benefit: Moderate</td>
</tr>
<tr>
<td><strong>Therapeutics: Leukotriene Modifiers</strong></td>
<td>For children with CF, ages 2 through 5 y, 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.</td>
<td>Grade: I; Certainty: Low</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health (2015), Grade: I, Certainty: Low</td>
</tr>
<tr>
<td><strong>Therapeutics: Azithromycin</strong></td>
<td>For children with CF, ages 2 through 5 y, the CF Foundation concludes that there is insufficient evidence to recommend for or against the chronic use of azithromycin.</td>
<td>Grade: I; Certainty: Low</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health (2015), Grade: C, Certainty: Moderate, Benefit: Small</td>
</tr>
<tr>
<td><strong>Therapeutics: S aureus</strong></td>
<td>For children with CF, ages 2 through 5 y, the CF Foundation recommends against the prophylactic use of oral antistaphylococcal antibiotics.</td>
<td>Grade: D; Certainty: Moderate; Benefit: Negative</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health (2015) Grade: D, Certainty: Moderate, Benefit: Negative</td>
</tr>
<tr>
<td><strong>Therapeutics: S aureus</strong></td>
<td>For children with CF, ages 2 through 5 y, the CF Foundation concludes that there is insufficient evidence to recommend for or against active attempts to eradicate <em>Staphylococcus aureus</em>, including methicillin-resistant <em>S aureus</em>, in asymptomatic patients.</td>
<td>Grade: I; Certainty: Low</td>
<td>Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health (2015) Grade: D, Certainty: Moderate, Benefit: Negative Cystic Fibrosis Foundation Evidence-Based Guidelines for Management of Infants with Cystic Fibrosis (2009) Grade: I, Certainty: Low, Benefit: Unknown.</td>
</tr>
</tbody>
</table>
Therapeutics: *Staphylococcus aureus*

30. For children with CF, ages 2 through 5 y, 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


Therapeutics: Ivacaftor

31. For children with CF, ages 2 through 5 y, 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


Nutrition, Behavior, and Gastrointestinal: Nutrition

32. For children with CF, ages 2 through 5 y, the CF Foundation recommends that weight-for-age be maintained at ≥10th percentile.

Grade: A; Certainty: High; Benefit: Substantial

Evidence-Based Practice Recommendations for Nutrition-Related Management of Children and Adults with Cystic Fibrosis and Pancreatic Insufficiency: Results of a Systematic Review (2008) Registry Data-based Recommendation

33. For children with CF, ages 2 through 5 y, the CF Foundation recommends weight-for-stature assessments use the 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 y, who are meeting optimal nutritional thresholds, the CF Foundation recommends ≥80–110 kcal/kg per day and protein intake based on dietary reference intakes and dietary guidelines recommendations: ≥13 g protein/d 2–3 y old, ≥19 g protein/d 4–5 y old.

Grade: A; Certainty: High; Benefit: Substantial

35. For children with CF, ages 2 through 5 y, 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 y, and at nutritional risk, the CF Foundation recommends patients be seen in 8 wk 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

Consensus Report on Nutrition for Pediatric Patients with Cystic Fibrosis (2002) Definition of Nutritional Failure and Patients at Risk

37. For children with CF, ages 2 through 5 y, 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

Evidence-Based Practice Recommendations for Nutrition-Related Management of Children and Adults with Cystic Fibrosis and Pancreatic Insufficiency: Results of a Systematic Review (2008) Grade: B
38. For children with CF, ages 2 through 5 y, 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

Evidence-Based Practice

40. For children with CF, ages 2 through 5 y, 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 nutrition 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

41. For children with CF, ages 2 through 5 y, 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.

42. For children with CF, ages 2 through 5 y, 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.

43. For children with CF, ages 2 through 5 y, 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.

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

45. For children with CF and PI, ages 2 through 5 y, 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.
that there is insufficient evidence to recommend for or against routine use of pulse oximetry as an adjunctive tool to detect lung disease. Table 1: Recommendation 7.

**Spirometry**

Spirometry is the most important and widely used tool to assess lung function in CF. Several studies have demonstrated that spirometry is feasible in preschoolers with CF, and has the potential to detect pulmonary exacerbations and airway obstruction despite minimal symptoms.\(^6\)\(^,\)\(^21\)\(^,\)\(^22\) In a cross-sectional, multicenter study, FEV in 0.5 second and flow-related volumes were found to be more sensitive than FEV for identifying abnormal lung function in asymptomatic, preschool-aged children.\(^23\) Another study demonstrated improvement of spirometric indices in both school-aged children and 10 preschoolers who were treated for pulmonary exacerbations.\(^24\) Because there is no risk to performing spirometry in preschool-aged children, and they benefit from practicing with technicians, the committee concluded that spirometry should be attempted as early as 3 years of age, depending on the child’s

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<tbody>
<tr>
<td>Nutrition, Behavior, and Gastrointestinal: Behavior</td>
<td>For children with CF, ages 2 through 5 y, 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.</td>
<td>Grade: B; Certainty: Moderate; Benefit: Substantial</td>
<td></td>
</tr>
<tr>
<td>Nutrition, Behavior, and Gastrointestinal: Behavior</td>
<td>For children with CF, ages 2 through 5 y, the CF Foundation recommends that all families are regularly assessed for the presence of mealtine behavior challenges and are provided with proactive behavioral assistance when needed.</td>
<td>Grade: A; Certainty: High; Benefit: Substantial</td>
<td>Evidence-Based Practice Recommendations for Nutrition-Related Management of Children and Adults with Cystic Fibrosis and Pancreatic Insufficiency: Results of a Systematic Review (2008) Grade: B</td>
</tr>
<tr>
<td>Nutrition, Behavior, and Gastrointestinal: Behavior</td>
<td>For children with CF, ages 2 through 5 y, who are at nutritional risk, or exhibiting challenging mealtine behaviors, or not meeting energy-intake goals, behavioral therapy provided by knowledgeable team members should accompany nutritional therapy.</td>
<td>Grade: A; Certainty: High; Benefit: Substantial</td>
<td></td>
</tr>
<tr>
<td>Nutrition, Behavior, and Gastrointestinal: Gastrointestinal</td>
<td>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.</td>
<td>Consensus Recommendation</td>
<td></td>
</tr>
<tr>
<td>Nutrition, Behavior, and Gastrointestinal: Gastrointestinal</td>
<td>For children with CF, ages 2 through 5 y, 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.</td>
<td>Consensus Recommendation</td>
<td></td>
</tr>
<tr>
<td>Nutrition, Behavior, and Gastrointestinal: Gastrointestinal</td>
<td>For children with CF, ages 2 through 5 y, and who are 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.</td>
<td>Consensus Recommendation</td>
<td>Consensus Report on Nutrition for pediatric Patients with Cystic Fibrosis (2002) Issues Related to Pancreatic Insufficiency: Identifying Pancreatic Insufficiency</td>
</tr>
<tr>
<td>Nutrition, Behavior, and Gastrointestinal: Gastrointestinal</td>
<td>For children with CF, ages 2 through 5 y, 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.</td>
<td>Consensus Recommendation</td>
<td></td>
</tr>
<tr>
<td>Nutrition, Behavior, and Gastrointestinal: Gastrointestinal</td>
<td>For children with CF, ages 2 through 5 y, who had terminal ileal bowel resection, the CF Foundation recommends annual measurement of serum vitamin B12 concentration.</td>
<td>Consensus Recommendation</td>
<td></td>
</tr>
</tbody>
</table>

AAP, American Academy of Pediatrics;
developmental level. Table 1: Recommendations 8–9.

**Bronchodilator Responsiveness**

Three articles demonstrated bronchodilator responsiveness in <20% of children with CF. Bronchodilator responsiveness may be associated with certain polymorphisms.25–27 Although there is insufficient evidence to recommend for or against routine monitoring of bronchodilator responsiveness, evaluation may be considered if there are concerns or symptoms suggestive of airway hyperreactivity. Table 1: Recommendation 10.

**Multiple-Breath Washout**

Multiple-breath washout (MBW) testing measures regional ventilation heterogeneity and appears to be more sensitive than spirometry in detecting pulmonary function abnormalities in young children with CF. Two prospective studies

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**TABLE 2 Routine Monitoring and Care**

<table>
<thead>
<tr>
<th>Age at Visit</th>
<th>2 y</th>
<th>3 y</th>
<th>4 y</th>
<th>5 y</th>
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<tbody>
<tr>
<td>Intervention</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Visit Done</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Care issues</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continue high-salt diet, supplement additional salt in hot weather</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>History and physical with weight and height</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Teach and assess airway clearance, review airway clearance techniques</td>
<td>X</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Assess weight gain, caloric intake, and PERT dosing</td>
<td>X</td>
<td>X</td>
<td>X</td>
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</tr>
<tr>
<td>Continue vitamins designed for patients with CF</td>
<td>X</td>
<td>X</td>
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<td>X</td>
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<tr>
<td>Introduce chronic dornase alfa and/or HS</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Seasonal influenza vaccination</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Pneumococcal polysaccharide vaccination</td>
<td>X</td>
<td>X</td>
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<td>X</td>
</tr>
<tr>
<td>Diagnostic testing</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Sweat test and genotyping confirmed documentation</td>
<td>X</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Pancreatic functional status testing</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Respiratory culture</td>
<td>X</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Chest radiograph or CT</td>
<td>X</td>
<td>C</td>
<td>C</td>
<td>C</td>
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<tr>
<td>Vitamin levels A, D, E, prothrombin time</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Serum electrolytes, SUN, creatinine, glucose</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Complete blood count</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>AST/ALT/GGT/bilirubin, albumin, ALP</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Spirometry</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
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<tr>
<td>Abdominal pain questioning</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teach and assess infection control</td>
<td>X</td>
<td>C</td>
<td>C</td>
<td>C</td>
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<tr>
<td>Document CF Foundation patient registry consent</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Discuss clinical research</td>
<td>X</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Referrals to community resources</td>
<td>X</td>
<td>C</td>
<td>C</td>
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<td>Tobacco smoke exposure avoidance education</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>Patient and caregiver engagement assessment</td>
<td>X</td>
<td>C</td>
<td>C</td>
<td>C</td>
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<tr>
<td>Set energy goals and assess progress</td>
<td>X</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Assess for presence of mealtme behavior challenges and provide proactive behavioral assistance</td>
<td>X</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Annual health supervision visits with PCP</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

**Legend:**
- A: attempt this task
- C: consider this task
- X: perform this task

**Notes:**
- ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; SUN, serum urea nitrogen.
- A single letter under one of the 4 yearly headings indicates the task should be performed, considered or attempted once a year. Further letters appear under quarterly visits when the task should be performed, considered, or attempted at >1 visit per year: A, attempt this task; C, consider this task; X, perform this task.
that included preschool-aged children reported that MBW indices, specifically lung clearance index (LCI), was more sensitive than spirometry in detecting abnormal lung function,\textsuperscript{5,28} and was generally abnormal in preschoolers with CF compared with healthy controls.\textsuperscript{20} The utility of MBW in the clinical setting and what constitutes a clinically significant change in the LCI has not yet been determined. The committee concluded that there is currently insufficient evidence to recommend for or against the routine use of MBW in CF. Table 1: Recommendation 11.

**Chest Radiographs**

Chest imaging can be performed at all ages and can identify structural changes that may be regional, early, and presymptomatic. Chest radiographs are relatively insensitive and nonspecific compared with CT scans, but require less radiation exposure, expense, and patient cooperation. Chest radiographs have been shown to detect the existence and progression of CF lung disease in infants,\textsuperscript{29} and preschool-aged\textsuperscript{30} and school-aged children.\textsuperscript{31} Chest radiographs demonstrate a higher correlation than FEV\textsubscript{1}/forced vital capacity with *Pseudomonas* acquisition in young children with CF.\textsuperscript{32} Chest radiograph scores are superior to FEV\textsubscript{1} in detecting concurrent abnormalities on chest CT scans,\textsuperscript{33} and in predicting future FEV\textsubscript{1} and chest radiograph scores.\textsuperscript{34} To monitor disease progression, chest radiographs should be obtained at a minimum of every other year following a baseline radiograph at diagnosis. Use of a scoring system, such as Brasfield,\textsuperscript{35} Chrispin-Norman,\textsuperscript{36} or Wisconsin\textsuperscript{37} scores, should be considered to monitor changes over time. Chest radiographs also should be considered in preschoolers with CF with a change in respiratory status that does not respond to appropriate interventions. Table 1: Recommendation 12.

**Chest CT**

Chest CT is a sensitive tool for monitoring early CF lung disease, as it detects early airway wall thickening, bronchiectasis, and gas trapping in infants and preschoolers,\textsuperscript{4,38,39} without symptoms or abnormal pulmonary function.\textsuperscript{40,41} Bronchiectasis in this age group often persists or progresses.\textsuperscript{42} The rate of structural lung disease progression on CT in preschoolers with CF is not well defined; however, CT scans have revealed progressive bronchiectasis in older children over a 2-year period, despite stable pulmonary function testing.\textsuperscript{40} In children <4 years of age experiencing a pulmonary exacerbation, CT detected regional differences in airway inflammation and scores improved after treatment.\textsuperscript{43} Although the carcinogenic risk of radiation exposure is small and continues to decrease with technological innovations,\textsuperscript{44} concerns remain regarding the risk of radiation exposure and expense. Controversy also persists regarding the significance of early changes seen on CT\textsuperscript{45} and the preferred methodology and reproducibility of scoring systems, especially in early or mild disease.\textsuperscript{46} There are currently no valid surrogates to replace CT. In a cohort of patients 5 to 19 years of age, a normal LCI almost excluded CT abnormality\textsuperscript{47}; in a younger cohort (mean age 7.8 years), LCI and high-resolution CT had similar sensitivity to detecting CF lung disease but provided complementary information.\textsuperscript{48} If routine monitoring is performed, it should replace chest radiographs, be performed every 2 to 3 years, and use the lowest radiation dose possible needed to obtain diagnostic-quality images. If used, consideration should be given to using a scoring system to standardize interpretation of repeated scans over time. Table 1: Recommendation 13.

**Microbiology**

Quarterly respiratory cultures are the standard of care for patients with CF.\textsuperscript{49} For infants\textsuperscript{1} and other nonexpectorating patients, an oropharyngeal (OP) swab is the usual respiratory sample, despite limited diagnostic accuracy compared with bronchoalveolar lavage (BAL).\textsuperscript{49} BAL is the only means by which to directly sample the lower respiratory tract and provides measures of lower airway inflammation that may have important prognostic value,\textsuperscript{5} but is invasive and costly. A randomized controlled trial in infants and preschoolers with CF\textsuperscript{50,51} found no difference in outcome at age 5 years when therapy was directed by OP culture as opposed to BAL. Induced sputum may have greater yield than OP culture,\textsuperscript{52–54} but it is time-consuming and impractical in standard clinic settings. Respiratory microbiology monitoring by OP cultures should be performed at least quarterly and routine airway monitoring by bronchoscopy is not recommended. However, bronchoscopy with BAL should be considered in patients with a change in respiratory status that does not respond to antibiotics directed toward pathogens isolated from OP swabs. Table 1: Recommendations 14–15.

**PULMONARY THERAPEUTICS**

**Pulmonary Exacerbations**

Based on our current understanding of early disease progression, the association of pulmonary exacerbations with worse outcomes, and evidence of improvement with antibiotic treatment,\textsuperscript{43} the recommendation for preschoolers with CF experiencing an exacerbation is oral, inhaled, and/or intravenous antibiotic treatment. Defining a pulmonary
Exacerbation is beyond the scope of this article; however, Fig 1 outlines the recommended approach to preschool-aged children with increased respiratory symptoms. There are no randomized clinical trials of pulmonary exacerbation treatment in preschool-aged children with CF; thus, these guidelines for management were based on consensus recommendations, and management decisions should be individualized. Oral antibiotics targeting bacteria detected on airway cultures are recommended for mild to moderate pulmonary exacerbations, whereas intravenous antibiotics are recommended for moderate to severe pulmonary exacerbations or mild exacerbations unresponsive to oral antibiotics. Inhaled antibiotics are recommended based on standard guidelines for treatment of new and chronic *Pseudomonas aeruginosa* infection.2,67

Table 1: Recommendation 16.

**Airway Clearance Therapy**

Airway clearance therapy (ACT) is an important maintenance treatment and is recommended for all individuals with CF.1,68 With early airway disease noted in the youngest population, ACT has the potential to prevent development of irreversible disease. Continuing ACT through preschool years will encourage maintenance throughout childhood. An active lifestyle consisting of vigorous physical activity and exercise, important components of maintaining lung health, should be encouraged and initiated in this age group. In preschoolers with CF, daily ACT is recommended and increased frequency and/or duration is recommended during pulmonary exacerbations. Table 1: Recommendations 17–18.

**Bronchodilators**

No studies were found that address bronchodilator efficacy in the absence of asthma or bronchial hyperresponsiveness in CF; therefore, the evidence is insufficient to recommend for or against the chronic use of inhaled bronchodilators in preschoolers. However, viral-triggered wheezing or asthma in preschoolers may respond to bronchodilator therapy. Table 1: Recommendation 19.

**Hypertonic Saline**

Several studies have demonstrated safety and tolerability of 7% hypertonic saline (HS) in infants and young children.69–71 Unlike a study in older individuals with CF,72 a randomized controlled trial of 344 children <5 years failed to show a reduction in the primary endpoint of pulmonary exacerbation rate.73 However, in 2 small studies that were part of this larger trial, infant lung function and the LCI did demonstrate improvement in subjects receiving 7% HS.73,74 Given these findings, the CF Foundation recommends that HS be offered to patients based on individual circumstances, either for chronic use or during acute pulmonary exacerbation. Further studies may alter this recommendation. Table 1: Recommendation 20.

**Dornase Alfa**

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 CF.75–81 Dornase alfa has been shown to have positive effects on CT changes and LCI82–84 and improved health-related quality-of-life scores in children >6 years.85 Safety and tolerability of dornase alfa has been demonstrated in children ages 3 months to 5 years.86,87 Potential benefits include its effect on mucus plugging, air trapping, and lung health in CF that may result in delayed pulmonary disease progression. Based on moderate evidence that dornase alfa is safe and effective, and the potential benefit is at least small, the CF Foundation recommends that dornase alfa be offered to patients based on individual circumstances, either for chronic use or during acute pulmonary exacerbation. Further studies may alter this recommendation. Table 1: Recommendation 21.

**Systemic and Inhaled Corticosteroids**

With the exception of treatment of allergic bronchopulmonary aspergillosis, systemic corticosteroids are not recommended for routine use in children with CF, as potential harm outweighs any benefit. Inhaled corticosteroids are not recommended for management of CF lung disease, as no clear benefit has been identified.2 Table 1: Recommendation 22–23.

**Ibuprofen**

High-dose ibuprofen is recommended for chronic use in individuals with CF older than 6 years with mild lung disease.2 We found no prospective trials that support its use in children younger than 6 years and conclude there is insufficient evidence to recommend for or against its use in preschoolers with CF. Table 1: Recommendation 24.

**Leukotriene Modifiers**

In the absence of comorbid conditions, such as asthma or recurrent wheezing, there is insufficient evidence to recommend for or against the chronic use leukotriene modifiers for preschoolers with CF. Table 1: Recommendation 25.

**Azithromycin**

Routine use of azithromycin is recommended for individuals with CF >6 years with persistent *P aeruginosa* infection.2 Azithromycin is safe, reduces lower airway inflammation and exacerbations, and improves
Increased respiratory signs or symptoms (cough, sputum production, new crackles, oxygen desaturation, wheezing, hemoptysis)

Mild-to-moderate pulmonary exacerbation
- 1-2 signs or symptoms present or symptom severity mild
- If seen in clinic: obtain respiratory culture
- Prescribe oral antibiotics based on most recent culture results.
- Prescribe inhaled antibiotics if indicated for *P. aeruginosa* infection
- Increase airway clearance

Symptoms resolve, return to routine care

Symptoms improve but not resolved
- Change antibiotics
- Repeat airway culture
- Follow-up

Symptoms continue, minimally improve or worsen
- Obtain respiratory culture,
- Attempt/perform spirometry
- Intravenous antibiotics based on most recent culture results
- Increase airway clearance
- Consider using albuterol with airway clearance treatments
- Consider use of dornase alfa and/or 7% hypertonic saline
- Consider chest radiograph particularly for new crackles, oxygen desaturation
- Consider bronchoscopy with bronchoalveolar lavage, if not responding to antibiotics directed to upper airway pathogens
- Oral corticosteroids only in patients with asthma or recurrent wheeze

Symptoms continue, minimally improve, or worsen
- Consider further evaluation: chest CT, bronchoscopy
- Repeat cultures
- Consider treatment of sinusitis/ENT evaluation if present
- Change antibiotics

FIGURE 1
Approach to preschool-aged children with increased respiratory symptoms.

Lung function and weight gain in older children with mild CF lung disease. There are conflicting data regarding the potential for higher nontuberculous mycobacterial infection rates in individuals with CF on chronic azithromycin. There is insufficient evidence to recommend for or against the chronic use of azithromycin in preschoolers with CF. Table 1: Recommendation 26.

**Chronic *P. aeruginosa* Infection**

The use of cycled inhaled tobramycin for the management of infants, children, and adults with persistent *P. aeruginosa* infection has been
previously recommended. Additional inhaled antibiotics, such as aztreonam, also have been effective and safe in improving lung function and reducing exacerbations outside of the infant and preschool age range. Microbiologic efficacy and safety of inhaled tobramycin has been demonstrated in infants and young children. The use of alternate-month inhaled antipseudomonal antibiotics for preschoolers with persistent *P. aeruginosa* infection is recommended. Table 1: Recommendation 27.

**Staphylococcus aureus Prophylaxis and Eradication**

In keeping with previous guidelines, the prophylactic use of oral antistaphylococcal antibiotics is not recommended given the risk of increased *P. aeruginosa* isolation. Several studies have addressed the utility of eradication attempts after first acquisition of *S. aureus*, particularly methicillin-resistant isolates, but none have been randomized or focused on young children with CF. Prophylactic use of oral antistaphylococcal antibiotics is not recommended; evidence is insufficient to recommend for or against attempts to eradicate *S. aureus* and for chronic use of oral antistaphylococcal antibiotics in preschoolers with CF who persistently culture *S. aureus*. Table 1: Recommendations 28–30.

**Ivacaftor**

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. This therapy has recently been approved for use in patients with additional cystic fibrosis transmembrane conductance regulator (CFTR) gating mutations: G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R, and R117H. A forthcoming study in preschoolers has demonstrated safety of ivacaftor in the preschool-aged child. The availability of oral granules now allows for appropriate dose adjustment in young children. Monitoring of liver function abnormalities will be important. Based on data in older subjects, forthcoming safety data, and recent Food and Drug Administration approval for this age group, the use of ivacaftor for preschoolers with specific gating mutations and R117H is a consensus recommendation of this committee. Table 1: Recommendation 31.

**TABLE 3 Routine Monitoring and Nutritional Care of Preschoolers with CF**

<table>
<thead>
<tr>
<th>Every visit</th>
<th>Yearly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurement of height and weight, using Centers for Disease Control and Prevention growth charts, should be performed to assess weight-for-height and BMI must be evaluated in the context of the child’s height. Stunting is a risk in CF and can obscure nutritional risk in a child. Preschoolers with CF should maintain a BMI ≥50th percentile. Recommended monitoring of growth and nutrition in this age group is found in Table 3. Table 1: Recommendations 33.</td>
<td></td>
</tr>
<tr>
<td>Serums levels of fat-soluble vitamins. As appropriate</td>
<td></td>
</tr>
<tr>
<td>Referrals to community food resources (Supplemental Nutrition Program for Women, Infants, and Children; food stamps; food pantries). Information on nutrition resources via enzyme assistance programs.</td>
<td></td>
</tr>
</tbody>
</table>

**CLINICAL AND BEHAVIORAL NUTRITION AND GASTROINTESTINAL CARE**

**Nutrition**

Normal ranges of weight-for-age, height-for-age, and BMI percentile are associated with better pulmonary function, height closer to the 50th percentile for age and gender, and survival. A recent study demonstrated that weight-for-age ≥10th percentile for age and gender at age 4 years was associated with superior survival at 18 years. Therefore, it is recommended that weight-for-age of preschoolers with CF be maintained at ≥10th percentile. Table 1: Recommendation 32.

Assessment of measurement of height and weight, with calculation of BMI percentile using Centers for Disease Control and Prevention growth charts, should be performed to assess weight-for-height and BMI. Table 1: Recommendations 33.

Energy and protein requirements should be assessed in preschoolers with CF. Energy and protein recommendations of ≥90 to 110 kcal/kg per day, and protein intake based on dietary reference intakes and dietary guidelines recommend ≥13 g protein per day for children aged 2 to 3 years and ≥19 g protein per day for children aged 4 to 5 years to meet optimal nutritional thresholds. Table 4 outlines general energy guidelines by age and gender for preschoolers with CF. Table 1: Recommendation 34.

**Nutritional Risk**

Nutritional risk is defined as a BMI <50th percentile, or rate of weight gain <50th percentile expected for age (≥6 g per day), or weight-for-age <10th percentile, or inappropriate weight loss. Families of preschoolers with CF at nutritional risk and CF...
health care professionals should establish a multifaceted care plan that addresses medical, behavioral, and nutritional issues and schedule more frequent follow-up to ensure rapid establishment of normal growth. Interventions to improve nutritional status can be guided by the algorithm in Figs 2A, 2B, 2C, and 2D. Collaboration with a PCP or a visiting nurse to obtain weight and height measurement is an option for preschoolers needing more frequent evaluation. Table 1: Recommendations 35–36.

Increased energy intake results in improved weight gain; however, fewer data support improved height with increased energy intake.121,122 There is conflicting evidence regarding the use of nutritional supplements to increase energy intake.122,123 Oral supplements may be beneficial to preschoolers with CF at nutritional risk. Supplements may increase protein and energy at a time when eating behaviors may interfere with daily food intake. The use of supplements should be integrated with other nutritional and behavioral approaches for this age group. Families and CF health care professionals should be aware of the substantial impact of behavior on optimal nutrition.124–127 Children who continue to be at nutritional risk despite having addressed pulmonary, social, and dietary factors should be referred to pediatric gastroenterologists, endocrinologists, and behavioral specialists for further evaluation and management. Gastrostomy tube feedings have been shown in older children and adults with CF to improve weight and pulmonary function.128–131 Table 1: Recommendations 37–40.

Vitamins

CF-specific multivitamins are recommended, in a form that the child will best accept, and at recommended doses based on manufacturer guidelines.1 Patients with low serum levels of a specific fat-soluble vitamin(s) should continue to receive CF-specific multivitamins in addition to supplementation of the specific fat-soluble vitamin associated with low serum levels. Serum levels should be remeasured to ensure adequate response to therapy. Frequency of remeasurement should depend on the level of deficiency, the dose used for treatment, and the risk associated with deficiency or toxicity of the vitamin. Specific CF guidelines for vitamin D management are published132; there has been limited evaluation of the efficacy of these guidelines.133 Table 1: Recommendations 41–43.

Salt

Preschoolers with CF are advised to continue a high-salt diet, especially in the summer, and for those who live in warmer climates. For those who may not select foods with a high salt content, supplementation with at least one-quarter teaspoon of salt per day (581 mg sodium) may be necessary. Caregivers should be advised to avoid overuse of salt.134 Table 1: Recommendation 44.

Pancreatic Enzyme Replacement Therapy

For preschoolers with CF who are pancreatic insufficient (PI), consistent administration of the appropriate doses of pancreatic enzyme replacement therapy (PERT) is essential. Recommendations for PERT follow previous guidelines to ensure adequate digestion and avoid risk of fibrosing colonopathy.135 Evaluation of PERT dose and adherence should occur at each visit (Supplemental Table 4). Table 1: Recommendation 45.

Behavior

To meet growth goals, families of preschoolers with CF and health care professionals should establish individualized energy-intake goals and routinely monitor progress.10,136–139 Table 1: Recommendation 46.

In multiple studies, families consistently reported challenges with mealtime energy-intake goals due to demanding mealtime behaviors, leading to significant stress.8,9,124–127 These mealtime behavioral challenges can predict calorie intake and weight gain.140 Regular assessment for mealtime behavior challenges should be performed and proactive behavioral assistance should be provided when needed Table 5.10,136,137,141–143 Table 1: Recommendation 47.

CF health care professionals with appropriate training should provide behavioral therapy for preschoolers with CF at nutritional risk, exhibiting challenging mealtime behaviors, or not meeting energy-intake goals. Behavioral and nutrition treatment can lead to improvements in attaining energy-intake goals.10,136–140,143,144 Table 1: Recommendation 48.

Gastrointestinal

Conditions associated with abdominal pain may contribute to malabsorption,
FIGURE 2A
Nutrition algorithm: Tier One Initial Evaluation.
impaired quality of life, reluctance to perform airway clearance therapies, and loss of appetite in children with CF. In a large retrospective study of children with CF, abdominal pain frequency in children <6 years of age was no different from the general population. Abdominal pain should not be attributed to pancreatic enzyme dosing. If pain persists after assessment for common causes of abdominal pain in CF, or “red flag” symptoms, listed in Supplemental Table 5, are present, refer to pediatric gastroenterology.
Studies of preschoolers with CF have shown that constipation,\textsuperscript{146} distal intestinal obstruction syndrome,\textsuperscript{147} gastroesophageal reflux disease,\textsuperscript{148} small bowel overgrowth,\textsuperscript{149} and celiac disease\textsuperscript{150} can occur. Providing parents with a questionnaire directed at gastrointestinal symptoms can assist in detecting disease.\textsuperscript{151,152} CF health care professionals unfamiliar with the diagnosis and management of these conditions should refer the child to a pediatric gastroenterologist.

Table 1: Recommendations 49–50.

Children with CF who are pancreatic sufficient (PS) do not necessarily have normal
**BMI and Weight for Age:**
(Valid Measures Rely on Trained Staff using Accurate Scales and Stadiometers)

**FIGURE 2D**
Nutrition algorithm: BMI and Weight for Age.

<table>
<thead>
<tr>
<th>BMI ≥ 50th %tile AND Wt/Age &gt; 10th %tile AND gaining ≥ 5-8 gm/d</th>
<th>BMI &lt; 50th %tile AND Wt/Age &gt; 10th %tile</th>
<th>BMI &gt; 50th %tile AND w/t age &lt; 10th %tile</th>
<th>BMI &lt; 50th %tile AND Wt/age &lt; 10th %tile</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROUTINE NUTRITIONAL CARE</td>
<td>REQUIRES CAREFUL CLINICAL JUDGMENT, EVALUATING WT, HT, AND BMI %TILE TRENDS</td>
<td>REQUIRES CAREFUL CLINICAL JUDGMENT, EVALUATING WT, HT, AND BMI %TILE TRENDS</td>
<td>REQUIRES URGENT NUTRITIONAL INTERVENTION</td>
</tr>
</tbody>
</table>

**“Tiers” do not necessarily imply a single clinic visit; there may be multiple. However, it is not recommended to remain cycling through a single Tier for an extended period of time, specifically Tier One (as this will delay correction of poor growth). While there is no “set” time for Tier completion, efficiency is encouraged.**

**FIGURE 2D**
Nutrition algorithm: BMI and Weight for Age.

**PHYSICAL EXAM**
In addition to routine physical exam done by MD, include evaluation of and intervention for any findings that may be nutrition related. Examples of this may include but are not limited to: Hepato-splenomegaly Skin changes (zinc deficiency rash) Etc.

**DIET**
- Specific methods used to increase calories
- Inquire about activity level and sleep schedule
- Inquire if meals are lasting longer than 15 minutes
- Inquire if there are any behaviors of the child at mealtimes that make it difficult to meet energy goals

**DIET Intervention**
- Caloric Increase by 10-20% in incremental fashion
- Education on increasing caloric density of diet
- Education of outside care providers on nutrition needs (daycare, PS, etc)
- Oral nutrition supplements
- Food Records
- Appetite stimulant
- Zinc supplement 1 mg/kg/day Max: 25 mg/day
- Discuss possibility of need for tube feedings in future
- Evaluate for oral aversion

**SOCIAL/PSYCH**
- Refer to financial assistance programs
- Parental Depression Screen
- Assess patient for depression
- Evaluation of family dynamics including outside care providers
- Home visit
- BPHAS questionnaire

**STOOL/PERT**
- Stool/GI Hx: Frequency Consistency Color Evaluate for abdominal distention/ pain, constipation
- PERT adherence-giving with snacks/milk/supplements/
- Suboptimal PERT administration (e.g. chewing, other)
- Check storage of enzymes, expired enzymes, etc.
- Intervention: PERT Adjustment Maximize daily dose to 10,000 lipase units/kg/day
- Consider H2 blocker or PPI

**VIT/MIN**
- Evaluate dose of multivitamins
- Evaluation of adequacy of salt intake
develop.156, 157 These individuals which may take 1 to 3 years to will become vitamin B12 deficient, with resection of the terminal ileum in the terminal ileum. Individuals Vitamin B12 is absorbed exclusively Recommendation 52.

aware that pancreatitis can occur in preschoolers, providers should be recommended behavioral and nutrition treatment to improve energy intake and growth whenever possible. A treatment plan focused on increasing energy intake and improving growth in preschoolers with CF will likely be more successful with inclusion of evidence-based interventions that are part of behavioral and nutrition treatment.

the development of hematologic signs to screen for deficiency. Table 1: Recommendation 53.

UNANSWERED QUESTIONS
With few clinical trials evaluating monitoring, therapeutics, and nutritional care, determining care pathways for preschoolers with CF is challenging. Additional research on monitoring for lung disease in preschoolers to advance early detection and potentially improve outcomes is needed. MRI and other imaging modalities that avoid radiation exposure may hold promise for evaluation of early CF lung disease. MBW, after further validation, may become incorporated into clinical care. Therapeutic trials evaluating efficacy of chronic respiratory medications, including dornase alfa and HS, are important; increasing treatment complexity with additional therapies must be weighed against the potential of preventing irreversible damage. CFTR modulators are a potentially life-changing therapeutic strategy for CF. The recent approval of ivacaftor for preschoolers will hopefully allow for early disease prevention. As modulators and correctors are developed for other mutations, it is important to recognize the substantial benefits for the youngest patients. Gaps in nutritional, behavioral, and gastrointestinal studies in this age group remain. Additional research on timing of nutritional interventions and of the conversion from PS to PI is needed. Determining the prevalence of key gastrointestinal disorders is needed to assist providers with testing and diagnostic decisions.

CONCLUSIONS
The care of the preschool-aged child with CF includes complex, time-consuming treatment regimes and overcoming behavioral challenges common in this age group to maintain lung health and optimize growth. We hope that these guidelines will help CF care teams and families make informed decisions regarding care of the 2- to 5-year-old children with CF.

ACKNOWLEDGMENTS
The authors acknowledge Elaine Skopelja, Indiana University, for her assistance with the literature review.

ABBREVIATIONS
ACT: airway clearance therapy
BAL: bronchoalveolar lavage
CF: cystic fibrosis
CFTR: cystic fibrosis transmembrane conductance regulator
CT: computed tomography
FEV1: forced expiratory volume in 1 second
HS: hypertonic saline
LCI: lung clearance index
MBW: multiple-breath washout
OP: oropharyngeal
PCP: primary care provider
PERT: pancreatic enzyme replacement therapy
PI: pancreatic insufficiency
PICO: population, intervention, comparison, outcome
PS: pancreatic sufficiency

TABLE 5 Behavioral Assessment and Management of Mealtimes

Assessment of behavior at mealtimes
It is important to assess for a regular schedule of meal and snack times, for mealtime duration, and for child behaviors and family stress related to difficulties in meeting energy-intake goals and a balanced variety of foods.

Setting energy-intake goals
For families of preschoolers to succeed with meeting growth goals, it is important that energy-intake goals individualized to the child are set and then monitored in terms of progress.

Inclusion of behavioral expertise when evaluating concerns about growth
Whenever concerns with growth and/or family stress related to mealtimes (and with meeting energy-intake goals) are present, it is critical to consider a multidisciplinary approach to understanding the problem, developing a treatment plan, and assessing the success (or need to further modify) the plan. Inclusion of expertise in child behavior management and knowledge of the evidence-based behavioral and nutrition treatment is strongly recommended whenever possible.

Recommendation 51.
Fecal elastase is the simplest, most available screening test. Table 1: Recommendation 51.

Children with PS and CFTR mutations associated with milder disease are at risk for acute pancreatitis, which may lead to episodes of acute, recurrent, or chronic pancreatitis. Specific CFTR mutations cannot reliably predict which children will get pancreatitis. Acute pancreatitis is a potentially life-threatening disease associated with severe pain, nausea, and vomiting. Although infrequent in preschoolers, providers should be aware that pancreatitis can occur in preschoolers who are PS. Table 1: Recommendation 52.

Vitamin B12 is absorbed exclusively in the terminal ileum. Individuals with resection of the terminal ileum will become vitamin B12 deficient, which may take 1 to 3 years to develop. These individuals should be screened by using serum B12 levels or urinary methylmalonic acid. Providers should not wait for

pancreatic function. Over time, they may develop PI. Diarrhea is an unreliable indicator of PI. Poor weight gain or growth may be a late indicator of PI, and micronutrient deficiency may be present. Fecal elastase, 72-hour stool for fecal fat, and cholecystokinin/secretin-stimulated pancreatic function testing may be used to diagnose PI. Fecal elastase is the simplest, most available screening test. Table 1: Recommendation 51.

TABLE 5 Behavioral Assessment and Management of Mealtimes

Assessment of behavior at mealtimes
It is important to assess for a regular schedule of meal and snack times, for mealtime duration, and for child behaviors and family stress related to difficulties in meeting energy-intake goals and a balanced variety of foods.

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For families of preschoolers to succeed with meeting growth goals, it is important that energy-intake goals individualized to the child are set and then monitored in terms of progress.

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review and assisted with manuscript preparation and revision; Drs Brady, Schwarzenberg, and Rosenfeld reviewed selected articles, and each compiled and edited contributions for major sections of the manuscript and drafted sections of the manuscript; Drs Cannon, Condren, Guill, Guillerman, Powers, Tompkins, and Zemanick and Ms Clark, Ms Leone, Ms Maguiness, and Ms Monchil reviewed selected articles and contributed written sections to the manuscript; and all authors reviewed and approved the final manuscript as submitted.

DOI: 10.1542/peds.2015-1784

Accepted for publication Dec 29, 2015

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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

FUNDING: Funding was provided by the Cystic Fibrosis Foundation.

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 NebuSol. 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.

REFERENCES


16. Committee on Environmental Health; Committee on Substance Abuse; Committee on Adolescence; Committee on Native American Child. From the American Academy of Pediatrics:


43. Davis SD, Fordham LA, Brody AS, et al. Computed tomography reflects lower airway inflammation and tracks changes in early cystic fibrosis. Am J Respir Crit Care Med. 2007;175(9):945–950


46. de Jong PA, Ottink MD, Robben SG, et al. Pulmonary disease assessment...


52. De Boeck K, Alifi er M, Vandeputte S.


152. Brunner HI, Johnson AL, Barron AC, et al; Gastrointestinal symptoms and their association with health-related quality of life of children with juvenile rheumatoid arthritis. validation


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*Pediatrics* originally published online March 23, 2016;

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