Use of Enteral Nutrition (EN) in the Treatment and Management of Cystic Fibrosis (CF)

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Cystic fibrosis is a fatal, chronic disease that is characterized by the excess production of mucus, impacting functionality of the respiratory and digestive tract. It is a recessive inherited disorder resulting from a mutation of the Cystic Fibrosis Transmembrane conductance Regulator (CFTR) gene. While there are nearly 1700 known variations in the genetic profile of patients with cystic fibrosis, a majority of cases are due to a variant in the DELTA F508 gene. Excess mucus impairs function of the cilia in the lungs and digestive system causing increased risk of lung infection, airflow restrictions, coughing, wheezing, runny nose, constipation, gas, nausea and diarrhea [1,2,3].

The disease has direct anatomical and indirect behavioral implications that impact nutrition status and ultimately total health and well-being. CF reduces nutrient absorption in the digestive tract due to impaired cilia and increased mucus. Decreased absorption effects growth and development and can eventually lead to osteoporosis. Mucus also impairs the flow of food through the GI tract and pancreatic enzyme production causing blockages and discomfort (nauseas, diarrhea). Impaired pancreatic activity can ultimately lead to CF Related Diabetes (CFRD). Indirect nutrition related effects include reduced appetite, lack of interest in food, eating schedule impacts due to treatment regime and hospitalizations, and limitations in dietary food choices due to CFRD [3].

The use of enteral nutrition has shown to improve growth in children, increase longevity, reduce the risk and incidence of malnutrition and increase the total well-being of CF patients [4, 5, 10, 11]. In 2016 the Cystic Fibrosis Foundation released evidence-informed guidelines endorsing tube feedings as a recommended (if not encouraged) method to reach nutritional goals [6 – 9]. Ongoing research is needed to optimize recommendations related to age of initiation,

macronutrient distribution, energy needs and fluid needs – however this research is limited due to ethical consideration of controls [12-15]. Even with compelling evidence supporting EN, many life style, social, and administration limitations exist [16-21]. For example, MNT must be coordinated in concert with time consuming treatments that include unplanned surgeries and hospitalizations. Last, despite the clear evidence that enteral nutrition impacts positive outcome, social stigmas exist and insurance coverage of medical nutrition is uneven at best - completely lacking in some states and some insurance plans. The Medical Nutrition Equity Act, working its way through congress this session, would require insurance coverage of enteral formula for CF patients. Closing the gap for insurance can increase access to EN, by reducing one aspect of patient resistance to treatment, potentially impacting many lives and improving the outcome for many families dealing with this complex, difficult disease [22].

How CF Impacts Nutritional Status

1. Spilsbury, R. (2019). *Gene diseases and gene therapies: Cystic fibrosis*. New York, NY: The Rosen Publishing Group, Inc.

The author provides a clear, simple, fact-based description of both the causes and symptoms of Cystic Fibrosis. In summary, Cystic fibrosis a disease that causes a multitude of symptoms, disrupting the homeostasis of the entire body. The most common CF genetic mutation, Delta F508, causes excess mucus build up resulting in inflammation, impacting the function of both the digestive and respiratory systems. The author describes the nutritional impact of CF as the "disruption of the entire digestive system from the mouth all the way through the excrement of waste".

There are two diet related co-morbidities associated with CF: diabetes and osteoporosis. The CF caused mucus build-up affects the pancreas, causing scarring and blockages that impact the pancreas' ability to release digestive enzymes. The abnormal function of the pancreas results in approximately 50% of all CF patients becoming diabetic due to the impaired ability of the pancreas to produce insulin. The newborn "heel prick" test for Cystic fibrosis screens for abnormally high levels of trypsinogen, a pancreatic enzyme. Osteoporosis is caused by limited nutrient intake and absorption combined with low activity levels due to respiratory issues. In order to address GI related symptoms - treatment includes enzyme supplementation to improve digestion and supplement pancreas function, high fiber diet to reduce constipation and diarrhea, and increased water consumption to thin mucus throughout the entire body. All three are important considerations when establishing a total enteral prescription.

2. Abramovitz, M. (2013). *Disease and disorders: Cystic fibrosis*. Farmington Hills, MI: Lucent Books, Gale, Cengage Learning.

The author casts the current state of Cystic fibrosis care as a collection of treatments designed to extend the life of the patient. When CF was originally discovered in 1938 by Dorothy Andersen, it was (and still is) considered a fatal disease. However, in the past it was considered a childhood disease, but because of treatments, that include aggressive nutrition and diet therapy, patients can live to a median age of 37, with increasing life expectancy.

The anatomy of digestive system impacts from CF centers on the small intestine. When food enters the small intestine, it is mixed with enzymes that are provided by the liver and pancreas for digestion. However, in a patient with CF, the epithelial cells lining the liver and pancreas become clogged by mucus – impairing function. As a result, fat and protein digestion that rely on pancreas enzymes like trypsin, chymotrypsin and lipase cannot occur. Similarly, bile salts cannot be pass through the "clogged" ducts of the liver, further impairing digestion. As a result, patients with Cystic fibrosis need increased protein, fat and digestive enzyme supplementation since their bodies cannot digest food through normal processes. This information is important when determining the appropriate formula, with balance of macro nutrients for enteral nutrition.

3. Gray, S. H. (2019). *Living with cystic fibrosis*. Chanhassen, MN: The Child's World.

This book is a practical, visual guide about the day to day lifestyle impacts of CF and the expected treatments provided in a clinical setting. It is focused on the type of needs expected from the community, family and patient's support system. The critical information this book provided is an outline of the time and effort required for treatment: breathing equipment and procedures, specifics about the number and type of digestive enzymes to take (sometimes 20

pills per setting) and the overall impacts that treatment makes to the daily life of a patient. These lifestyle considerations are critical when determining the type and administration method of enteral nutrition as a treatment for CF.

4. Sullivan, J.S., & Mascarenhas, M. R. (2017). Nutrition: Prevention and management of nutritional failure in cystic fibrosis. *Journal of Cystic Fibrosis,* 16, 587-593. http://dx.doi.org/10.1016/j.jcf.2017.07.010

The authors describe the clinical importance, as well as specific methods for monitoring CF patients for malnutrition as well as ways to evaluate for more subtle signs of nutritional risk. They also describe intervention tools that includes the use of enteral tube feeding. At issue are the following

- How frequently CF patients should be measured and monitored (weekly, monthly, annually)
- What parameters should be used (BMI, weight, growth percentile)
- Specific methods due to the complexity of CF (i.e. fluid retention and reduced bone mass): DEXA, bioelectric impedance.

The conclusion is that nutritional status should be evaluated frequently and very aggressive interventions should occur as early as possible in order to meet normal weight, BMI and growth guidelines. The interventions include – increasing fat percentage in the diet, zinc supplementation, essential fatty acid supplementation, appetite enhancing drugs, glutathione (antioxidant) supplements, growth hormone supplements, and enteral feeding.

5. Larson-Nath, C., & Goday, P. (2019). Malnutrition in children with chronic disease. *Nutrition in Clinical Practice, American Society for Parenteral and Enteral Nutrition*, 34 (3), 349-358. doi: 10.1002/ncp.10274

The authors describe the importance of avoiding malnutrition by meeting increased energy needs through oral and enteral formula. They also explore how standard anthropometric measures do not always reflect accurate nutrition status of CF patients. Regarding anthropometric data, the BMI measures of CF patients can be skewed due to underlying osteoporosis, where lower bone density contributes to an artificially low BMI.

Regarding energy needs, the authors state that best clinical practice is to provide 110 – 200% total calories above the recommendations for children without a disease state. The increased energy needs are based on the effort required for breathing, and digestion. Additionally, they recommend 30-40% of total calories come from fat (in comparison to the standard 20-30% recommendation). This is due to the limited absorption that occurs in the intestine due to lack of enzymes and increased mucus. They also point out the research associated with protein intake is mixed – rough guidelines estimate needs at 13- 19 grams per day for children age 2-5 years old.

The most compelling, and relevant data they compiled is the research basis for a clear link between nutrition status (weight) and respiration, hospitalizations, and life expectancy. This is fundamental evidence- based research that drives the use of enteral nutrition as a regularly accepted clinical practice for CF patients.

Guidelines for the use of Enteral Nutrition and Outcome Results

6. Schwarzenberg, S.J., & Hempstead, S.E. (2016). Enteral tube feeding for individuals with cystic fibrosis: Cystic Fibrosis Foundation evidence-informed guidelines. *Journal of Cystic Fibrosis,* 15 (6): 724-735. http://dx.doi.org/10.1016/j.jcf.2016.08.004

A team of 16 expert clinicians and researchers in the field of CF were convened to provide standards and clinical practice recommendations for the initiation and administration of enteral tube feedings. The retrospective literature review covered 1138 unique citations. The most fundamental recommendation is that enteral feeding should be initiated if the patient is unable to meet growth/weight goals, and the evaluation of need should continue throughout the entire lifetime of the patient. Interestingly, the consensus was NEUTRAL on a recommendation that enteral tube feedings stabilize pulmonary function (other research paints a contradictory recommendation). Of the 33 recommendations, many restate practices we have learned about in class: careful consideration of the options related to tube placement, use of laparoscopic procedures in place of open surgery whenever possible, use of NG tubes for short term feedings (less than 3 weeks), avoiding surgery when lung function is decreased or patient is ill, open discussion with patients and their families about tube management, availably of supplies, insurance consideration and possible long term side effects.

One critical recommendation relates to intermittent bolus feeding vs continuous feeding. The consensus recommendation is to use continuous nocturnal infusion as a preferred method. The primary reasons are increased nutrients, increased absorption, and the ability to consume nutrients orally during the daytime.

7. Woestenenk, J.W., Castelijns, S.J.A.M, van der Ent, C.K., & Houwen, R.H. (2013). Nutritional intervention in patients with cystic fibrosis: A systemic review. *Journal of Cystic Fibrosis*, 12, 102 – 114. http://dx.doi.org/10.1016/j.jcf.2012.11.005

A total of 17 research articles and investigations studies were reviewed to determine methods to improve nutritional status of CF patients. The ultimate conclusion of the research was that enteral supplementation is the most effective manner to achieve both weight gain and improve overall nutritional status. Other methods that were investigated – oral supplementation and behavior modification fell short in terms of impacting overall patient health.

8. Libeert, D., Declerq D., Wanyama, S., Thomas M., Van daele, S., De Baets, F., & Van biervliet, S., (2018). The effect of enteral tube feeding in cystic fibrosis: A registry- based study. *Journal of Cystic Fibrosis*, 17, 264-270. https://doi.org/10.1016/j.jcf.2018.01.004

The authors conducted a long- term study of 113 CF patients to determine the effect of enteral tube feeding. The study was conducted by Belgian researchers, and validated the use of tube feeding as way to reduce hospitalizations, increase BMI and improve pulmonary function. Interestingly, the picture the study depicts is not extremely positive. Overall the height of the patients did not increase, they had patient high patient mortality (8.9%) and significant amount of need for IV antibiotics. My conclusion is that this validates the need for enteral feeding, even though the study population was small and the delayed use of enteral feeding may have caused their study to enroll patients who were very sick, or in degraded nutritional status to start. Bottom line – the enteral feeding should have been initiated earlier as a method of patient treatment as evidenced by the low BMI at the start of tube feeding, and the median age of the patient of 10 years old.

9. Wolfe, S.P & Wilschanski, M. (2016). Nutrition in CF – two new important guidelines. *Journal of Cystic Fibrosis*, 15, 708 – 709. http://dx.doi.org/10.1016/j.jcf.2016.10.004

The authors provide a meta-analysis summary of CF guideline changes due to recent research. Both of these guidelines were developed by forming a team of researchers, doctors, nurses, registered dietitians from both academic and clinical settings. The team reviewed relevant, recent research and combined with expert opinion and evidence based clinical outcomes formulated a set of standard recommendations for management and treatment of CF. First is the guideline from the European CF society regarding nutritional care for adults and children with CF. It provides comprehensive and standard methods for assessing nutritional status, and subsequent intervention focused on preventing under nutrition beginning at birth and managed throughout the lifecycle. The second guideline provides detailed recommendations on the use of enteral tube feeding for cystic fibrosis. The guidelines include consensus-based statements about the use and placement of the tube, as well as addressing the importance of family involvement in the treatment decision.

10. Khalaf, R. T., Green, D., Amankwah, E.K., Peck, J., Carr, V., Goldenberg, N.A., & Wilsey M., (2019). Percutaneous endoscopic gastrostomy tubes may be associated with preservation of lung function in patients with cystic fibrosis. *Nutrition in Clinical Practice*, 34(2), 290-296. doi: 10.1002/ncp.10219

Although this was a small study, 60 patients in total, it showed compelling evidence that even when EN did not change a patients BMI, lung function was improved. The implication of this research is that establishing a nutrition regimen that affords a patient the opportunity to get a better macronutrient distribution and complete vitamin and mineral supplementation can affect lung function. This study could be key to helping CF patients overcome objections to EN therapy – regardless of weight gain, or other stigma associated with tube feedings. This evidence points

to the relationship between better nutrition and improved respiratory function, potentially improving life expectancy.

11. White H., Morton A.M., Conway S.P., & Peckham D.G. (2013). Enteral rube feeding in adults with cystic fibrosis; patient choice and impact on long term outcomes. *Journal of Cystic Fibrosis*, *12*, 616-622. http://dx.doi.org/10.1016/j.jcf.2013.05.003

Long term research into the outcomes associated with EN for adult CF patients is limited – for several reasons. One reason is the unfortunate nature of CF as a fatal disease, median life span is 35 years old (recent data has pushed median life expectancy to 37 years old), and a second reason is that there are ethical considerations about creating a control group when EN has shown positive results to BMI and overall health. However, the authors of this study monitored 23 adult patients over a three-year period – 17 who accepted enteral tube feeding (ETF) and 6 who declined ETF. Overall there was an increase in BMI, and improvement in lung function. The study was the first to evaluate long term impacts of ETF in adults and although it was a small study group, had results important to clinical care. Specifically, the incidence of CFRD increased from 33% to 50% of the population using EN. It is known that CFRD is a complication of EN, which means that glucose levels must be carefully monitored in the clinical setting. The time delay to accept EN ranged from 18-36 months and the sicker the patient was, the more likely they were to accept EN. These items together point to the need for earlier patient education of EN solutions together with earlier initiation of EN as a key component of treatment.

12. Trabulsi, J., Ittenbach, R.F., Schall, J.I, Olsen, I.E., Yudkof, M., Yevgeny, D., Zemel, B.S., & Stallings, V.A. (2007). Evaluation of formulas for calculating total energy

requirements of preadolescent children with cystic fibrosis. *The American Journal of Clinical Nutrition*, *85* (1), 144–151.

The research associated with this paper is 13 years old, however there is an important result – which is how to determine appropriate energy requirements for patients with CF. Energy requirements are a critical input into the calculation and formulation of an EN order. An overestimation of calories can result in earlier onset of CFRD and an undercalculation will undermine efforts to increase growth. Although most CF patients receiving EN in a clinical setting, also consume food orally- a total daily caloric need must be established for determining ways to increase weight, BMI and growth. The authors compared different measurement equations for total energy to the actual energy expended by using precise measurement using Indirect Calorimetry (IC) together with an evaluation of fat loss in stool samples. A mathematical analysis was performed comparing different EER formulas and the result was a specific recommendation for activity factors that mostly closely matched the IC measurements. The authors hypothesized the improved accuracy of CF specific EER formulas was due to the measurements of fecal samples – not estimations of activity levels.

13. Parrish, C.R. (2005). Elemental and Semi-Elemental Formulas: Are they superior to Polymetric Formulas? *Practical Gastroenterology*, *34*, 59-72.

An interesting aspect of the author's position is they not only evaluated the medical impacts of using elemental vs semi-elemental formulas, they hit right on the important lifestyle consideration - cost. As a very simple data point that is referenced in the paper, the cost of a semi-elemental formula: Novartis Peptinix is $21.60 per 1,000 kcal vs. the cost of a standard polymetric formula: Novasource 2.0, by the same manufacturer, is $3.04 per 1,000 kcal. Many patients with chronic conditions, also have insurance and cost considerations as part of their

acceptance of treatment regime. In fact, EN falls "in the cracks" of insurance coverage as it is not considered a prescription (regulated by the FDA) it is instead considered food. Insurance agencies argue that "food" is not covered as a medical treatment, even though evidence exists that EN substantially improves the health of CF patients, reducing mortality rates.

14. Curry, A.S., Chadda, S., Danel, A., & Nguyen, D. (2018). Early introduction of a semi-elemental formula may be cost saving compared to a polymetric formula among critically ill patients requiring enteral nutrition: a cohort cost-consequence model. *ClinicoEconomics and Outcomes Research, 10*, 293-300. http://dx.doi.org/10.2147/CEOR.S155312

This research seems to provide a contradictory result about the use of elemental formulas vs polymetric formulas. ASPEN states "no clear benefit to patient outcome…for the routine use of specialized formulas" and instead to use standard formulas for critical care patients - including CF patients. This study points out an exception – adults with upper GI distress benefit from semi-elemental formulas. The authors go even further and develop a cost model to show the saving obtained by fewer days in the ICU (on average 3 days less) far outweigh the cost of using a specialized formula (as shown above - a cost difference of 10x in comparison to standard polymetric formula). Given the fragile nature of the GI tract in a patient with CF, there may be benefit, in limited cases to using a semi-elemental formula: when the patient is in critical care and when the patient is experiencing upper GI distress (nausea, bloating, GERD).

15. Endo, A., Shiraishi, A., Fushimi, K., Murata, K., & Otomo Y. (2018) Comparative effectiveness of elemental formula in the early enteral nutrition management of acute

pancreatitis: a retrospective cohort study. *Annals of Intensive Care 8* (69), 2-8. https://doi.org/10.1186/s13613-018-0414-6

One of the life-threatening aspects of Cystic fibrosis is pancreatic insufficiency, evidenced by reduced production of pancreatic enzymes, with the possible result pancreatitis. Pancreatitis is inflammation of the pancreas, treated through support therapy (hydration, antibiotics, and respiratory care). The authors conducted a study of Japanese patients with pancreatitis to determine whether there was any benefit - measured in terms of days in the hospital, overall mortality rate, cost of care, to the use of elemental formula vs non-elemental formula. The study group was defined by identifying patients who were admitted to critical care with acute pancreatitis (with or without cystic fibrosis as an underlying disease state) over a 5-year period (2010 – 2015). In total, the medical records of 948 patients were reviewed as candidates for the study, and 382 received elemental formulas via enteral nutrition within three days of admission. The conclusion was there was no statistically significant advantage in the use of elemental formulas. This is relevant to CF treatment, as a reasonable hypothesis is that an elemental formula would be "easier" on the pancreas because there was would be less need for enzymes – particularly lipase in fat free elemental formulas. This study validated previous CF specific research that proved on a small scale no benefit to the use of elemental formulas in the overall outcome of CF (in fact the opposite is true).

16. Schwarzenberg, S.J. & Borowitz, D. (2019). Challenging barriers to an option for improved provision of enteral nutrition. *Journal of Cystic Fibrosis*, 18, 447-449. https://doi.org/10.1016/j.jcf.2019.06.002

The author's purpose in publishing this paper was to provide universal endorsement for the use of a technology called immobilized lipase cartridge (ILC) as a way to increase the nutritional status of patients with Cystic fibrosis. The ILC is a device that is integrated into the tube feeding system that provides lipase enzymes in a manner that mixes with the tube feeding formula to break down the fatty acids prior to them arriving in the digestive tract. The pre breakdown of fatty acids has shown considerable results in clinical settings. Approximately 2000 patients have used the device, with results as follows: 46- 59% of patients reported both improvement or a decrease of at least one gastrointestinal symptom (gas, abdominal pain, bloating, diarrhea), 100% reported increased weight gain. Each study collected weight measurements in different ways – some measured BMI, some measured weight for height/growth charts and standard deviations as well as increased omega-3 fatty acid consumption.

Unfortunately, ILC is considered a device, not a drug since the lipase activity occurs external to the body. It is not a new drug or chemical – simply a specialized device integrated into the feeding system. The FDA has approved the device but it is not approved for use by insurance. Despite the barriers – the authors unanimously recommend the use of this device. Approximately 100 nationally recognized experts in the field of CF treatment "co-signed" this recommendation.

17. Fisher, K.L., Patchell, C., Jones, S., Hull, L., Cooper, S., & Desai, M. (2013). Nutritional outcomes of enteral nutrition in children with Cystic fibrosis. *Conference on Gastroenterology and Nutrition*, 220.

The poster summarizes a study of 16 patients and the effect of enteral feeding on BMI. Although the study confirmed the use of EN as an effective treatment method to increase BMI, it unfortunately did not conclude that the long-term effects of EN were all positive. For example, a

result of EN feeding was vomiting and diabetes (however diabetes is a known existing comorbidity of CF due to pancreatic injury). The study showed that EN improved BMI within 3 months of initiation, however after two years a decline in impact was noted. The researchers hypothesized the reasons for decline could be attributed to lack of adherence, intolerance to the formula, or overall health decline of the patient due to the natural course of the fatal, chronic disease.

18. Abad-Jorge, A. (2013). Nutrition management of the critically ill pediatric patient. *Journal of Infant, Child and Adolescent Nutrition*, 5 (4), 221-230. doi: 10.1177/1941406413492821

This paper addresses the topic of appropriate nutrition guidelines when treating critically ill patients in the pediatric intensive care unit (PICU). The paper covered a list of primary causes for being admitted into the PICU - ranging from cardiovascular, trauma, and oncology, including cystic fibrosis caused respiratory failure, diabetes and gastrointestinal failure. ASPEN guidelines are: malnutrition screen, create a nutrition intervention plan, use EN when possible over PN, proactively plan for interruptions (surgery, treatment, etc.). Interestingly, the current guidelines related to the preferred use of EN over PN for pediatric nutrition mirror the adult guidelines however there are no controlled studies that support this guideline. The evidence resides with adult studies and for now, these are strictly clinical practices based on experience providers that need further institutionalization and formal practice instructions.

Daily Living Considerations for the use of Enteral Nutrition

19. Filigno, S.S., Brannon, E.E., Chamberlin, L.A., Sullivan, S.M., Barrnett, K.A., & Powers, S.W. (2012). Qualitative analysis of parent experiences with achieving cystic fibrosis nutrition recommendations. *Journal of Cystic Fibrosis, 11*, 125 – 130. doi:10.1016/j.jcf.2011.10.006

The authors interviewed families of eight children with CF to determine the type of behavior intervention and strategies they use to increase nutrient intake. An important fact the authors state right up front is that despite general CF treatment guidelines that patients should receive 120-150% caloric energy intake based on age, of which 40% should come from fat, only 12-16% of the population meets those guidelines. The barriers with meeting those guidelines include lack of parental education about food, macronutrient content, or calorie content. Another barrier is lack of appetite and difficulty structuring time to eat around treatment regimes. A third barrier is parental stress – centered around the challenges of raising a child with a chronic illness. The conclusion of the research is that intensive nutritional counseling and anticipatory guidance should be provided to the parents about the importance of nutrition and that specific tools and methods be provided to ensure a child with CF meets nutrition intake guidelines.

20. Wolfe, P. & Collins, C. (2017). The changing face of nutrition in cystic fibrosis. *Journal of Cystic Fibrosis*, 16, 436-438. http://dx.doi.org/10.1016/j.jcf.2017.05.006

The authors describe a positive trend in the awareness of the importance of careful management of nutritional status in cystic fibrosis patients. The history of dietary treatment reaches back as far as the 1930's when patients were fed beef serum, glucose and triglycerides. In 1988, key research proved the value of feeding high fat diets, as well as pancreatic enzymes. A newborn screen program accelerated the opportunity to use nutrition therapies early in the growth cycle, preventing stunting and other growth abnormalities. Some current treatment regimens use technology like food tracking Apps, and specialized formulas. However, the authors point out that diet adherence – across the board is a challenge. This further illustrates the value of using EN as a treatment, potentially long term since is provides consistent, balanced

nutrition, eliminating behavior or diet preference issues, providing a complete nutritional solution to the patient.

21. Current Research results for treatments, drugs, cure for cystic fibrosis. Retrieved from https://www.cff.org/News/

The Cystic Fibrosis foundation funds research at hospitals, Universities and in clinics. Much of the current focus is related to gene therapies to correct the defective gene but there are other funded research projects aimed at addressing nutritional status of CF patients. On the same CF Foundation web site, is an entire section devoted to tube feeding. A picture of a happy smiling child performing a gastric bolus feeding attempts to break down myths and pre-conceived notions surrounding tube feedings. The most compelling document on the web site is a "before and after" picture from a young patient using tube feeding. The visual differences are remarkable – in the before picture she looked malnourished, muscle wasted, had very thin hair, and a small head size. In the after picture she was a well-nourished looking child, with long healthy hair and increased body fat with healthy looking skin and features proportionate to her body size.

22. The Medical Nutrition Equity Act, retrieved from https://www.npkua.org/Portals/0/pdfs/MNEA-flyer_2pager.pdf

Although this reference is not related to research – it forms an important piece of the puzzle needed with clinical treatment of CF using EN. As stated in several of the research items above, there are cost and insurance considerations associated with using EN. Reducing cost impacts, which can be a barrier to treatment is critical because it will improve access to treatment, potentially enable patients to get treatment at a younger age, and prolong life expectancy. I have

personally advocated for this legislation on behalf of the PKU community, a group of patients who would also benefit from the new law, and after nearly 10 years, the legislation finally has enough co-sponsors that is could be finally passed!