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## Review

## Consensus-based guidance for the nutritional management of children with cystic fibrosis on ELEXACAFITOR/TEZACAFITOR/IVACAFITOR

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## ABSTRACT

**Introduction:** The introduction of CFTR modulators such as elexacaftor/tezacaftor/ivacaftor (ETI) has significantly altered the nutritional trajectory of children with cystic fibrosis (cwCF). While most eligible children in high-resource countries have commenced ETI, the rollout has outpaced the development of nutritional guidance. This study aimed to: (1) systematically review the literature on ETI and nutrition (2) develop expert consensus-based statements and (3) highlight existing research gaps and priorities.

**Methods:** A systematic review and guideline development process was registered on PROSPERO (ID: CRD42024587618). An expert panel of 22 professionals, including dietitians, gastroenterologists, respirologists, endocrinologists, and a parent representative was convened with attention to global representation. Research

**Abbreviations:** ACCORD, Accurate Consensus Reporting Document; BMI, Body mass index; CF, Cystic fibrosis; CFRD, Cystic fibrosis-related diabetes; CFTR, Cystic fibrosis transmembrane conductance regulator; CGM, Continuous glucose monitoring; cwCF, Children with cystic fibrosis; ETI, Elexacaftor/tezacaftor/ivacaftor; FE-1, Faecal elastase-1; FSV, Fat-soluble vitamins; HbA1c, Glycated haemoglobin; HDL-C, High-density lipoprotein cholesterol; ID, Iron deficiency; IDA, Iron deficiency anaemia; LDL-C, Low-density lipoprotein cholesterol; OGTT, Oral glucose tolerance test; PERT, Pancreatic enzyme replacement therapy; PI, Pancreatic insufficient; PICO, Population, Intervention, Comparison, Outcome; ppFEV1, Percent predicted forced expiratory volume in 1 second; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SIGN, Scottish Intercollegiate Guidelines Network; sTfR, Soluble transferrin receptor; TC, Total cholesterol.

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questions were developed using the Population, Intervention, Comparison, Outcome (PICO) framework. A comprehensive literature search was conducted across Medline, Embase, CINAHL, and Cochrane (January 2010 to April 2025). Studies were independently screened, assessed for quality using Scottish Intercollegiate Guidelines Network (SIGN) criteria, and extracted into evidence tables. Draft statements were developed and refined through iterative feedback and online discussion. Final consensus was achieved using real-time Delphi, with  $\geq 80\%$  agreement required for endorsement. Reporting followed Accurate Consensus Reporting Document (ACCORD) guidelines.

**Results:** 67 consensus-based statements were developed. The top research priorities were identified based on the greatest proportion of “strongly agree” responses.

**Conclusion:** ETI has altered nutritional requirements in cwCF, yet evidence remains limited. This study presents the first consensus-based guidance for the nutritional care of cwCF receiving ETI, providing interim, expert informed recommendations and highlighting research priorities, particularly the need to re-evaluate traditional BMI targets.

## 1. Introduction

Most cwCF who are eligible for ETI and reside in countries where it is accessible have already started this therapy. However, its global use is still in the early stages, and the rollout has advanced faster than the development of comprehensive guidelines. The evidence that is available regarding the impact of ETI on the nutritional status of cwCF is still evolving and is either insufficient or shows inconsistent findings. Until more comprehensive data becomes available, it would be advantageous for clinicians to have consensus guidance that leverages the expertise of specialists in this area from around the world. The aim of this study is to: 1. Systematically review the literature on the effect of ETI on the nutritional status of cwCF; 2. Develop consensus-based guidance to support all members of the CF multidisciplinary team in making informed clinical decisions regarding the nutritional management of cwCF on ETI; and 3. Highlight existing research gaps and priorities.

## 2. Methods

This project was prospectively registered on the PROSPERO platform (ID: CRD42024587618). The project was led by TK, a senior paediatric dietitian with expertise in CF nutrition and prior experience in guideline development. TK, BP, CYO assembled an expert panel of 22 individuals comprising Dietitians, Gastroenterologists, Respiriologists, Endocrinologists and a community representative (parent of a cwCF). Clinician experts needed to meet the following criteria: recognized experts in their field, previous involvement in CF-related guidelines, and at least two years of clinical experience managing cwCF on ETI. Efforts were made to ensure geographical diversity, aiming for representation from as many countries as possible across Australia, North America, Asia and Europe. Conflicts of interest were declared at the project’s outset, and employees of pharmaceutical companies were excluded. Evidence-based research questions were developed by TK using the PICO model and then shared with the expert panel for feedback and final approval. In this model, the “P” (Population) was defined as children aged 0–21 years with CF. The “I” (Intervention) was ETI, while the “C” (Comparison) included cwCF on a different CFTR modulator, those not on any CFTR modulator, or children without CF. The “O” (Outcome) focused on aspects of nutritional status that the expert group identified as being affected, either positively or negatively, by the use of ETI: anthropometry (weight, height and BMI-for-age z scores or percentiles, body composition); biochemical (vitamins, minerals, proteins and lipids); diet; endocrine pancreatic status; exocrine pancreatic status; ETI administration. A comprehensive literature search strategy was developed by TK and validated by a librarian: elexacaftor plus tezacaftor plus ivacaftor OR elexacaftor ivacaftor tezacaftor OR elexacaftor tezacaftor ivacaftor OR ivacaftor plus elexacaftor plus tezacaftor OR ivacaftor plus tezacaftor plus elexacaftor OR ivacaftor tezacaftor elexacaftor OR ivacaftor elexacaftor tezacaftor OR kaftrio OR tezacaftor plus elexacaftor plus ivacaftor OR tezacaftor plus ivacaftor plus elexacaftor OR tezacaftor elexacaftor ivacaftor OR tezacaftor ivacaftor elexacaftor OR trikafta OR

ETI OR HEMT OR highly effective modulator therapy OR elexacaftor AND newborn\* OR neonat\* OR infan\* OR pre-schooler\* OR pre-schooler\* OR child\* OR adolescent\* OR pediatric\* OR paediatric\* OR youth\* OR teen OR teens OR teenage OR teen-age\* AND cystic fibrosis. Electronic databases, including Medline, Embase, CINAHL, and Cochrane, were searched from 1st January 2010 up until 1st March 2025 using the assigned keywords to find relevant primary studies (including conference abstracts published in peer reviewed journals). Grey literature was not included.

Identified studies from each database were uploaded into Covidence [1] for deduplication. The final list of titles and abstracts were screened independently by TK and a member of the expert panel against a pre-defined set of inclusion and exclusion criteria for each PICO (Supplementary Table 1). Two “yes” votes moved the study to the full text screening stage, two “no” votes excluded the study, one “yes” and one “no” moved the paper to the conflict folder where CYO made the final decision. Expert panel members and TK were blinded to each other’s votes. Full texts were obtained for all included studies and further scrutinized for inclusion by TK and an expert panel member using the same method described. In cases where studies included a mixed adult/paediatric population, the paper was only included if paediatric data were presented separately. Only studies published in English were considered, if the abstract only was in English then that was included.

The number of records identified, included, and excluded, along with the reasons for exclusions, were documented using PRISMA (Fig. 1) [2]. Data was extracted from each study by TK using a customised data extraction form (Supplementary Table 2). Extracted data was checked by a member of the expert panel with disagreements managed in the first instance by these individuals. Any conflicts that could not be resolved were escalated to CYO as arbiter. Each study was assessed for quality and risk of bias by both TK and an expert panel member using the SIGN levels of evidence (1++ to 4) (Supplementary Table 3a) [3]. Where TK and an expert panel member could not agree on the overall quality of a study CYO acted as arbiter. The body of evidence for each PICO question was synthesised in evidence tables. Following discussion between TK and an expert panel member, the strength of the evidence was classified using the SIGN framework. Grade A required at least one meta-analysis, systematic review, or randomised controlled trial rated as 1++, or a body of evidence rated as 1+, in both cases directly applicable to the target population and showing consistent results. Grade B reflected a body of evidence rated as 2++ OR 2+, directly applicable to the target population and demonstrating consistent results, while grade O reflected evidence rated as level 3 or 4. (Supplementary Table 3b) [3]. Draft statements for each PICO were then generated alongside narrative summaries. Where direct evidence was lacking, statements reflecting the clinical expertise of the panel were formulated and designated as good practice points (GPP). Expert panel members were provided with the systematic review and draft statements via email and invited to submit feedback before finalising the statements. The panel then participated in the consensus process which involved iterative and anonymous voting using the real time Delphi method [4] via the online platform Surveylet

[5]. This involved panel members voting on each statement with the ability to revisit and modify their voting as often as they liked over a 3-week period (between 2nd September and 23rd September 2025). Each time they accessed the platform they were shown their own responses as well as the updated responses of others and their reasons for voting a certain way. Voting options included ‘Strongly Agree’, ‘Agree’, ‘Disagree’, ‘Strongly Disagree’, and ‘Abstained/Unable to answer’. The consensus threshold was pre-defined as  $\geq 80\%$  of panellists selecting either ‘Agree’ or ‘Strongly Agree’. The top research priorities were determined based on the highest proportion of “Strongly Agree” responses. Reporting of this process was done in alignment with ACCORD (Accurate consensus reporting document) [6].

### 3. Results

The complete systematic review evaluating the effect of ETI on nutritional status in cwCF, structured according to the PICO framework, is provided in Supplementary File 1. Data were limited, with only 28 full text articles available; most reported on anthropometric outcomes, and no studies reported on minerals (iron or sodium), protein, diet or ETI administration. Importantly, ETI is currently approved only for individuals aged 2 years and older, and therefore the findings and guidance in this document apply to this age group.

The following section presents the final consensus-based statements, accompanied by an evidence classification and the percentage agreement, reported as the combined proportion of panellists selecting “Agree” or “Strongly Agree.” A complete breakdown of response categories is provided in Supplementary Table 4a. All 67 statements reached

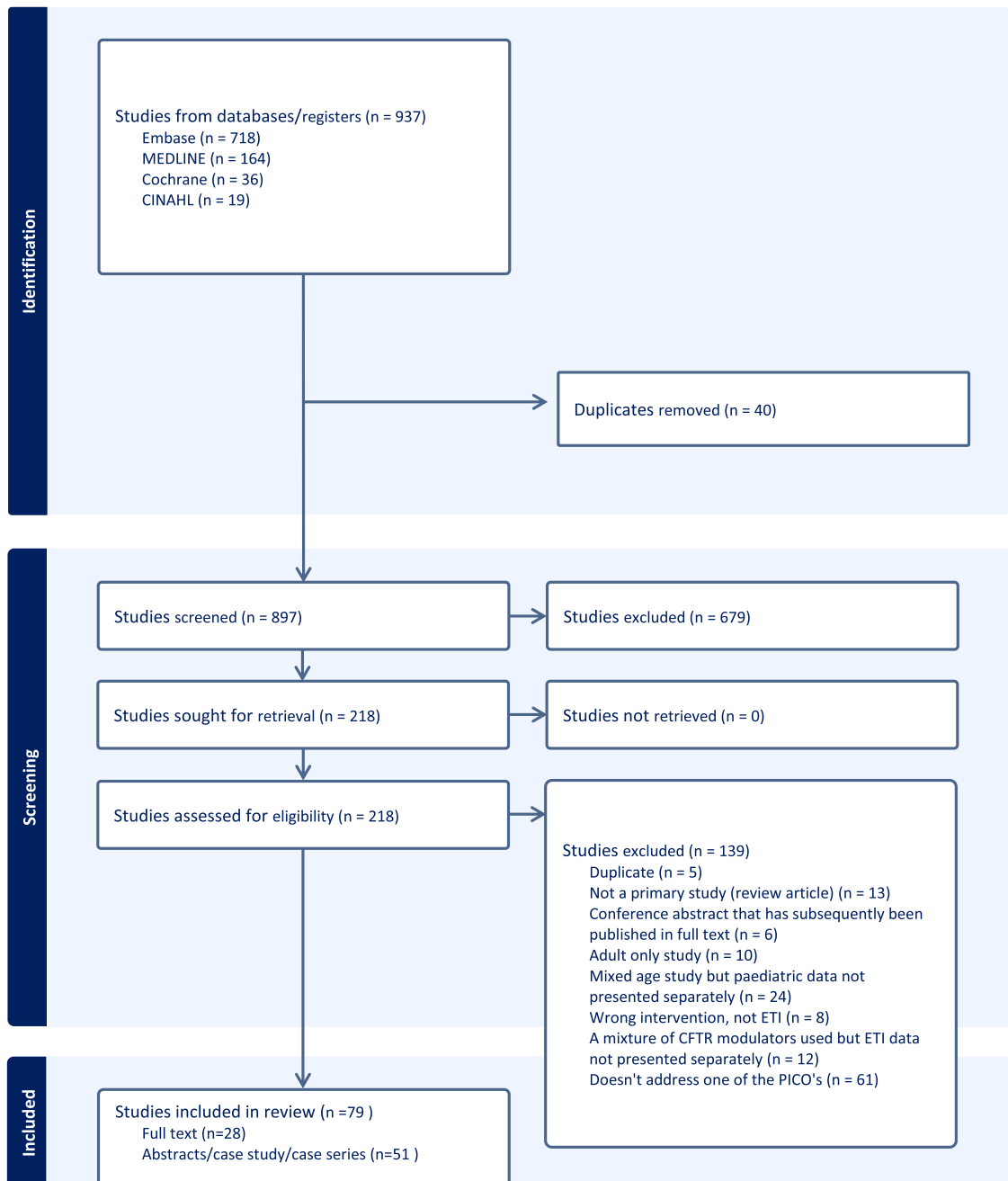


Fig. 1. Impact of CFTR modulator therapy (Elezacaftor/Tezacaftor/Ivacaftor) on the nutritional status of children with Cystic Fibrosis.

the predefined consensus threshold. For the majority of statements, direct evidence was limited, and they were therefore designated as Good Practice Points (GPP). All included studies were observational in design (cohort, case-control, or case series), such that the highest attainable evidence classification was grade B. In several instances, statements were assigned a grade O, reflecting inconsistency between studies or an insufficient number of studies to support a higher classification (Table 1).

Thirteen of the 67 statements were research-focused (Supplementary Table 4b). The highest priority areas for future nutrition research, identified by the greatest proportion of “Strongly Agree” responses, are outlined below. The remaining research statements achieved levels of agreement ranging from 63.16 % to 80 %. While numerous evidence gaps are identified in the systematic review, the research-focused statements reflect those prioritised by the expert panel during consensus discussions rather than the full scope of identified research needs.

1. **Nutritional Targets:** Longitudinal studies are needed to determine whether maintaining BMI-for-age at or above the 50th percentile (or BMI-for-age z-score  $\geq 0$ ) remains an appropriate nutritional target for cwCF on ETI or if updated nutritional targets are necessary (100 % strongly agree).
2. **Pancreatic Function:** Standardized clinical protocols are needed to guide pancreatic function reassessment and enzyme adjustment in children receiving ETI therapy (94.44 % strongly agree).
3. **Sodium Requirements:** Prospective studies are needed to investigate the impact of ETI on sodium requirements in cwCF (89.47 % strongly agree).
4. **Pancreatic Function:** Further prospective studies are needed to define predictors of pancreatic recovery, assess the durability of ETI-related improvements, and evaluate the impact of partial restoration of pancreatic function (88.47 % strongly agree).

4. Conclusion

This study presents the first consensus-based guidance addressing the nutritional management of cwCF receiving CFTR modulator therapy. Although focused on ETI, many of the issues discussed are likely to extend to newer generation modulators such as vanzacaftor, tezacaftor, deuterivacaftor. Early evidence highlights important changes in nutritional status following ETI initiation, however substantial knowledge gaps remain. A comprehensive synthesis of evidence underpinning this guidance is provided in the Supplement and should be consulted to support and contextualise the statements presented.

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CRedit authorship contribution statement

**Tamarah Katz:** Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Josie van Dorst:** Investigation, Supervision, Validation, Writing – review & editing. **Bernadette Prentice:** Investigation, Supervision, Validation, Writing – review & editing. **Christine L. Chan:** Investigation, Validation, Writing – review & editing. **Dimitri Declercq:**

Table 1

Consensus-based statements for the nutritional management of cwCF on ETI.

Statement	Grade	% Agreement*
<b>Anthropometry</b>		
Studies consistently report increases or maintenance of BMI-for-age z scores and weight-for-age z scores in cwCF following initiation of ETI therapy, with no studies indicating a decrease in these parameters.	B	95 %
Height-for-age z scores do not appear to significantly change over the short- to medium-term follow-up in cwCF receiving ETI therapy.	B	95 %
The magnitude of nutritional gains with ETI varies among individuals and may be influenced by factors including baseline lung function, age, CFTR genotype, prior modulator use, and colonization status with pathogens such as Pseudomonas aeruginosa.	B	100 %
Nutritional gains achieved on ETI may not be sustained if therapy is discontinued, highlighting the importance of ongoing treatment adherence.	O	100 %
Regular monitoring of BMI-for-age and weight-for-age z scores should be conducted in cwCF on ETI therapy to assess nutritional status and detect excessive weight gain early.	GPP	100 %
Further research is recommended to clarify the long-term effects of ETI on growth trajectories, including height, from childhood onwards.	GPP	100 %
Longitudinal studies are needed to determine whether maintaining a BMI for age at or above the 50th percentile (or a BMI-for-age z score of $\geq 0$ ) remains an appropriate nutritional target for cwCF on ETI or if updated nutritional targets are necessary.	GPP	100 %
<b>Body composition</b>		
Incorporating body composition assessment with standard anthropometry as part of the annual review offers a more comprehensive alternative to BMI alone, especially for tracking longitudinal changes in cwCF.	GPP	100 %
Future research should adopt standardised methodologies and consistent reporting metrics (including use of indices and z-scores) to improve comparability across studies and better understand the impact of ETI on body composition and clinical outcomes in cwCF. Ideally, studies would be multi-institutional to increase cohort size. Inclusion of children at many levels of health and nourishment would better represent the heterogeneity of the CF population.	GPP	100 %
<b>Fat soluble vitamins</b>		
Vitamin A levels may increase significantly in children receiving ETI, with some evidence suggesting an elevated risk of hypervitaminosis A.	O	100 %
Vitamin E levels do not appear to change significantly in children following ETI initiation.	B	100 %
Findings on vitamin D levels in children receiving ETI are inconsistent, and most studies did not adequately consider the effect of seasonality, which is a key factor in interpretation.	O	100 %
There is currently insufficient evidence to determine the effect of ETI on vitamin K status in children.	GPP	100 %
Given the increased bioavailability of preformed vitamin A (retinol) and the potential for toxicity, children on ETI should receive supplements containing predominantly provitamin A carotenoids ( $\beta$ carotene).	GPP	90 %
Children starting ETI should have their plasma/serum vitamin A levels measured before initiation and again within 1 to 3 months post to monitor for hypervitaminosis A. It is important to note that intracranial hypertension has been reported even in patients with normal vitamin A levels; therefore, observing an upward trend may be more clinically relevant.	O	100 %
Healthcare professionals should maintain a high index of suspicion for conditions linked to vitamin A toxicity, such as raised intracranial pressure, in children on ETI. Close monitoring for symptoms including headache, nausea, vomiting, and visual disturbances is essential. If clinical suspicion arises, fundoscopy to assess for	GPP	89.47 %

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Table 1 (continued)

Statement	Grade	% Agreement*
papilledema is warranted. Notably, intracranial hypertension has been reported when plasma/serum vitamin A levels are within the normal range or only mildly elevated.		
Prospective studies evaluating fat-soluble vitamin (FSV) status in children receiving ETI are warranted. These studies should account for relevant clinical context and include associated biochemical markers (e.g., C-reactive protein, lipid profiles, seasonality) to support accurate interpretation. Additionally, they should clearly report the reference cut-offs used for defining deficiency or excess and detail the composition and dosage of any vitamin supplements administered.	GPP	100 %
<b>Minerals, Iron</b>		
It is reasonable to assume that rates of iron deficiency (ID) and iron deficiency anaemia (IDA) may improve in cwCF receiving ETI therapy, potentially due to enhanced nutrient absorption, reduced inflammation and infection, correction of CFTR dysfunction, and greater attention to diet quality. However, routine assessment of iron status remains essential, given the high global prevalence of ID and IDA in children.	GPP	100 %
Prospective studies that include inflammatory markers alongside iron studies or use sTfR and account for dietary iron intake are needed.	GPP	100 %
<b>Minerals, Sodium</b>		
Urinary sodium:creatinine ratio is a useful tool to assess sodium status and can therefore be used to guide individualised dietary salt advice.	GPP	94.74 %
The urinary sodium:creatinine ratio provides a direct assessment of salt adequacy over the preceding 24 hours. It is particularly useful when there are significant changes in dietary intake or supplementation, when habitual intake appears excessive, or if elevated blood pressure is detected.	GPP	100 %
For cwCF and sweat chloride concentrations <30 mmol/L, sodium requirements are likely comparable to those of the general population. In this context, salt reduction advice may be appropriate depending on dietary intake.	GPP	84.21 %
For cwCF and sweat chloride concentrations >60 mmol/L, sodium requirements are expected to be elevated. However, if the child's diet already reflects a Western pattern high in energy-dense, nutrient-poor foods, baseline sodium intake may be sufficient. Additional supplementation should be individualised, taking into account overall diet, lifestyle, physical activity, and climate.	GPP	84.21 %
Prospective studies are needed to investigate the impact of ETI on sodium requirements in cwCF.	GPP	100 %
<b>Lipids</b>		
Low HDL-C is the most common lipid abnormality in cwCF, and early studies suggest this pattern persists following the introduction of ETI. Given that low HDL-C is an independent risk factor for cardiovascular disease, the underlying mechanisms and clinical implications of persistently low HDL-C in this population warrant further investigation.	GPP	95 %
Although significant increases in TC and LDL-C have been consistently observed in adults with CF on ETI, it remains unclear whether these are clinically significant and correlated with an increased risk in cardiovascular morbidity.	GPP	100 %
Universal cholesterol screening should be performed in the first decade of life, recommended at age 10. Earlier or more regular screening may be advisable in children with additional risk factors such as steatotic liver disease, obesity, normal weight obesity, a family history of high cholesterol or cardiovascular disease, poor diet, sedentary lifestyle, insulin resistance, or high blood pressure.	GPP	100 %
Prospective, longitudinal studies are needed to evaluate lipid profiles in cwCF as part of broader metabolic assessment. Results should report the proportion of	GPP	100 %

Table 1 (continued)

Statement	Grade	% Agreement*
children above and below reference ranges, rather than only mean changes, to better define cardiovascular risk.		
<b>Diet</b>		
Children with CF should focus on nutrient-dense, minimally processed, fibre-rich diets that emphasise fruits, vegetables, legumes, whole grains, nuts, and lean protein.	GPP	94.74 %
Focus on monounsaturated and preferably polyunsaturated fats while minimising saturated and trans fats.	GPP	100 %
Minimise processed meats.	GPP	90 %
Red meat should be consumed in alignment with population-level dietary recommendations.	GPP	100 %
Prioritise lean, minimally processed protein sources.	GPP	90 %
Minimise refined carbohydrates and sugar-sweetened beverages.	GPP	90 %
Choose wholegrain carbohydrates.	GPP	100 %
Consume fibre in line with population recommendations.	GPP	100 %
Assess energy requirements individually, considering lung function, pancreatic status, and overall growth needs. Dietitian-led assessment and ongoing monitoring are recommended.	GPP	100 %
For cwCF who continue to have elevated energy requirements, nutritional intake should be optimised to meet needs while maintaining diet quality. High energy needs can be met through nutrient dense foods rather than relying on energy-dense, nutrient-poor options.	GPP	100 %
Well designed, prospective studies are urgently needed to define optimal energy requirements, macronutrient composition, and overall dietary patterns for cwCF on ETI, including long-term outcomes related to growth, lung function, metabolic and gut health.	GPP	100 %
<b>Endocrine pancreas</b>		
Current evidence does not support changing recommendations for annual CFRD screening in people with CF following the introduction of ETI. While improvements in lung function and BMI post-ETI may prompt consideration of less frequent testing, ongoing research is needed to guide personalization of screening recommendations based on CFRD risk.	GPP	100 %
There is consistent evidence that HbA1c levels decrease in cwCF following initiation of ETI therapy (at least at the one-year mark), regardless of baseline glucose tolerance status. This suggests a potential improvement in overall glycaemic control. However, evidence beyond this time frame is currently limited.	B	95 %
Clinicians should be aware that ETI may enhance insulin secretion in some children, but this may be offset by a decline in insulin sensitivity, particularly in the context of ETI-associated weight gain.	O	100 %
There is currently insufficient evidence to recommend routine adjustments to insulin dosing in children with CFRD following ETI initiation. Management should continue to be guided by individualized clinical assessment.	GPP	100 %
Future prospective studies should stratify participants by baseline glucose tolerance and pubertal stage, include assessments of diet, physical activity, and body composition and incorporate long-term follow-up beyond one-two years to evaluate the durability of glycaemic outcomes.	GPP	100 %
<b>Exocrine pancreas</b>		
ETI therapy may improve exocrine pancreatic function in some children, particularly when initiated at a younger age. All PI cwCF commenced on ETI should have the opportunity for pancreatic function reassessment.	B	100 %
The likelihood of clinically meaningful pancreatic recovery is higher in younger children, suggesting a possible therapeutic window that supports early initiation of ETI.	GPP	100 %
FE-1 levels >200 µg/g may reflect recovery of sufficient pancreatic reserve to support improved digestive function, though this should not be interpreted as full restoration of normal pancreatic activity. Furthermore, this level of function may not be sufficient to maintain	GPP	94.74 %

(continued on next page)

Table 1 (continued)

Statement	Grade	% Agreement*
nutritional status during key developmental periods, such as puberty.		
FE-1 is the preferred method for assessing pancreatic function and should be considered together with clinical presentation to assess pancreatic function.	GPP	94.74 %
FE-1 should be measured 6 months after ETI initiation and annually thereafter, as some children may recover sufficient exocrine pancreatic function over time.	GPP	94.74 %
FE-1 levels >200 µg/g do not exclude mild or moderate pancreatic insufficiency, and interpretation should be made within the broader clinical context.	GPP	100 %
If FE-1 is >200 µg/g, a repeat test is recommended to confirm stability in level before considering any changes to PERT	GPP	100 %
If FE-1 is >500 µg/g, it is reasonable to trial cessation of PERT. Families should be counselled that PERT may need to be resumed based on ongoing clinical monitoring.	GPP	94.74 %
If FE-1 is between 200 and 500 µg/g, enzyme therapy should be tapered gradually, not stopped abruptly. Dose adjustments should be accompanied by close monitoring of growth, gastrointestinal symptoms, and nutrient absorption.	GPP	94.74 %
In children who tolerate serial PERT reductions without signs of malabsorption and with continued satisfactory growth, it is reasonable to discontinue enzymes. Families should be counselled that PERT may need to be resumed based on ongoing clinical monitoring.	GPP	100 %
Children who reduce or stop PERT should continue to undergo annual FE-1 testing, or more frequently if clinical concerns arise.	GPP	94.74 %
Families should be counselled proactively that if ETI adherence declines, or if ETI dose is reduced, or discontinued, FE-1 should be re-evaluated promptly, and enzyme therapy may need to be restarted.	GPP	100 %
Further prospective studies are needed to define predictors of pancreatic recovery, assess the durability of ETI-related improvements, and evaluate the impact of partial restoration of pancreatic function.	GPP	100 %
Standardised clinical protocols are needed to guide pancreatic function reassessment and enzyme adjustment in children receiving ETI therapy.	GPP	100 %
Prospective studies are needed to identify additional validated, non-invasive methods for assessing pancreatic function, ideally blood-based biomarkers that can be integrated into routine care to support monitoring and improve adherence.	GPP	100 %
<b>ETI administration and nutrition</b>		
Although product information recommends dosing ETI approximately 12 hours apart, strict adherence to this schedule may not align with typical mealtimes in children. To avoid the need for an additional snack solely for medication administration, thereby minimizing excess calorie intake and potential weight gain, clinicians may adopt a more flexible approach, such as dosing with breakfast and dinner.	GPP	100 %
ETI should be taken with fat-containing meals or snacks, but specifying exact grams of fat should be avoided until supporting evidence is available.	GPP	95 %
If a child typically skips meals (e.g., breakfast), is unwell, or prefers low-fat foods, they should still take ETI. However, if clinical response is inadequate, caregivers should be advised on the importance of including food, preferably containing some fat, with the medication.	GPP	100 %
Families should be routinely asked about the use of herbal or naturopathic supplements.	GPP	100 %
Due to the potential for many herbal products to affect CYP3A4/5 enzyme activity, it is advisable to avoid their use during ETI therapy. If there is strong parental preference for their use, consultation with their clinician and pharmacist is essential.	GPP	100 %
Future research should define the minimal fat content (in grams) needed in meals accompanying ETI to maintain drug concentrations within the therapeutic range.	GPP	100 %

\* Percent 'Agree' + percent 'Strongly Agree.'

Investigation, Validation, Writing – review & editing. **Tanja Gonska:** Validation, Writing – review & editing. **Jodi Grunert:** Investigation, Validation, Writing – review & editing. **Daina Kalnins:** Investigation, Validation, Writing – review & editing. **Christina N. Katsagoni:** Investigation, Validation, Writing – review & editing. **Amanda Leonard:** Investigation, Validation, Writing – review & editing. **Catherine M. McDonald:** Investigation, Validation, Writing – review & editing. **Paul McNally:** Validation, Writing – review & editing. **Monika Mielus:** Investigation, Validation, Writing – review & editing. **Anne Munck:** Investigation, Validation, Writing – review & editing. **Lutz Naehrlich:** Validation, Writing – review & editing. **Elizabeth Owen:** Investigation, Validation, Writing – review & editing. **Chris Smith:** Investigation, Validation, Writing – review & editing. **Sarah Jane Schwarzenberg:** Investigation, Validation, Writing – review & editing. **Vito Terlizzi:** Investigation, Validation, Writing – review & editing. **Michael Wilschanski:** Validation, Writing – review & editing. **Chee Y. Ooi:** Investigation, Supervision, Validation, Writing – review & editing.

#### Declaration of competing interest

All members of the expert panel provided declarations of potential conflicts of interest at the commencement of the project. Individuals employed by pharmaceutical companies were deemed ineligible for participation; this exclusion criterion was not applicable to any panel members.

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#### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.jcf.2026.02.004](https://doi.org/10.1016/j.jcf.2026.02.004).

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