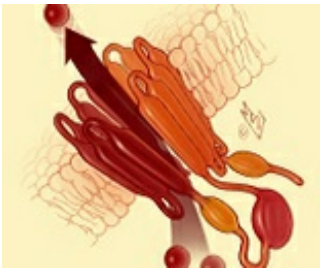
JOHNS HOPKINS MEDICINE
eLITERATURE REVIEW
Jointly provided by the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing
eCysticFibrosis Review
Vol 7: Supported by educational grants from Gilead Sciences, Inc., Vertex Pharmaceuticals Incorporated, AbbVie, Inc., and Chiesi USA, Inc.



New Guidelines in Nutritional Management for Patients with CF

Editor's Note: In our first newsletter/podcast on *CF Pulmonary Exacerbations: Known Unknowns?* learners were knowledgeable prior to the education. However, our post-assessment showed that **50%** of learners will make changes to their practice as a result of the education. We will report the results of issues 3 and 4 in an upcoming podcast.

In this Issue...

As the field of nutrition in cystic fibrosis evolves, new guidelines are needed to ensure that practitioners are provided up-to-date, evidence-based information, particularly in areas where no guidance existed.

In this issue, Amanda Leonard, an advanced nutrition practitioner from the Johns Hopkins Children's Center in Baltimore, reviews:

- the newly released CFF guidelines that provide recommendations for determining nutrition risk, intake, and interventions to promote successful outcomes in preschoolers with CF
- new guidance on enteral feeding that provides a clinical and educational pathway to guide clinicians, as well as patients and their families
- new research on the effects of a CFTR modifying agent (ivacaftor) on growth in prepubertal children with cystic fibrosis

Volume 7
Issue 5

Program Information
CME Information
Accreditation
Credit Designations
Intended Audience
Statement of Need
Internet CME/CE Policy
Faculty Disclosure
Disclaimer Statement

Length of Activity
1.0 hour Physicians
1.0 hour Nurses

Launch Date
May 23, 2017

Expiration Date
May 22, 2019

LEARNING OBJECTIVES

After participating in this activity, the participant will demonstrate the ability to:

- Describe the CFF Preschool Guidelines nutrition-related recommendations
- Discuss the guideline recommendations for enteral feeding
- Summarize the impact of ivacaftor on linear growth in prepubescent children

GUEST AUTHOR OF THE MONTH

Commentary & Reviews

Amanda Leonard, MPH, RD, CDE
Advanced Nutrition Practitioner
The Johns Hopkins Children's Center
Baltimore, Maryland

Guest Faculty Disclosure

Amanda Leonard has indicated that she has served as an advisor/consultant to Alcresta.

Unlabeled/Unapproved uses

Amanda Leonard has indicated that she has no financial interests or relationships with a commercial entity whose products or services are relevant to the content of this

COMPLETE THE POST-TEST

Click on link to download instructions for the post-test and evaluation

PHYSICIAN POST-TEST

NURSE POST-TEST

presentation.

IN THIS ISSUE

Program Directors

Peter J. Mogayzel, Jr., MD, PhD
Director, Cystic Fibrosis Center
Professor of Pediatrics
The Johns Hopkins University
Baltimore, Maryland

Noah Lechtzin, MD
Director, Adult Cystic Fibrosis Program
Associate Professor of Medicine
The Johns Hopkins University
Baltimore, Maryland

Suzanne Sullivan, RN, BSN
Senior Clinical Nurse
Johns Hopkins Hospital
Baltimore, Maryland

COMMENTARY

Nutrition and lung function are closely related in cystic fibrosis (CF), with better nutrition associated with better outcomes.[1-3] Clinicians strive to use the most current information when caring for people with CF, and new research findings provide insights into potential new ways to improve care for their patients. However, keeping up with current research and assessing when to implement changes can be a daunting task for a busy clinician. Guidelines are a means to critically review current research, determine recommendations based on existing data, and disseminate that information to the CF care community. As the field of nutrition in cystic fibrosis changes and evolves, new guidelines are needed to ensure that practitioners are provided up-to-date information. Adjusting clinical nutrition recommendations based on the guidelines may help provide better care and improve outcomes. In addition, guidelines frequently identify areas in need of future research; this research can then perpetuate the guidelines cycle of reviewing new data, updating guidelines, and improving care.[4]

Prior to the publication by Lahiri and colleagues (reviewed in this issue), nutrition guidelines for children with CF did not provide specific recommendations for issues frequently encountered in the preschool population.[5-6] Targeting nutrition in this population will potentially influence long-term outcomes, as weight for age at age 4 has been linked to survival at 18 years.[1] The recommendations for growth and intake specific to this age group will allow clinicians to appropriately assess and intervene for those at nutritional risk. The specific suggestions for determining nutrition risk, as well as steps to take to correct any nutritional concerns, provide valuable resources to use in a busy clinic setting. Another highlight is the recommendation to involve a multidisciplinary team that includes the patient and family. These guidelines promote early intervention, as well as an individualized approach to eating and behavior training. Clinicians can use this guidance to provide concrete recommendations for their preschool age patients. The algorithms provided will guide the team and suggest next steps when goals are not achieved.

Guidelines are often updated or revised as new information becomes available.[4] However, once treatment recommendations are published, it is not always clear if the benchmarks are being achieved in the CF community. The publication by Filigno and colleagues (reviewed in this issue), comparing the intake of a large group of preschool children to the new CFF preschool guidelines, provides novel information about preschool intake. The finding that preschool children may not be meeting their intake goals for fat and calories is helpful to the clinician and will allow for targeted assessment and intervention.

The group also found that protein intake was a significant predictor of height-for-age *z* score. This information highlights the importance of assessing protein intake in young children and can help guide the busy clinician. Information from this article can also be used to provide

targeted nutrition suggestions, including macronutrients goals, for preschoolers with CF. Additional studies of this nature will help inform future guidelines.

Enteral nutrition is another area in CF care that has not previously had detailed guidelines. The Cystic Fibrosis Foundation's evidence informed guidelines (Schwarzenberg et al, reviewed in this issue) provide recommendations for the entire enteral tube feeding process. The authors highlight the importance of patient and family involvement, education to better promote this involvement, and using a multidisciplinary team to provide the best care possible. Guidelines are provided for many aspects of care during the decision to have a tube placed, including placement of the tube and care after placement. These guidelines also provide a clinical and educational care pathway to guide the clinician and patient and family through the tube feeding process, providing tangible information to help clinicians and caregivers navigate this endeavor. However, many areas of care did not have enough research available to provide a specific recommendation—for instance, how to deliver enzymes with feeds and which formula to use. As previously stated, guidelines often bring to light unanswered questions and areas of further research. As new data becomes available, additional research will hopefully provide answers to these important questions.

New therapies also provide unanswered questions about care. Ivacaftor has been shown to improve nutritional status (weight and BMI).[7] Stavley and colleagues analyzed the impact of ivacaftor on linear growth (reviewed in this issue). Studies of this nature, looking at the impact of a drug on outcomes, are an important first step to developing guidelines. The authors postulate that there is an intrinsic defect in growth in children with CF that may be improved by CFTR modulation. The finding that linear growth, in addition to weight and BMI, is improved with ivacaftor may suggest that this group would benefit from different nutrition recommendations than those currently available for the CF population. As CF nutrition continues to evolve, it will likely be necessary to have mutation- or therapy-based nutrition recommendations.

The future of CF nutrition holds many exciting opportunities. The implementation of new guidelines will bring to light additional questions, highlighting where future research needs to focus to provide answers. As more data is collected, particularly about the impact of new therapies on nutrition and growth, new guidelines can then be developed and implemented to provide the best care possible.

References:

1. Yen EH, Quinton H, Borowitz D. Better nutritional status in early childhood is associated with improved clinical outcomes and survival in patients with cystic fibrosis. *J Pediatr.* 2013;162(3):530-535.
2. Konstan MW, Butler SM, Wohl ME, et al. Growth and nutritional indexes in early life predict pulmonary function in cystic fibrosis. *J Pediatr.* 2003;142(6):624-630.
3. Steinkamp G, Wiedemann B. Relationship between nutritional status and lung function in cystic fibrosis: cross sectional and longitudinal analyses from the German CF quality assurance (CFQA) project. *Thorax.* 2002;57:596-601.
4. *CFF Website, accessed 4/14/17*
5. Cystic Fibrosis Foundation, Borowitz D, Robinson KA, et al. Cystic Fibrosis Foundation evidence-based guidelines for management of infants with cystic fibrosis. *J Pediatr.* 2009;155(6 Suppl):S73-93.
6. Stallings VA, Stark LJ, Robinson KA, et al. Evidence-based practice recommendations for nutrition-related management of children and adults with cystic fibrosis and pancreatic insufficiency: results of a systematic review. *J Am Diet Assoc.* 2008;108:832-839.
7. Borowitz D, Lubarsky B, Wilschanski M et al. Nutritional status improved in cystic fibrosis patients with the g551d mutation after treatment with ivacaftor. *Dig Dis Sci.* 2016 Jan;61(1):198-207.

Back to top

Preschool Guidelines

Lahiri T, Hempstead SE, Brady C, et al. Clinical Practice Guidelines from the Cystic Fibrosis Foundation for Preschoolers with Cystic Fibrosis. *Pediatrics*. 2016 Apr;137(4). pii: e20151784.

View Journal Abstract View Full Article

These guidelines were developed by the Cystic Fibrosis Foundation (CFF) to provide guidance for the care of preschool age (2-5 years) children with cystic fibrosis (CF). The CFF convened a committee of 16 pediatric CF experts and parents to develop guideline recommendations for both CF clinicians and primary care providers (PCPs). The 53 recommendations were organized into four main topics: health maintenance; screening and monitoring; therapeutics; and nutrition, behavior, and gastrointestinal. This article highlights some of the 22 statements related to nutrition, behavior, and gastrointestinal topics.

Nutrition: The committee recommended that nutritional monitoring include measurement of height and weight, with calculation of BMI percentile using Centers for Disease Control and Prevention growth charts. Preschoolers with CF should maintain a weight for age at or above the 10th percentile and a BMI at or above 50th percentile. Intake recommendations include goals for energy (≥ 90 to 110 kcal/kg/day) and protein (≥ 13 g protein/day for children aged 2 to 3 years, and ≥19 g protein/day for children aged 4 to 5 years).

Nutrition Risk: The authors define nutritional risk for preschool children as one or more of: BMI < 50th percentile; rate of weight gain < 50th percentile expected for age (≥ 6 g/ day); weight for age < 10th percentile; or inappropriate weight loss. Lahiri and colleagues advise that children who continue to be at nutritional risk despite having addressed pulmonary, social, and dietary factors be referred to pediatric gastroenterologists, endocrinologists, and/or behavioral specialists for further evaluation and management.

Behavior: The committee recommends that mealtime behavior challenges be assessed and active behavioral assistance provided when needed. CF health care professionals with appropriate training should provide behavioral therapy for preschoolers with CF who are at nutritional risk, those exhibiting challenging mealtime behaviors, and/or those not meeting energy intake goals.

Gastrointestinal: Recommendations related to gastrointestinal issues include that all providers be aware of the presenting symptoms for gastrointestinal tract disorders, including constipation, gastroesophageal reflux disease, small bowel overgrowth, distal intestinal obstruction syndrome, and celiac disease. The authors recommend a referral to pediatric gastroenterology if pain persists after assessment for common causes of abdominal pain in CF, if red flag symptoms are present, or if the CF health care professionals are unfamiliar with the diagnosis and management of these conditions.

Main themes of the nutrition-related statements were early intervention and monitoring and an individualized approach to eating. Behavioral training for preschoolers was also emphasized. The committee developed a three-tiered algorithm to provide specific recommendations for nutrition evaluation and treatment. These guidelines will help guide caregivers and clinicians in their care of children ages 2-5 years.

Back to top

Nutrient Intake in Preschoolers

Filigno SS, Robson SM, Szczesniak RD. et al. Macronutrient intake in preschoolers with cystic fibrosis and the relationship between macronutrients and growth. *J Cyst Fibros*. 2017 Feb 6. pii: S1569-1993(17)30017-6.

View Journal Abstract View Full Article

This analysis — using data from an RCT involving children aged 2-6 years with CF and pancreatic insufficiency (PI) — compared the macronutrient intake of preschoolers with cystic fibrosis to the recently published Clinical Practice Guidelines from the Cystic Fibrosis Foundation (CFF) for Preschoolers with CF. The authors sought to describe the baseline dietary intake of preschoolers, compare that intake to new guidelines, and assess the relationship between macronutrient intake and growth. Seventy-five children who had at least three diet records at the baseline assessment were included in the analysis. Weight and height were measured at each visit.

The authors report that the mean age of children included in the analysis was 3.8 years. The cohort of 75 children had a baseline weight for age *z* score (WAZ) of - 0.41, height for age *z* score (HAZ) of - 0.51, and 44% had BMI < 50th percentile. Intake was assessed using a seven-day diet record. For the group the average intake was 35.3% fat, 12.7% protein, and 52% carbohydrates. All of the children met the CFF protein recommendations: 45% met the 110% recommended daily allowance (RDA) for calories recommendations; 53% met the recommendation for 35% of the calories from fat. Children with better BMI had higher intake.

Filigno and colleagues also evaluated macronutrient intake by meals. The investigators found that lunch and dinner had the highest percentage of fat intake, while snacks had a higher percentage of calories from carbohydrate and a lower percentage of energy from protein. When macronutrient intake and growth were assessed, it was noted that change in the percentage of energy from protein was a significant predictor of change in HAZ from baseline to posttreatment ($P < .001$). While change in percent energy from protein was not a significant predictor of change in WAZ over time, there was trend toward significance ($P = .08$).

The authors conclude that preschool children with CF may not be meeting benchmarks for fat and calorie intake. One suggestion to alleviate this issue would be to establish an approach to feeding during preschool years that involves monitoring, goal setting and feedback. Filigno et al also suggest refining nutrition recommendations to include tracking and monitoring macronutrients in addition to energy as a way to potentially improve intakes. Specifying recommendations with meal-targeted suggestions (ie, more protein at snacks and breakfast) could also help toddlers achieve the benchmarks for macronutrient intake.

Back to top

New Enteral Feeding Guidelines

Schwarzenberg SJ, Hempstead SE, McDonald CM, et al. Enteral tube feeding for individuals with cystic fibrosis: Cystic Fibrosis Foundation evidence informed guidelines. *J Cyst Fibros*. 2016 Nov;15(6):724-735.

View Journal Abstract View Full Article

The CF Foundation assembled a multidisciplinary team, including pediatric and adult clinicians, a parent of a child with CF, and a person with CF, to develop these 2016 enteral feeding guidelines for people with CF. A total of 33 guideline statements were developed in three main areas: shared decision-making, enteral feeding tube management, and management after placement. Highlights of the guidelines include:

The recommendation for enteral tube feeding as a means to improve nutritional status in people with CF who are not able to meet their nutritional needs by mouth after evaluation and intervention by a multidisciplinary team. The team should assess for causes of inadequate nutrition, including inadequate caloric intake, gastrointestinal and endocrine complications, pulmonary exacerbation, and behavioral and psychosocial factors. There is not sufficient data to recommend for or against enteral tube feeding to improve or stabilize pulmonary function in people with CF.

The recommendation for early introduction of enteral tube feeding as a potential treatment option to allow the patient and family to become comfortable with the available choices and to participate in the decision-making process. The authors highlighted education as an important aspect of the enteral feeding process to inform a pre-, peri- and postoperative clinical plan, as well as discharge needs. After home enteral feeding is established, education should continue to include care of the enteral feeding tube, problem solving, and required follow up. Schwarzenberg et al recommend that insurance coverage and out-of-pocket costs of enteral nutrition be explored well before enteral feeding tube placement.

Postoperative recommendations deal with airway clearance, pain management, and bowel regimen. The group recommended optimal postoperative pain management to facilitate reinitiation of airway clearance within 24 hours of feeding tube placement. Initiating a bowel regimen to prevent postoperative constipation or distal intestinal obstruction syndrome was also recommended.

In infants with enteral feeding tubes, the evidence-based guidelines for managing infants with CF should be followed to determine the type of feeding used. The guidance recommends continuous nocturnal infusion for individuals with CF who are receiving supplemental enteral tube feeding. The group does not recommend for or against the use of a specific type of formula (polymeric, semielemental, elemental) or a specific method of providing pancreatic enzyme replacement therapy for enteral tube feeding in individuals with CF (because of lack of data).

The guidance also recommends evaluation by a CF-trained registered dietitian/nutritionist (RDN) to calculate energy needs when enteral tube feeding supplementation is recommended, as well as to monitor growth, BMI, and tolerance of enteral tube feeding (to for allow changes if the person with CF is not meeting goals or is not tolerating the current regimen). Monitoring for the development of an oral aversion, disordered eating, or other related behavioral concerns was also noted as an important follow-up measure. The authors recommend that people individuals with CF who have had an enteral feeding tube placed be monitored at least annually by a gastroenterologist, in addition to their quarterly CF care center visit.

Main themes of the guidelines focus on the need for a multidisciplinary care team, which includes the patient and family, and the importance of education. The recommendations provide a clinical and educational care pathway to guide the clinician and patient/family throughout the enteral tube feeding process. Schwarzenberg and colleagues identified multiple areas, such as formula choice and enzyme administration, that lacked sufficient data to provide recommendations, and are areas where future research should be directed.

Back to top

Ivacaftor and Linear Growth In Prepubertal Children

Stalvey MS, Pace J, Niknian M, et al. Growth in prepubertal children with cystic fibrosis treated with Ivacaftor. *Pediatrics*. 2017 Feb;139(2). pii: e20162522.

View Journal Abstract View Full Article

In this post hoc analysis, Stalvey and colleagues investigated the impact of ivacaftor on growth in prepubertal children with cystic fibrosis. Ivafactor, a CF transmembrane conductance regulator (CFTR) potentiator, has been shown to improve lung function, weight, and body mass index, but no studies have looked at the impact of ivacaftor on linear growth in children with CF. The investigators hypothesized that targeting the biological defect in the CFTR protein may affect growth outcomes.

This study analyzed linear growth and weight in 83 children, ages 6-11 years, with one copy of the G551D *CFTR* mutation. Data from two clinical trials evaluating the effects of ivacaftor — the longitudinal-observation GOAL study and the placebo-controlled ENVISION study — were used. Prepubertal children were selected for assessment to avoid changes in growth due to pubertal influence.

In GOAL, height and weight were used to calculate *z* scores at baseline, 3 months and 6 months. Baseline growth velocity (GV) was calculated using registry data collected the previous year. Weight and height *z* scores were compared in ENVISION at baseline, 24, and 48 weeks. GVs for height (cm/year) and weight (kg/year) were assessed for the entire 48 weeks.

The 35 patients evaluated from the GOAL study showed a baseline height *z* score that was below average based on the Centers for Disease Control growth curves. A significant increase in height *z* score was observed at 6 months ($P < .05$). A significant increase in weight z-score was also noted at both 3 and 6 months ($P < .05$ and $P < .001$, respectively). Height GV showed a significant increase between 3 and 6 months ($P < .01$), and after 6 months of ivacaftor treatment weight GV was improved compared to results seen before enrollment ($P < .0001$).

The ENVISION study enrolled 48 prepubertal children. At baseline the height z score was average in the ivacaftor arm and below average in the placebo arm. In the ivacaftor arm a significant increase in the height *z* score was noted from baseline at both 24 and 48 weeks ($P < .01$ and $P < .001$, respectively). In the placebo arm there was a slightly positive but not significant change from baseline at 24 weeks; at 48 weeks a slightly negative but not significant change was reported. At baseline the weight *z* score in the ivacaftor arm was average and in the placebo arm was below average. Ivacaftor treatment was associated with a statistically significant increase in weight z score at both 24 and 48 weeks ($P < .001$ for both). Placebo subjects showed a significant decrease in weight *z* score at 48 weeks ($P < .05$). Patients in the ivacaftor arm showed significantly greater height and weight GV ($P < .05$ and $P < .001$, respectively).

The authors report that this study provides evidence that correcting the abnormally functioning CFTR channel is associated with improved linear growth. This concept also supports the hypothesis that defective CFTR function directly contributes to impaired linear growth in CF. Data presented by the authors provides evidence that improvements in linear growth and GV are seen after therapeutic intervention with ivacaftor in children with the G551D *CFTR* mutation; however the studies were not designed to specifically investigate this issue. Improvements are seen with weight gain as well as with improved pulmonary function, which could confound the influence of CFTR on linear growth.

Back to top

KEY TAKEAWAYS

- New CFF preschool guidelines provide guidance for assessing nutritional risk and providing calorie and macronutrient goals and interventions for preschool age children.
- New CFF enteral feeding guidelines provide guidance for clinicians and family before, during, and after enteral tube feeding placement.
- Post hoc analysis shows an improvement in linear growth of prepubescent children with cystic fibrosis on ivacaftor.

Back to top

IMPORTANT CME/CE INFORMATION

ACCREDITATION STATEMENTS

Physicians

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing. The Johns Hopkins University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Nurses

The Institute for Johns Hopkins Nursing is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation

CREDIT DESIGNATION STATEMENT

Physicians

eNewsletter: The Johns Hopkins University School of Medicine designates this enduring material for a maximum of 1.0 AMA PRA Category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Nurses

eNewsletter: This 1.0 contact hour Educational Activity is provided by the Institute for Johns Hopkins Nursing. Each Newsletter carries a maximum of 0.5 contact hour, or a total of 3 contact hours for the 6 newsletters in this program.

POLICY ON SPEAKER AND PROVIDER DISCLOSURE

It is the policy of the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing that the speaker and provider globally disclose conflicts of interest. The Johns Hopkins University School of Medicine OCME has established policies in place that will identify and resolve all conflicts of interest prior to this educational activity. Detailed disclosure will be made in the instructional materials.

INTERNET CME/CE POLICY

DISCLAIMER STATEMENT

STATEMENT OF RESPONSIBILITY

STATEMENT OF NEED

CONFIDENTIALITY DISCLAIMER FOR CME ACTIVITY PARTICIPANTS

INTENDED AUDIENCE

HARDWARE & SOFTWARE REQUIREMENTS

Respiratory Therapists For United States: Visit this page to confirm that your state will accept the CE Credits gained through this program.

POLICY ON SPEAKER AND PROVIDER DISCLOSURE

It is the policy of the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing that the speaker and provider globally disclose conflicts of interest. The Johns Hopkins University School of Medicine OCME has established policies in place that will identify and resolve all conflicts of interest prior to this educational activity. Detailed disclosure will be made in the instructional materials.

Respiratory Therapists For United States: Visit this page to confirm that your state will accept the CE Credits gained through this program.

This activity was developed in collaboration with DKBmed.

COMPLETE THE POST-TEST

Click on link to download instructions for the post-test and evaluation

PHYSICIAN POST-TEST

NURSE POST-TEST