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Cystic Fibrosis and Nutrition Risk

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by

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Abstract:
Introduction: Cystic Fibrosis (CF) is an autosomal recessive disorder with serious pulmonary and nutritional implications. Nutrition status has a direct affect on lung function and longevity. Screening patients for growth velocity makes it possible to identify patients at nutritional risk. This identification is the first step towards appropriate nutritional interventions. The current screening tool used for children and adolescents with CF is not reliable and leaves too much room for clinical judgment. It is for this reason that a new screening tool was developed. Methods: The Cystic Fibrosis Foundation established a panel of experts for the purpose of developing an evidence based screening tool to be used for children and adolescents with CF aged 2 to 20 years. Catherine McDonald, PhD, RD, was then given the responsibility to develop the actual tool and solicit feedback from other clinical nutrition experts. This feedback included a qualitative feedback questionnaire and a validation survey. The qualitative comments were used to edit and revise the tool. The revised tool went through a validation process which included three phases. The final draft was then created and validated. Results: The qualitative feedback questionnaire showed that clinicians felt the proposed nutrition screening tool was capable of accurately reflecting nutrition risk most of the time to some of the time. The validation study was still underway at the time this paper was written. Conclusion: The new screening tool for children and adolescents with CF will be a reliable, valid, and useful tool. It is anticipated that because clinical nutrition professionals have been involved in the development process, the screening tool will be widely accepted and used. This would make it an integral part of the treatment process for children and adolescents with CF aged 2 to 20.

Introduction:

Normal growth is the goal for all patients with CF. These individuals often experience nutritional inadequacy resulting in impaired growth, suboptimal lung function, and decreased longevity. (1,2) It is for these reasons that early identification of nutritional inadequacy and intervention are needed. Nutrition screening is the first step in the identification process.

The Cystic Fibrosis Foundation (CFF) recommends that patients with CF be seen on a routine basis, every 3 months. The CF care team has the potential of having a powerful and positive effect on appropriate growth and lung function. Patients' growth is monitored and recorded at each visit. This facilitates the identification of suboptimal growth and supports the provision of anticipatory counseling. Monitoring growth helps identify CF patients at nutrition risk. It also helps facilitate early intervention and the prevention of further decline. (1)

An effective nutrition screening tool has 5 characteristics. (3) It must be applicable to the patient being screened. It is important that the nutrition screening can be accomplished quickly and be able to provide readily available information. Reliability and validity are crucial characteristics. The tool must be capable of assigning levels of nutrition risk consistently to patients based solely on risk factors and established parameters. This should occur independent from the clinician administering the screen.

The most current screening tool used for children and adolescents with CF was not reliable and many felt it left too much room for clinical judgment. Another concern was the terminology used by the tool when assigning nutritional status. Patients were labeled as being "acceptable", "at-risk", or "nutritional failure". (See Figure 1) It is for

these reasons that a new screening tool was developed. The CFF sponsored efforts to produce a new and improved nutrition screening tool for children and adolescents with CF aged 2 to 20 years. (1)

Figure 1 (1)

Nutritional status	Length or height	Percentage IBW[1] All ages	Weight-for-length percentile[2] 0 to 2 years	BMI percentile[3] 2 to 20 years	Action
Acceptable	Normal growth	≥90%	>25th	>25th	Continue to monitor with usual care
At-risk[4]	Not at genetic potential	≥90%, with weight loss or weight plateau[5]	10 to 25th	10 to 25th	Consider nutritional and medical evaluation; some but not all patients in this category are at risk for nutritional failure
Nutritional failure	<5th ile	<90%	<10th	<10th	Treat nutritional failure

1. From References 6 and References 7
2. From 2000 NCHS/CDC growth charts (weight for length) available for children, ages 0 to 2 years.
3. From 2000 NCHS/CDC growth chart, available for children and adolescents, ages 2 to 20 years.
4. Delayed puberty should also be considered a marker of patients at risk for nutritional failure (no breast development past age 13 in girls; no menarche by age 16 or more than 5 years after the start of breast development in girls; no testicular enlargement or genital changes by age 14 in boys).
5. Weight plateau is defined as no increase in weight for >3 months in a patient under 5 years of age, or no increase in weight for >6 months in a patient over 5 years of age.

This paper will explain the development process of the new proposed screening tool. It will also provide an overview of the genetic etiology and pathophysiology responsible for the development of CF. Nutrition complications and recommended interventions will be included which support the necessity of an accurate and valid nutrition screening tool.

Methods:

The Cystic Fibrosis Foundation established a panel of experts for the purpose of developing an evidence based screening tool to be used for children and adolescents with CF aged 2 to 20 years. Catherine McDonald, PhD, RD, was then given the responsibility to create a screening tool based on the literature and parameters agreed upon by the committee. She was responsible to create and format the actual nutrition screening tool and then solicit feedback from other clinical nutrition experts for further refinement.

A team of pediatric dietitians at Primary Children's Medical Center participated in a trial of a preliminary screening tool. The dietitians used the nutrition screening tool

to screen six case studies for nutrition risk. There was a 92.1% agreement of assigned nutrition risk. This exercise was useful because it revealed weaknesses in the tool and pointed to areas requiring further clarification. This trial made significant contributions to the development of the nutrition screening tool.

Revisions were made and the tool was distributed to 17 pediatric dietitians throughout the United States. The team consisted of pediatric dietitians involved in the provision of nutrition care for pediatric patients with CF. These nutrition professionals were asked to use the screening tool on 5 to 10 patients and then report on their experience through a qualitative feedback questionnaire.

The participating clinicians reported that it took an average of 5 minutes to complete the screening process per patient. They also reported that they felt it was capable of accurately assessing and reflecting the nutrition risk of CF children and adolescents most of the time to all of the time. Additional comments and suggestions were solicited and encouraged. They were then used to edit and revise the nutrition screening tool.

A new version was then distributed to the same 17 pediatric dietitians. They used this draft to screen four case studies. Three of the four case studies had an agreement of 100% for assigned nutrition risk. The fourth had an agreement of 71%. This error helped identify additional revisions necessary to ensure reliability and validity.

The screening tool was then edited and revised producing a final draft. The proposed nutrition screening tool (figure 2) and an algorithm representing the methodology (figure 3) were included on the following pages. The final draft and 18 case studies were distributed to a new set of 7 registered dietitians.

Patient Name: _____ Gender: ____ Age: ____ yr ____ mo ____

Tanner Stage: _____ if > 9 years (F) and > 10 years (M)

Weight for stature

Determine current **BMI percentile for gender & age** (CDC BMI chart): _____

Weight velocity

Current wt (kg): _____ Date: _____

Wt (kg) last clinic visit : _____ Date: _____

Net change in wt: _____

Number of days between weights: _____

Daily wt gain (gm/day)_____ **(Round to nearest whole integer)**

Expected weight gain per day (gm/day)_____

Height velocity

Current Ht (cm):_____ Date:_____

Ht (cm) ≥ 1 year; ≤ 2 yr prior to current visit:_____ Date:_____

Net change in ht: _____

Number of years between height measurements _____

Annual height gain (cm/year) _____**(Round to nearest whole integer)**

Expected height gain per year (cm/year) _____

Expected Daily Weight Gain and Annual Height Gain

Minimally acceptable rate of weight and height gain when **BMI is equal to or greater than 50th percentile**.

Average rate of weight and height gain at the 10th percentile				
	DAILY WEIGHT GAIN (gm/d)		ANNUAL HEIGHT GAIN (cm/yr)	
Age, y	Males	Females	Males	Females
2.0-2.99	3	3	7	7
3.0-3.99	3	3	6	6
4.0-4.99	3	2	5	5
5.0-5.99	3	2	5	5
6.0-6.99	3	2	5	5
7.0-7.99	3	3	4	4
8.0-8.99	3	3	4	4
9.0-9.99	2	3	4	4
10.0-10.99	3	3	4	4
11.0-11.99	3	4	4	4
12.0-12.99	4	1	4	3
13.0-13.99	4	<1	4	1
14.0-14.99	4	<1	3	<1
15.0-15.99	<1	<1	1	<1
16.0-16.99	<1	<1	<1	<1
17.0-17.99	<1	<1	<1	<1
18.0-18.99	4	2	.5	.1
19.0-19.99	3	1	.2	.1

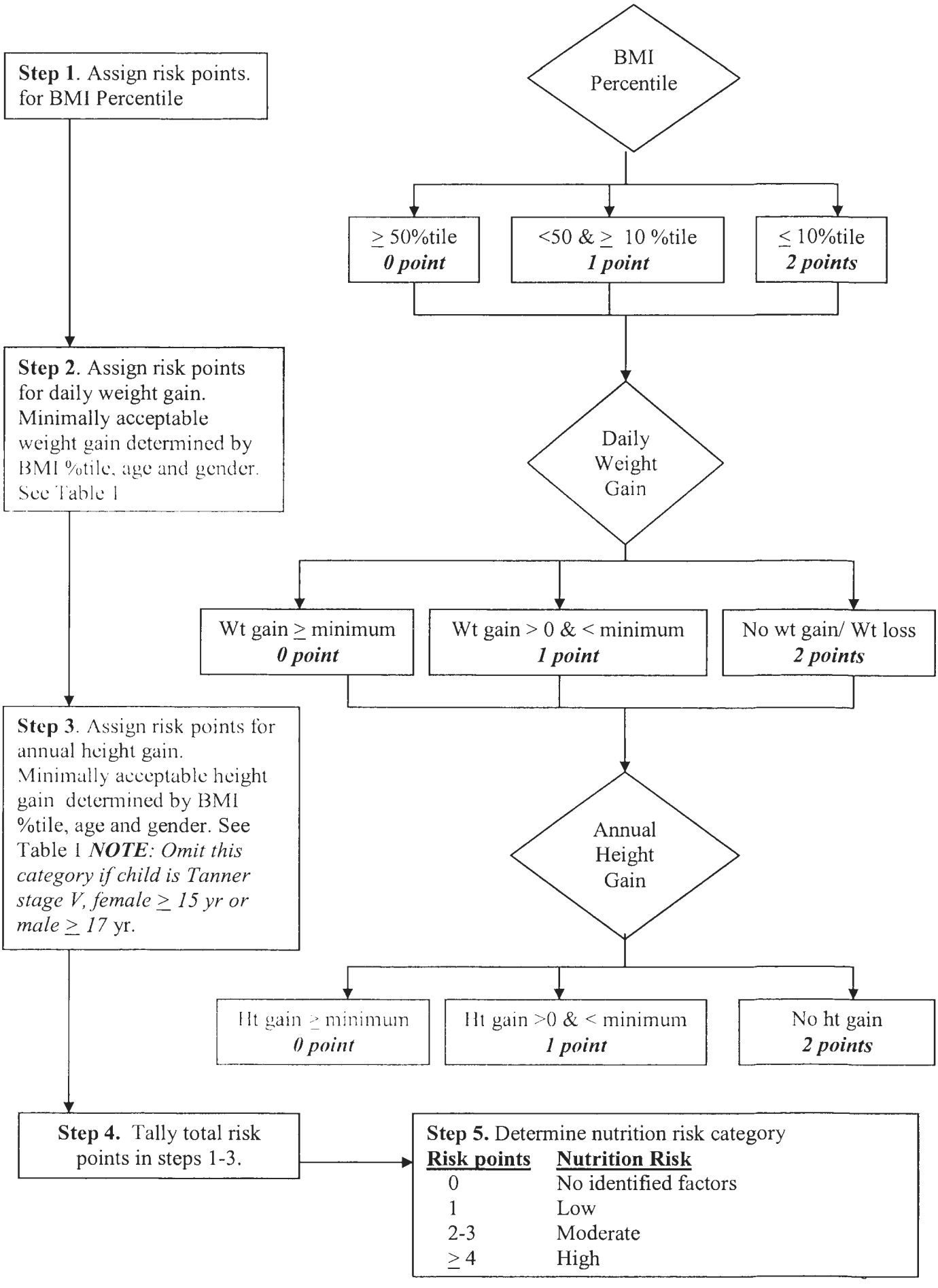
Minimally acceptable rate of weight and height gain when **BMI is less than 50th percentile**.

Average rate of weight and height gain at 50th percentile				
	DAILY WEIGHT GAIN (gm/d)		ANNUAL HEIGHT GAIN (cm/yr)	
Age, y	Males	Females	Males	Females
2.0-2.99	5	5	9	9
3.0-3.99	5	5	7	8
4.0-4.99	6	5	7	7
5.0-5.99	7	6	7	7
6.0-6.99	7	7	6	6
7.0-7.99	8	7	6	6
8.0-8.99	8	8	6	6
9.0-9.99	9	8	5	6
10.0-10.99	9	11	5	6
11.0-11.99	11	14	5	7
12.0-12.99	15	14	6	6
13.0-13.99	18	11	8	3
14.0-14.99	19	7	7	2
15.0-15.99	13	4	4	1
16.0-16.99	8	4	2	<1
17.0-17.99	5	2	1	<1
18.0-18.99	5	3	.4	.1
19.0-19.99	4	3	.2	.1

Nutrition Risk:

	0 Points	1 Point	2 Points
BMI Percentile	≥ 50%tile	<50 & ≥ 10 %tile	≤ 10%tile
Daily Weight Gain	≥ minimum	> 0 & < minimum	No wt gain/ Wt loss
Annual Height Gain	≥ minimum	>0 & < minimum	No ht gain
Total Points:	**Nutrition Risk:**		

Figure 2. Proposed Nutrition Screening Tool for Children and Adolescents aged 2 to 20.


Step 1. Assign risk points. for BMI Percentile
BMI Percentile
≥ 50%tile
0 point
<50 & ≥ 10 %tile
1 point
≤ 10%tile
2 points
Step 2. Assign risk points for daily weight gain. Minimally acceptable weight gain determined by BMI %tile, age and gender. See Table 1
Daily Weight Gain
Wt gain ≥ minimum
0 point
Wt gain > 0 & < minimum
1 point
No wt gain/ Wt loss
2 points
Step 3. Assign risk points for annual height gain. Minimally acceptable height gain determined by BMI %tile, age and gender. See Table 1 NOTE: Omit this category if child is Tanner stage V, female ≥ 15 yr or male ≥ 17 yr.
Annual Height Gain
Ht gain ≥ minimum
0 point
Ht gain >0 & < minimum
1 point
No ht gain
2 points
Step 4. Tally total risk points in steps 1-3.
Step 5. Determine nutrition risk category
Risk points Nutrition Risk
0 No identified factors
1 Low
2-3 Moderate
≥ 4 High

Results:

The qualitative feedback questionnaire showed that clinicians felt it was capable of accurately reflecting nutrition risk most of the time to some of the time. The validation of the final draft had not been completed when this paper was written.

Discussion:

Cystic fibrosis (CF) is the most common autosomal recessive disorder affecting the Caucasian population. It affects 1 in 2,500 live births. The median life expectancy for those affected with this disease is 35.2 years. The first publication in the United States describing CF was in 1938, and the underlying genetic basis was not presented until 1989. CF is caused by genetic mutations in the cystic fibrosis tansmembrane regulator (CFTR) gene which results in defective chloride channels, causing the formation of excessive mucous in the lungs and the gastrointestinal system. This mucous has several nutrition related consequences, such as, nutrient malabsorption and malnutrition, fat soluble vitamin deficiency, osteoporosis, CF related diabetes, impaired lung function, decreased quality of life, and early death. (2)

Genetic Etiology:

CF is an autosomal recessive disease. It results from a mutation in the cystic fibrosis tansmembrane regulator (CFTR) gene. The CFTR gene is a single large gene located on chromosome 7q. It encodes for the CFTR protein. This protein is composed of 1480 amino acids. It functions as an integral part of chloride channels located on the surface of epithelial cell membranes. These cAMP regulated channels assist in the regulation of chloride and sodium transport. (2,4)

CF is due to a mutation or mutations in the CFTR gene. There have been more that 1200 sequence changes identified which result in clinical disease. The type of sequence change and resulting genetic mutation dictates the severity of the disease. There are four classes of CFTR gene mutations:

1. Defective protein production: Premature termination of the mRNA can result from a splice-site, frameshift, or nonsense mutation. The result is a complete absence of the CFTR protein.
2. Defective protein processing: The CFTR protein is unable to locate and attach to the correct cellular location.
3. Defective regulation: The protein has decreased channel activity in response to ATP.
4. Defective conduction: The protein is produced and attached correctly to the cell surface. Chloride currents are generated in response to cAMP stimulation. The mutations cause a reduction in the rate of ion flow and the duration of channel opening. (4)

Pathophysiology:

The exocrine glands are most affected by the genetic mutations in the CFTR protein. Altered sodium and chloride channel regulation leads to abnormal physical and chemical secretions. This abnormality manifests itself in the respiratory tract, sweat and salivary glands, pancreas, intestine, liver, and reproductive tract. These systems produce abnormally thick mucus which obstructs glands and ducts.

Impaired lung function is one of the biggest obstacles patients with CF face. Malfunctions in the CFTR protein result in defective cAMP dependent chloride secretion

from the respiratory epithelium. This failure of CFTR-mediated regulation of chloride channel activity leads to increased airway lumen absorption of sodium. The result is an alteration in airway secretions, which are thick and difficult to clear.

In addition to congestion, the high chloride concentration of epithelial secretions may also leave the patient more susceptible to infection with unique bacteria. Pseudomonas aeruginosa, Haemophilus influenzae, and Staphylococcus aureus species are some of the most commonly observed infections. This increased risk of infection is thought to be due to the dependency of neutrophils and beta-defensins on normal chloride concentrations. (4)

Abnormal inflammation is another pulmonary related issue experienced by patients with CF. The CFTR-expressing tissue from patients with CF has been analyzed. Researchers have found that these tissues have altered fatty acid metabolism. The result is elevated arachidonic acid and its metabolites. It is thought that these may contribute to the abnormal inflammation which is characteristic of CF. (5)

In addition to pulmonary complications, CF patients often experience malfunction within their digestive system. The thick mucus acts as a plug preventing and limiting pancreatic secretions into the small intestine. The blockage decreases the amount of pancreatic enzymes which are able to reach the small intestine, causing enzyme insufficiency and maldigestion of food. The ultimate result is malabsorption and malnutrition. It is estimated that 85% to 90% of the CF population experiences pancreatic insufficiency. (1,2)

Proper management of gastrointestinal and pulmonary symptoms makes normal weight and/or growth status achievable for individuals with CF. Another important

factor which helps support appropriate growth is adequate nutrient and energy intake. There are also psychosocial and financial issues which must be properly managed. Malnutrition is observed when there is a discrepancy between nutrition needs and actual dietary intake. (6) In 2004, 23% of U.S. children with CF were less than the 10^{th} percentile weight for age and gender, and 22% of adults with CF aged 18 to 30 years are below a body mass index (BMI) of 19. These statistics were found in the 2004 CFF Patient Registry Report. (7)

There is evidence from population based studies indicating that normal weight-for-age, weight-for-height, and height-for-age percentiles are associated with better FEV1 and longevity for adults and children with CF. (2) It is recommended that children with CF strive to maintain normal weight and stature-for-age and gender. Adults should strive to maintain normal weight-for-height. (2)

The CFF has made the following recommendations:

1. Individuals with CF should consume energy intakes 110 to 200% of standard energy needs for the healthy general population. These elevated energy recommendations are necessary to support weight gain at an age-appropriate rate.
2. Children with CF aged 1 to 12 years at risk for or with growth deficits should receive intensive treatment including behavioral intervention in conjunction with nutrition counseling.
3. Nutritional supplements (oral and enteral) should be given to children with CF who experience growth deficits and adults who experience weight deficits. This supplementation will improve the rate of weight gain. (6)

Conclusion:

The CFF recently identified nutrition status as the leading indicator of lung function and longevity. (1,6) A registered dietitian is a fundamental part of the CF care team. (1) Increased attention and efforts should be given to improving the nutrition status of individuals with CF. Improved nutrition means improved lung function, longevity, and quality of life.

The new screening tool for children and adolescents with CF will be a reliable, valid, and useful tool. This is because the values and parameters are evidence based and have been approved by a multidiscipline panel of experts. It is anticipated that because nutrition clinicians have been involved in the development process, the screening tool will be widely accepted and used. This would make it an integral part of the treatment process for children and adolescents with CF.

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