

CHAPTER 7 MACRONUTRIENTS

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7.1 Energy, Protein, Fat and Fibre

Historically, CF nutrition guidelines have routinely recommended a high energy and high fat diet ¹ due to a high prevalence of undernutrition. Early diagnosis through newborn screening, significant improvements in the nutritional status of CF populations and the emergence of overweight and obesity in some individuals dictate that this approach as a routinely recommended diet needs to be moderated.

This chapter explores the variable energy requirements of people with CF, and the specific role of macronutrients (i.e. carbohydrates, fat, protein and fibre).

Disease Aetiology

An overall deficit in both dietary energy and protein can result in catabolism and undernutrition ³⁰¹.

ENERGY

A positive energy balance is associated with storage of energy, deposition of tissue, weight gain and normal growth. In contrast, negative energy balance is correlated with depletion of tissue, weight loss and if prolonged, poor linear height, particularly in children ^{43,301}. In CF, energy balance is complicated by pancreatic insufficiency resulting in malabsorption of fat and protein, which is largely, but not totally, resolved with adequate pancreatic enzyme replacement therapy (PERT).

Most studies looking at energy expenditure in CF refer to resting energy expenditure (REE) due to the significant variability and challenges in measuring in total energy expenditure (TEE). While early studies hypothesise that altered REE in CF is due to a genetically linked abnormality, recent studies have found that altered REE is likely due to disease progression ³⁰². The following have been reported in the literature in regards to REE in CF:

- Comparison between CF and general population
 - Some studies have found REE is similar in both the CF and non-CF population ^{33,37,39,303}.
 - Most studies report that people with CF have a higher REE compared with controls and predictive values derived from standard equations ^{30,38,268,304-308}.
- Correlation between REE and fat free mass (FFM), pancreatic function and pulmonary function
 - Most studies have found that FFM, pancreatic function and pulmonary function are associated with REE in CF ^{30,39,41,42,49,309}.
 - Some studies found no association between increased REE and lung disease severity ^{38,305,306,310}.
- REE and respiratory exacerbations
 - Some studies have found REE to be increased at the beginning of a CF respiratory exacerbation ^{32,34,40} while other studies report no change ^{311,312}.
- REE and puberty
 - In comparison to the general population, REE is elevated in both males and females with CF and pancreatic insufficiency during pubertal maturation ³⁸. This increase in REE has been shown to be greater in females than males ³⁸.
 - REE remains elevated post-puberty in females with CF in comparison to the general population where REE decreases ^{31,42}.

When applying these findings to clinical practice, it is important to remember that an increase in REE may not result in an increase in TEE as the increase in REE may be offset by a reduction in activity in CF, particularly for those with worsening and end-stage lung disease ²⁷⁶.



PROTEIN

Protein is composed of both amino acids and nitrogen and is vital for the structure and metabolic operation of the human body including enzymatic, hormonal and transport functions⁴³. Some amino acids cannot be synthesized by the body, and these are referred to as essential amino acids. These essential amino acids must be provided by dietary sources. Importantly, people with CF are known to have decreased protein synthesis ([Chapter 6](#)).

FAT

One of the main roles of fat in a CF diet is to provide a concentrated form of energy. Fats also assist in the transportation of fat soluble vitamins and in the formation of phospholipids and adipose tissue⁴³. Since the implementation of a high energy and high fat CF diet, the overall caloric intake and growth of people with CF has improved^{313,314}.

The following should be considered when looking at fat digestion and absorption in people with CF:

- Potential impact of mucous obstructing the pancreas and gall bladder
 - Pancreatic lipase, bile salt and colipase are provided by bile and pancreatic juices and play a key role in the absorption of fat³¹⁵.
- Absorption of medium chain triglycerides (MCT)
 - Unlike long chain triglycerides (LCT), which are absorbed via the lymphatic system, MCT are absorbed via the small intestine and transported directly to the liver via the portal vein for metabolism³¹⁶.
 - MCTs may be beneficial for people with CF who have cholestasis or short bowel syndrome³¹⁷

FIBRE

Dietary fibre is the edible portion of plant-based foods that is not absorbed in the small intestine but instead undergoes fermentation in the large intestine⁴³. Fibre is known to play a key role in optimising digestive and bowel health, reducing cholesterol, and in stabilising blood glucose in the general population⁴³. Conversely, little is known about the role of fibre in the CF population. To date, most studies looking at the role of dietary fibre in CF have found conflicting results in regards to adequacy of fibre intake on gastrointestinal symptoms and the incidence of constipation and distal intestinal obstruction syndrome (DIOS)^{142,143,318} ([Chapter 11](#)).

Assessment

DIET

As part of a thorough nutritional assessment, an individual's intake of energy, protein and fat should be considered. This should be done in conjunction with individual enzyme requirements, anthropometric measures and physical activity levels.

ENERGY

- Refer to [Chapter 5](#) for information on the assessment and calculation of energy requirements for people with CF.
- Macronutrient distribution i.e. percent energy provided by protein, fat and carbohydrate should be considered (see practice points below).

PROTEIN

- Pay particular attention to protein intake in people who are vegan or vegetarian, restrictive eaters and athletes.
- Animal protein sources such as meat, fish, poultry (including eggs) and dairy foods, together with plant sources such as legumes/lentils and nuts are the major dietary protein sources.

FAT

- Oils, margarine, butter, cream, dairy foods, fish, meat, processed foods and takeaway foods are major dietary fat sources.
- Consider the source and quality of the fat ingested i.e. polyunsaturated and monounsaturated versus saturated fats³¹⁹.

FIBRE

- Sources of soluble fibre include fruits, vegetables, oats, barley and legumes ³²⁰. Soluble fibre plays a role in lowering of LDL cholesterol ³²¹.
- Sources of insoluble fibre include wholegrain breads and cereals, nuts, seeds, skin of fruit and vegetables. Insoluble fibre adds bulk to stools and also plays a role in the prevention of constipation ³²¹.
- Sources of resistant starch include cooked and cooled potato and rice ³²⁰. Resistant starch ferments in the large bowel and produces short chain fatty acids that play a role in improving bowel health ³²¹.

ALCOHOL

- While not a macronutrient, alcohol intake contributes to total daily energy intake and should be considered as part of a nutrition assessment for adults with CF.

Intervention

Are energy requirements increased in the CF population compared to the general population? PICO 7.1.1

[Grade D] Limited evidence to guide determination of energy requirements for people with CF of all ages. Until further evidence is available, health professionals should be guided by the consensus recommendation of 110-200% of the general population energy target. Use clinical reasoning and an individualised approach to setting energy targets. ³⁰⁻⁴²

ENERGY TARGETS

When setting energy targets the aim is to achieve normal nutritional status and growth, whilst avoiding undernutrition or overweight/obesity ¹. It is recommended that practitioners in Australia and NZ consider most recent international recommendation of 110-200% ⁷⁸ when setting energy targets for people with CF. However, in the absence of strong evidence, this should only be considered a guide.

The following should be considered when assessing and revising individualised energy targets for people with CF ¹:

- Nutritional status
- Dietary intake
- Growth pattern
- Clinical status (including pulmonary function)
- Pancreatic function
- Physical activity levels
- Any additional requirements for weight gain/growth and nutritional repletion
- Increased dietary requirements with pregnancy and lactation
- Likelihood of changes in REE and/or TEE post lung transplant

Are protein requirements increased in the CF population compared to the general population? PICO 7.1.2

[Ungraded] Insufficient evidence to make a recommendation about protein requirements



PROTEIN TARGETS

In the absence of new research, practitioners should use 15-20% of total energy from protein as a guide ^{78,322}. This aligns with the current recommendations for the general population ⁴³. A varied diet which meets individual energy requirements should provide adequate protein for people with CF ³²².

Additional protein considerations:

- Protein quality
 - Emerging evidence suggests that there should be a strong focus on high-quality protein intake in CF. It has also been proposed that essential amino acid mixtures may be effective in inducing protein anabolism in people in a catabolic state ^{323,324}.
- Intact versus hydrolysed protein
 - There is inadequate evidence to support the use of hydrolysed protein over intact protein for enteral tube feeding in most people with CF ^{325,326}. For those people with CF and significant CF co-morbidities i.e. GI complications, a more specialised enteral feed that may include partially or fully hydrolysed protein may be appropriate.
- Impact of high protein diet
 - Short-term protein synthesis and thus net nitrogen retention may be increased by a high protein diet (5g/kg/d) ³²⁷. However, this has only been demonstrated in a cohort of stunted paediatric patients and the longer-term implications of a high protein diet are unknown ³²⁷.
 - A case report shows an adolescent with CF-related liver disease and portal hypertension developing acute hepatic encephalopathy after consuming 4.5g/kg protein over 6-hours at a festival ³²⁸. Although there is some evidence indicating the need for high-quality protein, further research is needed to assess the optimal level of protein (including essential amino acids) in clinically stable CF children and adults as well as those recovering from acute exacerbations.

What is the evidence to support the routine recommendation of a high fat diet for people with CF? PICO 7.1.3

[Grade D] There were no new studies included in this systematic literature review (2002-2016) to make changes to the existing recommendation for fat intake in CF from the '2006 Australasian Clinical Practice Guidelines for Nutrition in CF'. Continue to recommend an unrestricted diet that contains adequate fat to meet energy requirements. Target an intake of 100g/day if over five years of age based on the premise that a diet high in fat is less bulky and energy targets are more achievable than a diet that is low in fat.

FAT TARGETS

Fat provides a significantly higher amount of energy per gram than the other macronutrients ⁴³.

- Fat = 37kJ/g (9kcal/g)
- Protein and carbohydrate = 16.7kJ/g (4kcal/g)
- Alcohol = 29kJ/g (7kcal/g)

What are the recommendations for fibre in people with CF? PICO 7.1.4

[Ungraded] Insufficient evidence to make a recommendation about fibre intakes.

FIBRE TARGETS

A moderate fibre intake in line with recommendations for the general population may be suitable for people with CF. See Table 7a for further information.

Table 7a. Nutrient Reference Values for Fibre ⁴³ available at <https://www.nrv.gov.au/nutrients/dietary-fibre>

Patient groups	Adequate Intake (g/day) for fibre	
	Males	Females
Young children		
1-3 years	14	14
4-8 years	18	18
Older children & adolescents		
9-13 years	24	20
14-18 years	28	22
Adults	30	25
Pregnancy		
Adolescents	N/A	25
Adults		28
Lactation		
Adolescents	N/A	27
Adults		30

An alternative and potentially more achievable recommendation for fibre intake in the paediatric population is:

$$\text{Fibre intake (g/d)} = \text{age (years)} + 5 \text{ }^{329}.$$

ALCOHOL

For adults with CF without a contraindicating condition or medication, advice regarding alcohol should follow the Australian Dietary Guidelines²⁵⁴ (i.e. no more than two standard drinks on any one day, and no more than four standard drinks on a single occasion). Recommendations for the New Zealand population are available at <http://www.health.govt.nz/your-health/healthy-living/addictions/alcohol-and-drugs/alcohol>. For some adults with CF, avoidance of alcohol is advised. This may include those with liver disease, pancreatitis, any concurrent condition in which alcohol use is discouraged or contraindicated, and those taking medication where alcohol interacts or is contraindicated. People with CF-related diabetes need to be aware of the risks of hypoglycaemia with alcohol use.

SPORTS NUTRITION CONSIDERATIONS FOR THE CF POPULATION

Advice regarding dietary intake and macronutrient distribution is particularly important for the CF population who are athletes, highly active, engaging in regular exercise and/or working out to improve lean body mass and muscle bulk. It is important that an individualised approach with thorough clinical reasoning is taken when providing sports nutrition advice to people with CF. Specific considerations for the general population that can be applied to CF include;

- Protein requirements of 1.2-2.0g/kg/d are recommended for athletes, with the upper limit of this range recommended for those involved in strength training ³³⁰. Many people with CF are likely to achieve this protein target given the high energy intake of their diet. Consumption of protein above 2g/kg/d is thought to be of no benefit to athletes ³³⁰.
- Prior to exercise, encourage food choices that are relatively low in fat and fibre to promote gastric emptying, high in carbohydrate for blood glucose maintenance and are moderate in protein ³³¹. Where possible, familiar foods that the individual knows is well tolerated should also be encouraged ³³¹.
- For exercise that is greater than one hour in duration, rehydration with a carbohydrate containing beverage is recommended for the non-CF population ³³¹. However, carbohydrate containing beverages, in particular sodium containing rehydration solutions, may be beneficial for the CF population in exercise of any duration. See [Chapter 9](#) for further information.



- After exercise, advice is tailored around the replacement of losses. A high energy meal or snack with adequate carbohydrate to replace muscle glycogen stores as well as protein to provide amino acids for muscle repair and growth should be encouraged³³¹. A carbohydrate to protein ratio of 3-4:1 is recommended by the International Society of Sports Nutrition (ISSN) and 20-25g of high quality protein is recommended by the International Olympic Committee (IOC)³³⁰. Again, these are reasonable targets for the CF population. Fluid and electrolyte losses should also be replaced after exercise³³¹. When providing advice for people with CF who is undertake high intensity exercise and/or body building, it is important the dietitian is aware of the role and use of sports supplements that are available and marketed to these individuals. Sports practitioners and trainers providing nutrition advice to people with CF should be aware of the implications of CF and inform the CF team of any advice they provide.

Monitoring & Evaluation

Macronutrient requirements of people with CF may change over time. This may be due to infective exacerbations, changes in physical activity levels, changes to drug therapies and/or transplantation. It is important that the adequacy of energy, protein and fat intake is reviewed by a dietitian on a regular basis to ensure individual needs are being met².

Practice Points PICO 7.1.1

Energy requirements are likely to be elevated for people with CF. Aim for 110-200% of the recommended daily energy intake for age and gender when setting energy targets for the CF population. Take into account the following when setting individualised energy targets for people with CF:

- Nutritional status
- Dietary intake
- Growth pattern – aiming to achieve normal growth (avoid both undernutrition and overweight/obesity)
- Clinical status (including pulmonary function)
- Pancreatic function
- Physical activity
- Any additional requirements for weight gain/growth and nutritional repletion
- Pregnancy and lactation
- Transplantation

Practice Points PICO 7.1.2

Aim for 15-20% energy from protein. Take into account the following when setting individualised protein targets for people with CF:

- Protein intake generally increases as energy intake increases
- A mixed high energy diet should provide adequate protein for people with CF
- Vegans, vegetarians, fussy/restrictive eaters, people with allergies i.e. cow's milk protein allergy and the obese CF population on an energy restricted diet, will require specific dietary advice regarding protein intake

Further research is needed into the impact of protein quality on health outcomes in CF. Protein requirements may be elevated with malabsorption and catabolism. It is particularly important to consider the adequacy of protein intake for people with CF who have signs/symptoms of malabsorption, are unwell e.g. with a respiratory exacerbation or poorly controlled diabetes.

Upper Limit for protein: The NHMRC recommends an upper limit for protein of 25% of energy intake for the general population,⁴³ however there is no evidence to guide a CF-specific upper limit. Evaluate individual dietary practices contributing to protein intake when intake is above 25% of energy intake; to identify if the high protein intake is contributing to a specific nutritional goal, or if other sources of energy and nutrients can be substituted without compromise to overall nutritional intake and status.

Practice Points PICO 7.1.3

Providing the person is not overweight or at risk of overweight/obesity, avoid restricting fat intake in people with CF

- Aim for 100g/day of fat for people with CF aged >5 years

Take into account the following in setting individualised fat targets for people with CF:

- Source and quality of fat i.e. polyunsaturated and monounsaturated versus saturated fat
 - Potential implications of a high saturated fat diet on cardiovascular health
 - Potential benefits of long chain polyunsaturated fatty acids on inflammation
- Macronutrient distribution
 - Initially aim for 20-30% energy from fat, according to the recommendations for the general population

Up to 35-40% energy from fat is considered acceptable for the paediatric CF population and for those requiring a high energy density diet (e.g. for nutritional repletion).

Practice Points PICO 7.1.4

Aim for a moderate fibre intake in line with the general population recommendations of 14-30g dietary fibre per day. Refer to the Nutrient Reference Values for Australia and New Zealand webpage, <https://www.nrv.gov.au/nutrients/dietary-fibre> for specific age and gender recommendations.

7.2 Essential Fatty Acids

Research since 2002 has focused on the lipid profile and supplementation of essential fatty acids (EFA). Omega-6 (pro-inflammatory) and omega-3 (anti-inflammatory) polyunsaturated fatty acids are both considered essential as they cannot be synthesised by the human body⁴³. EFA disturbances and deficiency are among the many metabolic abnormalities that may affect a person with CF³³²⁻³³⁶.

- **Omega-6**
 - mostly comes in the form of linoleic acid (LA), a precursor of arachidonic acid (AA)
- **Omega-3**
 - includes alpha linolenic acid (ALA), a precursor of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and docosapentaenoic (DPA)

Disease Aetiology

EFA deficiency was first described in CF more than 50 years ago³³⁷. In CF, fatty acid disturbances are largely characterised by lower LA and DHA concentrations in the serum, plasma, erythrocytes or whole blood³³⁶⁻³³⁸. The metabolism of AA is also thought to be altered in some people with CF^{335,339}.

Hypotheses looking at the aetiology of EFA deficiency in CF have changed over time. It was initially thought that EFA deficiency in CF was a consequence of malnutrition, pancreatic insufficiency and fat malabsorption³³⁵. More recent studies report that altered fatty acid composition in CF is likely due to intrinsic metabolic alterations that occur in cells lacking cystic fibrosis transmembrane conductance regulator (CFTR) function³³⁸. The precise mechanism and significance of EFA deficiency in CF remains unclear³³⁸. The overall prevalence of EFA deficiencies in CF remains unknown.

EFA disturbances may have significant consequences on the progression of CF. Animal studies have shown that EFA deficiencies can impair lung defence mechanisms^{335,340,341}. The postulated links between EFA deficiency and inflammation in CF are:

- Inflammation related to increased production of pro-inflammatory AA derived eicosanoids³³⁵
- The reduction in anti-inflammatory benefits associated with reduced DHA levels³³⁵

The impact of EFA disturbances on CF health outcomes were also recently summarised in the 2016 ESPEN guidelines⁷⁸ whereby the following was noted:

- LA deficiency is correlated with poor growth and pulmonary status in the paediatric population
- Elevated AA to DHA ratio is associated with impaired bone mineral density
- EFA deficiencies are found to be positively correlated with impaired immune, hepatic and renal function



Assessment

DIET

Review dietary sources of EFAs

PLANT-BASED SOURCES

- Provide ALA (omega-3)
- Found in plant-based fats and oils such as canola oil and soybean oil, and also in linseeds, chia seeds and walnuts ⁴³

ANIMAL (MARINE) BASED SOURCES

- Provide EPA and DHA
- Predominantly found in oily fish such as salmon, sardines, blue-eye trevalla, mackerel, herring, canned salmon, canned sardines and some varieties of canned tuna ⁴³

CLINICAL

EFA SUPPLEMENTATION

- Check for any use of EFA supplementation including fish oils

EFA DEFICIENCY

Signs and symptoms of inadequate EFA intake may include ³⁴²⁻³⁴⁷:

- Rough and/or scaly skin
- Dermatitis
- Increased trans epidermal water loss
- Increased susceptibility to infection
- Impaired wound healing
- Thrombocytopenia and reduced platelet aggregation
- Poor growth
- Learning difficulties (in children)

BIOCHEMICAL AND LABORATORY DATA

SERUM EFA PROFILE

Measurement of serum levels of EFA is generally only undertaken in a research setting with the following most often reported ^{43,78}:

- Serum LA
- Triene : tetraene (T3:T4)

Intervention

LIPID PROFILES

Preliminary research shows that dietary fat intake patterns of children with CF may directly influence lipid profiles, suggesting that changes in dietary practices, particularly promotion of omega-3 containing foods, may result in better fatty acid profiles resulting in improved clinical outcomes and inflammation ^{334,348}. Conversely, another study concluded that adjusting intake of dietary fat patterns is unlikely to affect lipid profiles ³⁴⁹. More research is needed in this area before any practice recommendations can be made.

Does dietary supplementation with omega-3 essential fatty acids improve health outcomes in people with CF? PICO 7.2.1

[Grade C] Dietary supplementation with omega-3 fatty acids may improve health outcomes for people with CF, however, the evidence is insufficient to recommend routine use of omega-3 supplementation. ⁴⁴⁻⁴⁶

EFA SUPPLEMENTATION

The body of evidence regarding omega-3 supplementation in CF lacks consistency due to significant variability in dosing, biochemical analysis of EFA and outcome measures. Long term safety and efficacy data as well as PERT recommendations with omega-3 supplementation in CF is also lacking³⁵⁰. As a result, until larger clinical trials have been completed, routine supplementation of omega-3 fatty acids is not recommended for the CF population³⁵⁰.

Despite a lack of evidence to support additional omega-3 supplementation in CF, it is still important that people with CF meet fatty acid recommendations for the general population. The National Heart Foundation recommends the following³⁵¹:

- Aim to eat 2-3 serves of fish (including oily fish) per week
- Aim to eat 1000mg of plant-based omega-3 per day
- Consume a healthy diet that includes vegetables and legumes, fruit, wholegrain cereals, lean meats and their alternatives, nuts and seeds, milk, cheese and yoghurt and healthier fats and oils.

EFA SAFETY CONSIDERATIONS

Omega-3 EFA supplementation must be commenced with some caution, as intakes above 5000mg per day have been associated with the following^{336,352}:

- Oxidative stress, leading to an increased requirement for dietary antioxidants
- A sensation of fullness
- Cramping, abdominal pain, steatorrhea and nausea

In CF there have also been some reports of steatorrhea and abdominal pain with omega-3 EFA supplementation, however, there have also been many studies which report no adverse events with supplementation³⁵³⁻³⁵⁵. Overall there is an absence of data on the long-term efficacy of omega-3 EFA supplementation in the CF population.

Monitoring and Evaluation

The adequacy of EFA intake, particularly omega-3 EFAs should be considered as part of the annual nutrition assessment. More regular review is suggested for people with CF who show signs and symptoms of EFA deficiency.

Practice Points PICO 7.2.1

People with CF may be at risk of EFA deficiency

- The prevalence of EFA deficiency in CF is unknown

Omega-6 fatty acids - Includes linoleic acid (LA), a precursor of arachidonic acid (AA)

- LA occurs in seed oils (sunflower, safflower and corn)
- AA occurs in meat, poultry and eggs
- Can exert a pro-inflammatory effect

Omega-3 fatty acids - Includes alpha linolenic acid (ALA), a precursor of the long-chain PUFAs (Eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and docosapentaenoic acid (DPA))

- ALA occurs in legumes, canola oils, margarine, linseed oils and nuts (walnuts)
- Long-chain omega-3 PUFAs occur in fish oils
- Known for their anti-inflammatory properties

Source of supplementation

- Insufficient evidence to suggest that any type or combination of omega-3 EFA (dietary or commercial) is superior.

Take into account the following prior to recommending omega-3 supplements to people with CF:

- Safety - intakes above 5000mg/d have been associated with an increase in oxidative stress and gastrointestinal discomfort
- Efficacy - long term efficacy of omega-3 supplementation in CF is unknown
- Cost of commercial omega-3 supplements
- Impact on burden of treatment and adherence

May be better tolerated with meals (and PERT)

