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Gastrointestinal and Nutrition Implications in Cystic Fibrosis

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The management of cystic fibrosis (CF) care continues to evolve rapidly with new medications and treatments. The advancements in specialized CF care have added years of life as well as improved life quality for people with cystic fibrosis (pwCF). Currently, more than half of the CF population is over the age of 18 years. As life expectancy for CF increases, the importance of overall physical and mental health maintenance has received more attention. Medical nutrition therapy (MNT) for children and adults with CF has shifted away from the so-called "CF legacy diet" with high fat, high energy foods to higher quality, individualized dietary patterns. Despite considerable improvements in respiratory function for many pwCF, gastrointestinal (GI) complications and nutritional deficiencies may persist. Effective management of GI symptoms assists in achieving nutrition goals and improving quality of life in this patient population.

INTRODUCTION

Cystic fibrosis (CF) is a genetic, multi-organ disorder affecting nearly 40,000 children and adults in the United States (US) and an estimated 105,000 people across 94 countries worldwide.[1] Mutations in the CF transmembrane conductance regulator (CFTR) gene result in dysfunctional CFTR protein in the cell. Over 1,700 CF-causing CFTR mutations have been identified. Different mutations impact the production and function of the CFTR protein in a variety of ways, but the outcome is essentially similar for all mutations. Abnormally functioning CFTR protein limits chloride movement across cell surfaces, causing the presence of thick sticky mucus in the lungs, pancreas, liver, and GI tract resulting in significant morbidity and mortality.[1]

This review addresses practical nutritional guidance for pwCF as follows: 1) current recommendations in MNT in the era of CFTR modulator therapy and 2) management of common GI issues.

CFTR Modulator Therapy

The treatment and prognoses of pwCF have changed dynamically since the 2012 introduction of CFTR modulator therapy (CFTRm).[2] CFTRm can be "potentiators" (i.e., keeps the chloride channel open) or "correctors" (i.e., fixes the

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CFTR structure). These medications enable more normal chloride transfer across cell surfaces, thus treating the underlying causes of CF rather than just symptoms. At present, four CFTRm combinations are approved by the US Food and Drug Administration with more therapies under investigation (**see Table 1**).[3-7] As of 2022, 86% of adults and an increasing number of children with CF in the US are receiving CFTRm therapies.[2]

CFTRm improves or alleviates respiratory symptoms and may also improve non-respiratory symptoms associated with other organ systems in pwCF. Overall, median predicted survival for pwCF has increased while pulmonary exacerbations requiring intravenous antibiotics and lung transplants have decreased.[2] People with CF receiving CFTRm are leading longer and healthier lives. Reported pregnancies in women with CF doubled between 2019 and 2022.[2]

The percentage of underweight adults with CF declined to 4.4% in 2022. Conversely, >40% of adults with CF are now categorized using body mass index (BMI) as overweight (BMI between 25 to < 30 kg/m^2) with 12.8% classified as obese (BMI ≥ 30 kg/m^2).[2,8] MNT is evolving rapidly to individualize nutrition and dietary intervention for pwCF in the era of CFTRm.[9-11] An emphasis on a nutrient-rich, healthy diet is important to prevent obesity and associated co-morbidities. Despite advances in CF care and therapies, there remain pwCF with advanced lung disease as well as pwCF who are not eligible for, cannot access, or do not tolerate CFTRm.[2] Individualized nutrition therapies with the assistance of a dietitian with expertise in CF care must be employed to address specific needs for each pwCF in accordance with therapies received. [9-11]

Although pulmonary manifestations of CF respond well to CFTRm, pwCF continue to experience a high gastrointestinal symptom burden.[12] Common GI symptoms in pwCF, regardless of age, include constipation, bloating, distension, early satiety, abdominal pain, and gastroesophageal reflux disease (GERD). Symptoms can be chronic and can negatively impact nutritional status and quality of life.[2,12]

Historical Perspective

In the early days of treatment for CF, MNT aimed to control malabsorption and associated GI symptoms by limiting dietary fat intake.[13] Consequently, poor weight gain and growth stunting in children were common.[14] In 1988, an epidemiological study compared two accredited CF centers one in Canada (Toronto) and the other in the US (Boston).[15] The pwCF seen at the Canadian center received a more liberalized diet and pancreatic enzyme replacement therapy (PERT) regimen compared to those at the CF center in the US. As a result, the pwCF at the Canadian center were taller, weighed more, and had a survival advantage of nine years.[15]

With this substantial difference in survival, the nutritional guidance for pwCF shifted from a low-fat to a high-fat and high calorie diet (the so-called "CF legacy diet") to promote weight gain and to potentially extend survival. As a result, diet quality for pwCF received less attention. Subsequent dietary intake studies in pwCF indicated a reliance on energy-dense, nutrient-poor foods.[16,17]

Current Nutrition Guidance

No evidence exists that pwCF require routine modification from a healthy, well-balanced, age-appropriate diet although energy needs may vary.[9-11] A wide variety of culturally acceptable foods associated with positive health outcomes in the general population should be emphasized for pwCF.[10] It is reasonable to advise supplementation

Table 1. Current CFTR Modulators

CFTR Medication Brand	Chemical Name	Mechanism
Kalydeco® (Vertex)	Ivacaftor	CFTR potentiator for patients with *G551D* mutation
Orkambi® (Vertex)	Lumacaftor/ivacaftor	CFTR potentiator / corrector for patients with homozygous *F508del* mutation
Symdeko® (Vertex)	Tezacaftor/ivacaftor	CFTR potentiator / corrector for patients with homozygous *F508del* mutation, heterozygous *F508del* mutation / residual CFTR function
Trikafta® (Vertex)	Elexacaftor/tezcaftor/ivacaftor	CFTR potentiator / corrector for patients with at least one *F508del* mutation or 177 other mutations

with energy and/or protein dense foods and/or oral or enteral nutritional supplements as needed to achieve or to maintain normal growth in children and a normal BMI status in adults (18.5-24.9 kg/m^2).[10,18,19] High nutrient density oral supplements are listed in **Table 2**. The use of these supplements should be tailored to the individual's preferences, clinical status, nutritional needs, GI tolerance, and reimbursement options.[18]

Vitamins and Minerals

Malabsorption of fats in pwCF is associated with deficiencies in fat-soluble vitamins (A, D, E, and K), calcium, and zinc.[1] Most pwCF benefit from CF-specific vitamin/mineral supplementation (**see Table 3**).[20,21.]

All forms of multivitamin supplements designed for pwCF include vitamin K, but not all over-the-counter multivitamins do. Most CF specific multivitamin supplements contain zinc. No CF-specific multivitamins contain either calcium or iron. Initiation of CFTRm may impact vitamin/mineral absorption, but further data are needed. Annual serum levels for fat soluble vitamins are recommended to guide supplementation.[1,9,10,21]

Fiber

The dietary fiber intake recommended for the general population does not increase the risk of constipation, distal intestinal obstruction syndrome or other GI symptoms for pwCF. Low amounts of dietary fiber may increase the risk of constipation and abdominal pain. Increased fiber intake above usual guidelines may exacerbate GI symptoms such as constipation, gas, and bloating in some pwCF. Dietary fiber recommendations should be adjusted according to individual tolerance and GI symptoms.[10,11,21]

Sodium

Excessive salt loss in sweat can cause electrolyte imbalances and hyponatremia in pwCF, and growth failure in infants and children with CF.[19,21] Salt requirements are affected by physical activity, climate, and GI losses. The usual recommendation for pwCF is to eat salty foods and to use the saltshaker freely at meals and snacks.[1,9,10,21] Guidelines from Australia and New Zealand suggest salt (sodium) supplementation for all pwCF (up to 500-1000 mg sodium/day for infants, 1000 mg sodium/day for children, and 6000 mg sodium/day for adolescents and adults) to compensate for loss in sweat.[21] Individual requirements are guided by signs and symptoms of sodium depletion, exercise levels, and rate of sweat.[9,11,21]

Salt recommendations are being re-evaluated for pwCF who receive CFTRm as such patients may experience reduced salt and chloride excretion in their sweat. Decreased salt losses along with high salt intake may cause hypertension in some pwCF who use CFTRm.[9] Blood pressure should be monitored at all clinical encounters for pwCF.[9] Hypertension has been noted to range between 2.2 and 11.8% of adults with CF in the US, UK, and internationally.[2,21]

Salt recommendations may need to be modified on an individual basis, especially for pwCF who receive CFTRm or for individuals who are post-organ transplant and on immunosuppressive therapy.[9,10,11,21]

Adiposity

Nutritional quality of diet has been associated with body composition and clinical outcomes in adults with CF.[22] A significant, positive association has been observed between fasting blood glucose concentration and visceral adipose tissue.[23] Excess dietary sugar is significantly and positively associated with visceral adipose tissue in adults with CF.[24]

In pwCF, a normal BMI and body composition with sex- and age-appropriate fat mass and fat-free mass should be achieved and maintained to improve lung function and to prolong survival.[4,5,10,22] Obesity should be avoided as it is associated with an increased risk of hypertension, hypercholesterolemia, liver steatosis, and diabetes.[9,24,25] Gradual weight reduction is appropriate in cases of overweight or obesity.[10] Rapid or extreme weight loss should be discouraged for pwCF as there can be detrimental effects on pulmonary function.

The effect of CFTRm upon body weight and BMI varies according to the genetic variants of the individual with CF and the specific CFTRm prescribed. Increased weight gain and BMI in some pwCF have been documented with each of the CFTRm currently available, especially the triple combination elexacaftor/tezacaftor/ivacaftor.

Table 2. Examples of High Nutrient Density Oral Supplements

Manufacturer	Supplement
Abbott	Ensure®, Ensure Plus®, Pediasure®
Fairlife Elite	1.5 Core Power®
Kate Farms	Kate Farms Standard® and Peptide®
Nature's One	Pediasmart®
Nestle	Boost®, Boost Plus®, Boost VHC®, Boost Kid Essentials®, Nutren Jr®, Nutren 1.5®, Nutren 2.0®

Anticipatory MNT should be provided prior to starting CFTRm with discussions of possible weight gain and potential body image concerns.[9,10,11,25] Incorporation of healthy dietary patterns, and exercise routines should be encouraged.[9,10,11,21] Individualized advice and regular nutrition monitoring should continue as part of standard CF care across the lifespan.[9,10,11,21,25]

CF-Related Diabetes and Glucose Impairment

Current guidelines recommend screening pwCF for glucose intolerance and CF-related diabetes (CFRD) with annual oral glucose tolerance tests beginning at age 10 years if not previously diagnosed with CFRD.[24,25,26] The prevalence of CFRD is increased across the lifespan, reaching above 40% in pwCF ≥40 years.[2] Consultation with an endocrinologist who has expertise in CFRD is recommended.[9,11,21]

The primary nutrition goals for CFRD are to achieve and to maintain healthy weight and body composition with normalized blood glucose levels.[21,23,24,26]

Common Gastrointestinal Complications of Cystic Fibrosis

GI symptoms, including fecal straining, abdominal distension, and abdominal pain, are quite common in pwCF but often go unrecognized.[12] GERD with potential erosive esophagitis and aspiration have an estimated prevalence of 35% to 81% in pwCF.[27,28] Thus, GI disorders and its associated symptoms are a significant burden for pwCF (**see Table 4**).[12]

Mouth

The sense of smell is impaired in many pwCF due to inflammation of the olfactory cleft which is the predominant location of olfactory neurons. Thus, pwCF experience an impaired sense of taste which can decrease food enjoyment and caloric intake.[29] Factors such as oral aversion can lead to feeding problems and resultant weight loss common to many children with CF.[30]

Esophagus and Stomach

As food is masticated and passed into the esophagus, pwCF can experience GERD which leads to classic "heartburn" symptoms, increased cough, aspiration, and in severe cases, weight loss. GERD appears commonly in pwCF with up to 90% of patients potentially having associated symptoms.[31,32] Other esophageal diseases such as eosinophilic esophagitis (EoE) may be increased in pwCF compared to the general population, especially in the pediatric age group.[33,34]

Although GERD is common, it is unclear if acid suppression therapy, including proton pump inhibitor (PPI) therapy, is beneficial in pwCF. Gastroesophageal reflux of bacteria-containing gastric fluid due to aggressive acid blockage from PPI use may increase risk for pneumonia and CF pulmonary exacerbations.[35,36] It is unclear if anti-reflux surgery such as fundoplication is beneficial in reducing lung function decline in pwCF who have GERD, especially in children.[37] Adult pwCF have an increased risk of Barrett's esophagus.[38]

Gastric issues tend to be less concerning in pwCF compared to other aspects of GI physiology although gastroparesis and dumping syndrome can occur in this population. No increased risk of *H. pylori* infection is associated with pwCF.[39,40] Gastroparesis may be more common in pwCF although research studying this phenomenon has not been standardized.[41] Conversely, pancreatic enzyme replacement therapy (PERT) may be effective in slowing rapid gastric emptying (thus, reducing dumping syndrome risk) in pwCF via increasing levels of glucagon-like peptide 1 (GLP-1).[42]

Small Intestine

CFTR is present throughout the small intestine, and CFTR mutations impair transport of small intestinal fluid leading to inflammatory and obstructive intestinal mucous, similar to CF pathologic processes in the lungs.[43] As a result, malabsorption and symptoms of small intestinal bacterial overgrowth (SIBO) can occur. SIBO is common in pwCF presenting as abdominal pain, diarrhea, malabsorption, and distention.[44,45] PPI use may precipitate SIBO due to the associated lack of gastric acid production leading to overgrowth of pathogenic bacteria.[46] Antibiotics with enteral efficacy and minimal systemic absorption, such as rifaximin, can be used to treat SIBO.[47]

CF enteropathy is associated with enterocyte inflammation and probable intestinal dysbiosis which affects lung function through the "gut-lung axis."[48] CF enteropathy is associated with an elevated fecal calprotectin level, and adult patients with this disorder have a negative correlation between fecal calprotectin levels and pulmonary function. Exocrine pancreatic insufficiency (EPI), CFRD, and use of PPIs also are risk factors for CF enteropathy.[49] CF enteropathy is not a type of inflammatory bowel disease such as Crohn's disease, but use of azathioprine has been reported as effective for some pwCF with this disorder.[50]

Although seemingly unrelated, celiac disease (CD), an autoimmune disease of the small bowel associated with gluten exposure, has been noted in pwCF. Research suggests that CD may be more common in pwCF compared to the rest of the population.[51-53] The association between CF and CD is unclear, but the production of sticky, inflammatory mucous in CF and the increased response in inflammatory GI conditions such as CD suggest that changes in the intestinal microbiome to more pathogenic bacteria such as *Escherichia* coli may be causative.[34,51-54]

Diagnosis of CD in pwCF does not differ from the rest of the population. Typically, CD diagnosis requires tissue transglutaminase IgA antibody (TTG IgA) serum testing with or without confirmatory duodenal biopsies (depending on TTG IgA level of elevation).[55,56,57] The treatment of CD in pwCF is life-long adherence to a gluten free diet, and consultation with a dietitian who has expertise in CD is of paramount importance.[55,58]

Pancreas

The most well-known aspect of the GI tract in CF occurs with the pancreas in the setting of EPI; EPI is present in at least 85% of pwCF and presents as malabsorption, fat soluble vitamin insufficiency, and poor growth.[59] Additionally, EPI is associated with worse lung function outcomes long-term.[60] Due to CFTR malfunction, pwCF and EPI experience pancreatic ductal obliteration, pancreatic fibrosis, and pancreatic fatty infiltration.[61] Diagnosis of EPI for pwCF typically is made through testing of fecal elastase-1 levels.[62]

Treatment of EPI requires appropriate PERT, fat soluble vitamin replenishment, and adequate fat intake. Consultation with a dietitian with expertise in CF is essential.[10,63,64] **Table 5** describes typical PERT dosing.[65] No evidence exists for the timing of PERT dosing relative to intake, but PERT is commonly dosed immediately prior to the ingestion of fat-containing food or beverages. If meals are longer than 30 minutes, PERT can be dosed half at the beginning of the meal and the other half midway through the meal.[1] Excessive PERT dosing (≥10,000 lipase units/kilogram/day) is associated

Table 3. Potential Vitamin and Mineral Deficiencies in Cystic Fibrosis

1. **Fat-soluble vitamins: A, D, E, K**
2. **Iron**
3. **Sodium**
4. **Zinc**
5. **Calcium**
6. **Magnesium**
7. **Essential fatty acids**
8. **Water-soluble vitamins**

*Supplements are available in drops, softgels, chewables and gummies with variable vitamin D levels ranging from 19 mcg to 125 mcg per dose including MVW Complete Formulation®, MVW Modular Formulation® and DEKAsPlus®

Vitamin comparison chart available at:

https://mvwnutritionals-assets.s3.amazonaws.com/wp-content/uploads/2024/04/11111124/Vitamin-Comparison-Chart-4_11_2024-FINAL.pdf

(last accessed 30 Sept 2024)

with the rare but serious complication of fibrosing colonopathy.[66,67] It should be noted that pwCF with endocrine pancreatic sufficiency can develop associated endocrine pancreatic insufficiency or CFRD as pancreatic damage progresses.[65]

CFTRm has reversed EPI in young children with CF, but not in older pwCF, although this issue remains under investigation as recovery of pancreatic function after CFTRm may occur after several years. Currently, no evidence-based algorithms exist for adjusting PERT with CFTRm for pwCF.[68] Measurement of fecal elastase-1 after CFTRm initiation in young children or anyone suspected of a change in pancreatic status is clinically appropriate.[4,69]

Although less common than EPI, pwCF can develop pancreatitis (acute, acute recurrent, and chronic) in the setting of less severe CFTR genotypes. Pancreatitis also has been reported in the setting of CFTRm use in pwCF who have EPI. In such clinical scenarios, pancreatitis should be considered in pwCF presenting with severe abdominal pain.[70,71]

Terminal Ileum/Colon

The terminal ileum is the site of early manifestations of CF in the setting of meconium ileus occurring during infancy. Dehydrated and acidic mucous due to CFTR dysfunction can lead to abdominal distention, emesis, and GI obstruction in the neonatal setting.[72] Such patients typically are diagnosed by barium enema in which the obstruction is noted,

Table 4. Common Nutrition and GI Disorders in CF and Potential Therapy

Nutrition/GI Disorder	Possible Therapies
Vitamin / mineral deficiency risk	• Supplementation and monitoring
Fiber	• Same use as general population
Essential fatty acid deficiency	• Serum fatty acid profile with triene:tetraene ratio monitoring, adjust PERT, EFA supplementation with absorbable structured lipid (Seracal™)
Sodium	• Increased salt use need compared to general population
Adiposity	• Prevention of underweight/overweight over time
CFRD	• Annual oral glucose tolerance test • Insulin/consultation with endocrinology
Esophagus (GERD, EoE, Barrett's esophagus)	• PPI use, therapies for EoE • Consider upper endoscopy with biopsy
Stomach (gastroparesis, dumping syndrome)	• Treatments for gastroparesis (prokinetics, pyloric botulinum toxin) • Treatments for dumping syndrome (PERT, dietary changes)
Small intestine (SIBO, CF enteropathy, celiac disease)	• Judicious enteral antibiotic use • Judicious PPI use • TTG IgA antibody titer • Upper endoscopy with biopsy
Pancreas (EPI, pancreatitis)	• Treatments for EPI (PERT, fat soluble vitamin supplementation, appropriate fat intake) • Treatments for pancreatitis (diagnostic amylase/lipase, diagnostic imaging including abdominal ultrasound or magnetic resonance cholangiopancreatography) • Typical medical/surgical treatments for pancreatitis, as warranted
Terminal ileum (meconium ileus, DIOS)	• Hyperosmolar enemas • Surgical intervention if warranted
Colon (constipation, increased colon cancer risk)	• Laxative therapy • Early colon cancer screening
Gallbladder (delayed emptying, cholelithiasis)	• Cholecystectomy if warranted
Liver (CFLD spectrum)	• Screening for progression of liver disease • Consultation with hepatology /liver transplant program if warranted

Table 5. PERT Dosing Guidelines

Age	Range	Upper Limit
Infants	1000-2500 lipase units/kg/feed	10,000 lipase units/kg/day
1-4 years	1000-2500 lipase units/kg/meal*	10,000 lipase units/kg/day
4+ years	500-2500 lipase units/kg/meal*	10,000 lipase units/kg/day

**Snack dose is half of a meal dose*

and many of these neonates with CF will have an associated microcolon due to ileal blockage and colon disuse. Treatment is urgent removal of the obstruction either through the use of hyperosmolar enemas observed by fluoroscopy for stable infants or surgical intervention in unstable infants or infants who do not respond to enema therapy.[73,74]

Distal intestinal obstructive syndrome (DIOS) may manifest after the neonatal period and potentially can occur at any stage in life in pwCF. Fecal obstruction of the terminal ileum and colon occurs with DIOS and presents with severe constipation, signs and symptoms of a bowel obstruction, and a palpable right lower quadrant mass that can be demonstrated radiographically.[75] Most cases of DIOS can be managed by high-volume osmotic therapy (such as with polyethylene glycol 3350) with surgical intervention required for severe cases. Constipation prevention via routine use of osmotic laxatives, especially polyethylene glycol 3350, is critical in reducing risk of DIOS in pwCF.[76,77]

Constipation, associated with hard stools, abdominal distention, and pain with defecation, is extremely common in pwCF affecting up to 41%.[78,79] Such patients have associated prolonged colonic transit time.[78] Treatment is supportive using osmotic laxative therapy (typically daily polyethylene glycol 3350).[77] Fiber intake in line with the dietary reference intake for the general population and adequate hydration are recommended for pwCF for the prevention and management of constipation.[10]

The risk of colorectal cancer in adults with CF is 5-10 times greater than the general population and is even higher in pwCF who receive a lung or other solid organ transplant.[80] Colonic adenomas with the risk of malignant transformation occur in pwCF at a younger age compared to the general population.[81] It is recommended that pwCF undergo screening colonoscopies no later than 40 years of age with repeat screening every 5 years. Such patients should undergo screening within 3 years if adenomas are noted.[82] If a pwCF has undergone a solid organ transplantation, they should undergo screening at age 30 years if they are within 2 years of transplantation.[82]

Gallbladder and Liver

Abnormal gallbladder anatomy such as micro-gallbladder formation occurs in pwCF. Delayed gallbladder emptying and cholelithiasis (typically black pigmented stones from bile acidification) are common in pwCF.[83] Most pwCF who have gallbladder abnormalities require simple observation over time, although cholecystectomy is warranted for symptomatic cholelithiasis.[83,84]

Liver manifestations in pwCF are defined as "cystic fibrosis-related liver disease" (CFLD), occurring in up to 30% of pwCF.[82,85] CFLD is caused by CFTR mutations which decrease bile transport disrupting the intestinal microbiome changes leading to hepatic inflammation. Risk factors for CFLD include male sex, history of meconium ileus, and history of EPI.[85,86] CFLD can vary from rare entities (neonatal cholestasis and sclerosing cholangitis) to more common presentations (steatosis). Hepatic fibrosis in pwCF can progress over time from focal biliary cirrhosis to multinodular biliary cirrhosis with associated portal hypertension and potential liver failure.[87-90]

Treatment of pwCF with CFLD requires optimizing nutrition status, including normal weight and muscle stores, and appropriate vitamin and mineral stores, in a manner necessary for all pwCF, and treating end-stage complications of liver disease such as treatment of portal hypertension and potential liver transplantation.[90] It is unclear if ursodeoxycholic acid use in pwCF with associated CFLD prevents progression to more severe liver disease.[91]

CONCLUSION

As the future for many pwCF anticipates less severe respiratory disease, longer lifespan, and less risk of undernutrition, more attention should be focused on preventive health management.[92] Many challenges remain for both clinicians and pwCF to achieve optimal nutrition in an era of CFTRm.[9,10,11,20,92] Not all pwCF are eligible for CFTRm, and some pwCF still face severe respiratory disease and many GI complications.[2] Some individuals are at risk of malnutrition with increased medical needs, especially pwCF not eligible for CFTRm. Others are at risk of overweight/obesity and associated metabolic and cardiovascular complications as well as oncological sequelae such as colon cancer.[92]

As described above, pwCF now are at an increased risk of major adverse cardiovascular events with associated obesity, diabetes, and hypertension.[19] In aging CF populations, individualized nutritional interventions, adequate hydration, and physical activity should aim to improve fat-free mass or to prevent its loss.[9,10,11,20,92]

Historically, these long-term complications were infrequently described due to the shortened life span for most pwCF. In the era of CFTRm, specific metabolic and cardiovascular screening programs need to be established. In the absence of specific recommendations for pwCF, standard screening guidelines for the general population should be employed.[9,10,11,20,92]

The future health of children and adults with CF, whether receiving or not receiving CFTRm, benefit from individualized MNT and GI management conducted in collaboration with pwCF, their family, and the entire healthcare team. Nutritional management for infants, children, and adults with CF continues to evolve but remains essential for optimal outcomes for all pwCF. ■

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Answers to this month's crossword puzzle:

1 C	H	2 O	L	3 A	N	4 G	I	5 T	I	6 S	■	7 V	A	8 S
I	■	P	■	C	■	O	■	W	■	E	■	E	■	T
9 R	E	S	E	C	T	■	10 M	O	S	Q	U	I	T	O
R	■	■	■	E	■	■	A	■	■	U	■	N	■	M
11 H	E	12 A	L	S	■	13 D	Y	14 S	15 P	E	16 P	S	I	A
O	■	L	■	17 S	18 I	R	■	19 P	I	N	E	■	■	■
20 S	I	T	E	■	21 C	E	L	I	E	C	T	22 O	23 M	24 Y
I	■	E	■	25 S	O	S	■	L	■	I	■	26 B	M	I
27 S	28 T	R	A	I	N	S	■	29 L	I	N	K	S	■	E
■	O	■	■	E	■	■	■	■	■	G	■	T	■	L
30 R	O	31 T	A	V	I	32 R	U	S	A	■	33 B	A	N	D
E	■	Y	■	E	■	A	■	■	■	34 C	■	C	■	■
35 N	E	P	H	R	I	T	I	36 S	■	37 O	S	L	E	38 R
I	■	E	■	T	■	I	■	O	■	A	■	E	■	N
39 N	E	O	N	■	40 C	O	L	O	P	T	O	S	I	S