

CHAPTER 14 SPECIAL CONSIDERATIONS FOR LIFE STAGE AND GENOTYPE

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This section covers the nutritional implications of pregnancy and genetic modulator therapies.

14.1 Pregnancy

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Pregnancy in women with CF is increasingly common. In Australia, approximately one in seven adults with CF have had children (majority: fathers)⁶⁷³. Most adult CF centres will need to provide pre-natal and post-partum care.

Many pregnancies in women with CF have been reported in the literature, generally with very good outcomes for both mother and baby, although some women do experience difficulties including maintaining adequate nutrition and an unpredictable effect on lung function⁶⁷⁴. Every pregnancy in CF should be considered as potentially high risk for both the mother and the foetus due to the effect on lung function⁶⁷⁵. The role that maternal nutrition plays prior to conception and throughout pregnancy is extremely important. Positive outcomes for both the woman with CF and her infant are associated with better nutritional status. Before pregnancy, a BMI greater or equal to 22kg/m² is recommended^{633,676}.

Assessment

A comprehensive nutrition assessment prior to conception provides an opportunity to optimise the nutritional status of a woman with CF. When the pregnancy is unplanned prompt nutrition assessment and counselling is essential. Ongoing nutrition assessments during the pregnancy and post-partum are also essential⁶⁷⁷.

DIET

Review diet history including a quantitative assessment of dietary intake and an assessment of vitamin and mineral supplementation, enzymes, oral and enteral nutrition support to address the requirements of pregnancy combined with CF.

CLINICAL

Key points to consider as part of a clinical nutrition assessment include:

- Anthropometry – including weight history prior to and during pregnancy
- Factors that may affect dietary intake:
 - nausea, vomiting, reflux and constipation
 - increased shortness of breath and coughing may become more frequent in the 3rd trimester
- Respiratory function tests and history prior to and during pregnancy

SCREENING FOR GESTATIONAL DIABETES MELLITUS

Pregnant women with CF should be screened for gestational diabetes mellitus. The following is recommended:

- A 2hr 75g fasting OGTT is recommended for any woman with CF who is planning a pregnancy or is confirmed pregnant if there has not been a normal CF-related diabetes screen in the last 6 months
- A 2hr 75g fasting OGTT with blood glucose measures at 0, 1, and 2 hours is also recommended at both 12–16wk and 24–28wk gestation in pregnant women with CF not known to have CF-related diabetes
- Post-pregnancy screening for CF-related diabetes using a 2-h 75g fasting OGTT is recommended 6–12wk post-partum¹⁴⁶

People with CF may be diagnosed with gestational diabetes mellitus (GDM) based on recommendations of HAPO Study Cooperative Research 2008⁶²⁴ and the Australasian Diabetes in Pregnancy Society⁶²⁵ (see table 14a).



Table 14a. Recommendations for diagnosis of gestational diabetes mellitus in people with CF

Gestational diabetes mellitus diagnosis	Blood glucose levels
Fasting plasma glucose (FPG)	>5.1mmol/l / (92mg/dL)
OR 1 hour plasma glucose	> 10 mmol/l / (180mg/dL)
OR 2 hour plasma glucose	>8.5 mmol/l / (153 mg/dl)

People with CF and diagnosed gestational diabetes mellitus are not considered to have CF-related diabetes. However, they do require screening for CF-related diabetes 6-12weeks post-partum. The 2hr 75g fasting OGTT is again recommended ^{146,624,625}.

BIOCHEMICAL AND LABORATORY DATA

The following laboratory data should be collected ⁶³³:

- Serum vitamin A
 - prior to conception or at the onset of pregnancy and at the beginning of the second and third trimesters
- Serum vitamin D
 - prior to conception or at the onset of pregnancy and/or at the beginning of the second and third trimesters
- Serum vitamin E
 - prior to conception or at the onset of pregnancy
- Iron studies at 20 weeks and supplementation considered if deficiency is developing

[Chapter 8](#) and [Chapter 9](#) respectively, provide further information on fat soluble vitamins and minerals.

Intervention

What are the nutrition considerations of the management of pregnancy in CF? ^{PICO 14.1.1}

[Ungraded] There is insufficient evidence to make a CF-specific recommendation.

Practitioners should be guided by the most recent guidelines for pregnancy and CF ⁶³³.

FOOD SAFETY

As with the general population, all women with CF who are planning a pregnancy, or as soon as possible after pregnancy is confirmed, should be informed about correct food handling procedures in order to minimise the risk of infections (eg. listeriosis, toxoplasmosis and salmonellosis) and mercury poisoning from fish, which are potentially harmful to the foetus. Furthermore, information should be provided on alcohol, caffeine and fish consumption akin to that for the general population ¹⁵².

FOLIC ACID

The role of folic acid in pregnancy is well established in the literature for the general population. However, recommendations for supplementation vary between countries. Factors specific to CF have not been identified.

Australian recommendations (general population):

- All women planning a pregnancy should take a daily supplement of 0.4mg folic acid per day per day pre-conception and in the first trimester to prevent neural tube defects ⁶⁷⁸.

New Zealand recommendations (general population):

- All women should take 0.8mg folic acid per day pre conception and in the first trimester ¹⁵³.
- Women with risk factors such as family history of neural tube defects, taking certain medications or having insulin dependent diabetes should be considered for additional supplementation of 5mg folic acid per day ¹⁵³.

VITAMIN A

What recommendations around vitamin A supplementation and monitoring should be provided to women with CF who are pregnant or planning a pregnancy ^{PICO 14.1.2}

[Ungraded] There is insufficient evidence to make a CF-specific recommendation.

Both vitamin A deficiency and excess are teratogenic and associated with adverse reproductive outcomes ^{675,677}. Assessment of vitamin A intake and status should be undertaken in the pre-conception period to establish that levels are within the normal range. Particular attention should be given to preformed vitamin A (i.e. retinol). Unlike preformed vitamin A, beta-carotene is not known to be teratogenic ³⁰². The total retinol equivalent (RE) intake, which will include the preformed and provitamin A intake, and the contribution of beta-carotene, should be adjusted based on serum retinol levels, with the goal of maintaining serum levels within the normal reference range. If serum vitamin A levels are normal, supplementation should continue at a dose <10,000 IU/day ^{411,633}. If levels are high it is considered prudent that the level of vitamin A supplementation is reduced ^{279,285}. Supplementation above upper recommended limits should only be recommended with caution. For people with CF are pancreatic insufficient and pregnant, vitamin A supplementation is still required in most circumstances. It is not currently recommended to cease all vitamin A supplementation in pregnancy and monitoring of its need is important. It is essential to review all non-prescription, over the counter and herbal vitamins/products that women may be taking. [Chapter 8](#) provides further information regarding supplementation, assessment and monitoring of vitamin A.

OTHER CONSIDERATIONS

Due to increased requirements in pregnancy, both the Australian and New Zealand health bodies recommend that all women who are pregnant or considering pregnancy, take an iodine supplement of 150 micrograms (µg) each day ^{152,153}.

The recommended dietary intake (RDI) for iron in pregnancy is 27mg/day and when lactating 9mg/day ⁴³. For this reason, iron supplementation may also be required for women with CF diagnosed with an iron deficiency during their pregnancy. The RDI for calcium in both the pregnant and lactating woman is 1000mg/day, unchanged from the RDI for adult females ⁴³. [Chapter 9](#) discusses assessing, monitoring and supplementation of minerals in greater detail. Vitamins D and E should continue to be monitored and supplemented to maintain levels in the recommended reference range. See [Chapter 8](#) for further information

WEIGHT AND NUTRITION STATUS PRE CONCEPTION, DURING PREGNANCY AND POST PREGNANCY

An overall weight gain of 12.5kg is considered typical for pregnancy and a weight gain of at least 11 kg has been recommended for women with CF ⁶⁷⁹. It may be useful to set a goal weight for each trimester to ensure overall weight targets are achieved. The recommended energy requirements for pregnancy vary from an extra 800-1200kJ/day per day. Women with CF, poor nutrition and low BMI prior to conception may need even more energy ⁶⁷⁴. Women with inadequately malabsorption control due to pancreatic insufficiency, and increased energy loss may require even greater energy intake to support adequate weight gain for pregnancy.

For women with or without CF, preconception weight, rate of weight gain during pregnancy, and total weight gain are crucial for both the health of the baby and the woman postpartum. Both the Australian and New Zealand governments have recommendations for total weight gain based on pre-pregnancy BMI, see Table 14b below ^{152,680}. Although not specific to CF this is useful to guide practice.

Table 14b. Recommendations for total weight gain during pregnancy, by pre-pregnancy or early pregnancy (less than 10 weeks) BMI

Pre-pregnancy or early pregnancy (<10 weeks)	Total weight gain
BMI <18.5 Kg/m ²	12.5 – 18 Kg
BMI 18.5 – 24.9 Kg/m ²	11.5 – 16 Kg
BMI 25.0-29.9 Kg/m ²	7 – 11.5 Kg
BMI ≥ 30 Kg/m ²	5 – 9 Kg



In order to achieve an optimal nutritional status prior to pregnancy and/or adequate weight gain during pregnancy, dietary intake and absorption should be maximized. If nutritional status cannot be optimised by a high energy diet alone, oral nutrition supplements or enteral nutrition support should be considered ⁶⁸¹. In those requiring tube feeding for the first time; it is best considered early in pregnancy when best tolerated. See to [Chapter 6](#) for further information.

GESTATIONAL DIABETES

CF-specific blood glucose targets for the woman with gestational diabetes have not been established. Recommendations from the American Diabetes Association ¹⁴⁶ for women with gestational diabetes should be followed. These targets are recorded in table 14c.

WOMEN WITH EXISTING CF-RELATED DIABETES

Women with established CF-related diabetes, who are planning a pregnancy or who are already pregnant, should optimise glucose control by adjusting their insulin regimen according to review by specialist endocrine and obstetric teams ⁶³³. The Australasian Diabetes in Pregnancy Society (ADIPS) has recommended BGL targets at fasting, one and two hours post prandial, as follows ⁶²⁵:

Table 14c. Targets for blood glucose levels in pregnancy for CF-related diabetes and gestational diabetes mellitus

	CF-related diabetes in pregnancy	Gestational diabetes mellitus
Fasting	5.0	5.3
1-hr postprandial	7.2 – 7.8	7.8
2-hr postprandial	6.7	6.7
A1C	6.0-6.5% recommended <6.0% may be optimal as pregnancy progresses	

BREASTFEEDING

The mother's choice of infant feeding method should be supported and it is prudent to discuss options during pregnancy. Many women with CF will be motivated to try to establish breastfeeding. Breast feeding in the mother with CF can be successfully undertaken, however close monitoring of nutritional status and fatigue should be undertaken ⁶³³. Breastfeeding further increases maternal energy, nutrient and fluid requirements and it can also be challenging for the mother to perform her regular treatment whilst looking after a newborn ⁶⁷⁵. It is important to support the mother in order to achieve optimal health for both herself and her newborn. Some women with CF will successfully maintain adequate health and nutritional status whilst breastfeeding with support from their healthcare team and family supports.

Monitoring & Evaluation

Aim to monitor the following closely:

- Weight gain
- Hydration status
- Development and/or management of gestational diabetes

Excellent communication between the CF specialist team and the obstetric service is required to ensure the best outcome for both the mother and infant ⁶⁷⁵.

Practice Points PICO 14.1.1

- Before pregnancy a BMI greater or equal to 22kg/m² is recommended.
- Undertake a comprehensive nutrition assessment prior to conception and ongoing during pregnancy and post-partum, including standard pregnancy counselling around food safety, alcohol, caffeine and fish consumption recommendations as per Australian¹⁵² and NZ recommendations¹⁵³.
- Clinicians should be guided by local country recommendations for supplementation amounts of folic acid. Assess the need for additional supplementation of 5mg folic acid per day in women with risk factors such as family history of neural tube defects, taking certain medications or with insulin dependent diabetes.
- Screening for Gestational Diabetes Mellitus is recommended via a 2hr 75g fasting OGTT when pregnancy is confirmed, at 12-16 weeks and 24-28 weeks gestation. Screen for CF-related diabetes at 6-12 weeks post-partum.
- Measure levels of fat soluble vitamins A, D and E at first review after pregnancy confirmation and the beginning of the second and third trimesters. Monitor levels and supplement to maintain in the reference range (refer to PP 14.2 for specific information about vitamin A supplementation).
- Undertake iron studies at 20 weeks' gestation and assess the need for supplementation if deficiency is developing. Tolerance of supplementation can be problematic in pregnancy further aggravating gastrointestinal symptoms especially constipation. Preventative management strategies including use of stool softening agents can be helpful.
- Weight gain of at least 11 kg has been recommended for women with CF. If nutritional status cannot be optimised by a high energy diet alone, explore oral nutrition supplements or enteral nutrition support. In those requiring tube feeding for the first time; it is best commenced early in pregnancy when best tolerated
- It is important to discuss infant feeding options during pregnancy with women with CF. Breast feeding in the mother with CF can be successfully undertaken, however close monitoring of nutritional status and fatigue should be undertaken
- It is important to monitor the weight of the woman with CF post-partum. Significant weight loss due to breast-feeding, and potential time burden that may compromise self-care can impact on overall health. Optimising nutrition at this time is vital.
- For any complex issues in the pregnant woman with CF, consult a CF specialist adult centre.

Practice Points PICO 14.1.2

- Measure fat soluble vitamin A level at first review after pregnancy confirmation and at the beginning of the second and third trimesters.
- If normal vitamin A levels, supplementation should continue at a dose <10,000 IU/day of retinol. These levels are in line with recommendations for the healthy population in pregnancy.
- Reassure the woman that supplements are being prescribed to prevent vitamin A deficiency which like vitamin A excess, is also teratogenic.
- If vitamin A levels are high, it is recommended to reduce vitamin A supplementation. A different multivitamin supplement may be required with lower vitamin A (particularly preformed vitamin A, retinol). Assess adequacy of other fat soluble vitamins if the CF-specific multivitamin is ceased.
- More frequent monitoring of vitamin A levels may be required following changes to supplement formulation and/or dose.
- Review dietary intake of vitamin A including oral and enteral supplements with particular attention to high retinol sources.
- Review all non-prescription, over the counter supplements with particular consideration for high retinol supplements (e.g. cod liver oil).



Translating into Practice

- The common multivitamin preparation used in CF management vitABDECK contains 0.4mg folic acid, but nil iodine. Iodine is available in other multivitamin preparations or through a folic acid and iodine combination supplement.
- VitABDECK contains Vitamin A as preformed retinol 2500IU and beta-carotene 3mg (1665IU). People with CF who are pregnant and taking vitABDECK prior to pregnancy should continue use unless alternate management is recommended by CF healthcare provider following thorough assessment.
- Iron supplementation can be problematic in pregnancy further aggravating gastrointestinal symptoms especially constipation. Preventative management strategies including use of stool softening agents can be helpful. A review of salt, fluid and fibre intake may also be beneficial.
- It is important to monitor the weight of the woman with CF post-partum. Significant weight loss due to limited time and self-care can impact overall health and optimizing nutrition at this time is vital.
- Breastfeeding mothers require close monitoring to ensure maintenance of adequate nutritional status

14.2 Genetic modulator therapies

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CF is caused by over 1700 different mutations in the CFTR gene, which are classified into six different classes based on the protein defect that causes disease^{682,683}, as shown in table 14d below. Recent advancements in therapies target correction of the function of this underlying defective protein. These treatments are called genetic modulators⁶⁸⁴. Gene modulators are targeted towards specific gene mutations, and are categorized into two groups: CFTR potentiators and CFTR correctors.

Genetic modulator therapy is an emerging field, and so it is important to note that the information provided in this section reflects the publication date.

Table 14d. Classifications of Gene Mutations That Cause Cystic Fibrosis*

Class	Example mutations	Description
I	G542X, R1162X W1282X	Mutations impair protein production, and being often nonsense mutations (with premature stop codons) they lead to mRNA degradation by a process called nonsense-mediated decay.
II	F508del R560T A561E	Affect CFTR processing due to misfolding which is recognized by endoplasmic reticulum quality control retention and which targets proteins with abnormal conformations to degradation.
III	G551D	Disrupt CFTR channel regulation through impaired gating.
IV	R334W	Decrease chloride ion conductance (flow) through chloride channel.
V	3272-26A>G	Significantly reduce normal protein levels, often by affecting splicing and generating both aberrant and normal transcripts
VI	F508del after rescuing to cell surface	Lead to decreased retention/anchoring at the cell surface, often associated with decreased protein stability at the plasma membrane

*Adapted from Bell, et al.⁶⁸³

IVACAFTOR

Ivacaftor (also known as VX-770 and Kalydeco®) is a CFTR potentiator which improves CFTR protein function at the epithelial cell surface⁶⁸⁴. Due to its mechanism of action, Ivacaftor is only suitable for people with class III and IV CFTR mutations (e.g. G551D, G1244E, G1349D, G178R, G551S, S1251M, S1255P, S549N, S549R and R117H)⁶⁸⁴. Ivacaftor has been proven safe and efficacious in people aged six years and over^{155,158}. A recently published study by Davies et al also demonstrated the safety of Ivacaftor for children ages two to five years over a period of 24 weeks⁵³⁰. Longer follow up trials are yet to be completed.

In Australia approximately 300 people, aged six years or more with one of the nine specified gating mutations, are eligible to be prescribed subsidised Ivacaftor through the Pharmaceutical Benefits Scheme (PBS)^{685,686}. Although Ivacaftor is approved in the United States of America for people with CF over the age of six who have one R117H mutation, this does not extend to Australia. The New Zealand Medicines and Medical Devices Safety Authority (MEDSAFE) have also approved the safety of Ivacaftor but funding is yet to be addressed.

Significant improvements in respiratory, nutritional and quality of life outcomes have been documented for people receiving Ivacaftor^{154-159,161,162,530}, which may change the nutritional needs of people with CF.

Due to the molecular target of Ivacaftor, it is not suitable for more than 90 percent of the CF population based on their CFTR mutations. Research into targeted therapies for more common CF genotypes is a priority⁶⁸⁴. Phase III trials of the CFTR corrector/potentiator therapy Lumacaftor/Ivacaftor (also known as VX-809 and Orkambi®) for people who are homozygous F508del have shown minimal improvements in respiratory outcomes, hospitalization frequency and BMI⁶⁸⁷. Improvements observed with this medication offer minimal clinical advantage (i.e. lung function clinical benefit was much lower than that demonstrated by Ivacaftor and the gating mutations). Ongoing studies with an alternative CFTR corrector (VX-661) in combination with Ivacaftor continue in both F508del homozygous and heterozygous populations. Lumacaftor/Ivacaftor is approved in Australia for those people homozygous for F508del alleles aged 12 years; however, this medication is not currently reimbursed by the government and thus it is not widely available. No CFTR corrector therapies are approved for use in New Zealand.

Whilst the success of these early CFTR modulators has dominated the literature in recent years, other gene specific therapies such as correctors and read-through-agents offer great promise for future therapeutic options⁶⁸⁴.

Disease Aetiology

What are the implications of Ivacaftor on nutritional status in children >2 years and adults with cystic fibrosis who have at least one G551D or other gating mutation allele? PICO 14.2.1

[Grade A] There is evidence to suggest that continued use of Ivacaftor therapy leads to significant improvements in weight and BMI in adults and children > 2 years.¹⁵⁴⁻¹⁶¹

Weight gain is likely to be multifactorial and is currently not well understood. The weight gain seen in adult populations is mostly within the first month and then plateaus^{154,156,158}, while paediatric patients continue to gain weight over time, as would be expected^{155,157,158}. Due to the wide range of ages of children and adolescents collectively studied it is difficult to interpret weight gain patterns.

Whilst not included in the formation of the evidence-based recommendation above, an ongoing study shows that, in adults, acute weight gained after commencement of Ivacaftor reflects an increase in total body water⁶⁸⁸. Increase in fat free mass does not occur until 1 month after treatment. Further validation is underway.

Are there any other nutritional considerations (energy, salt intake) that practitioners should take into consideration for people on Ivacaftor therapy? PICO 14.2.2

[Grade D] Well-nourished individuals on Ivacaftor therapy may benefit from dietary advice consistent with the general healthy population recommendations, although at this stage there is insufficient evidence to recommend routine changes of energy and salt intake for people with CF receiving this medication.¹⁵⁴⁻¹⁶³

Significant improvements in sweat chloride levels are noted across studies^{154,155,157,159,530}; however, the relationship between sodium intake and sweat chloride levels is currently unknown¹⁵⁶. In 2015, McKay et al. demonstrated that the majority of patients receiving Ivacaftor therapy (approximately 80 percent) had substantially improved fat intake and decreased fat excretion⁶⁸⁹.

Several factors contributing to improvements in nutritional outcomes post Ivacaftor have been hypothesised including gut pH increases (i.e. less acidic) and energy balance changes⁶⁹⁰. A recent publication has also shown that the histological changes of CF revert to normal after Ivacaftor use⁶⁹¹. Changes in gut pH may have implications for the use of acid regulation medication which is often required concurrently with enzyme therapy to enhance enzyme activity and fat absorption (e.g. PPIs). In addition, one small pilot study of five individuals suggests that Ivacaftor



therapy may improve glucose tolerance ¹⁶³. Secondary analysis of Phase III randomized control trial data by Borowitz, et al. ⁶⁹² revealed that there were no linear correlations between changes in body weight seen and improvements in FEV1 or chloride levels. A recent study also showed significant improvements in faecal elastase concentration (a measure of pancreatic function) after treatment with Ivacaftor, with some participants aged 2-5yo converting from abnormal to normal pancreatic function after 24 weeks of treatment ⁵³⁰.

Further research is required on the nutritional implications of Ivacaftor therapy, specifically its effects on body composition, bone mineral density, energy and salt requirements, enzyme dosing and acid regulation.

Assessment

What is role of gastrointestinal and/or other nutritional outcome measures in people with CF receiving Ivacaftor therapy? ^{PICO 14.2.3}

[Ungraded] There is insufficient evidence to make a CF-specific recommendation.

There is currently no specific evidence available to guide practice in this area. Nevertheless, practical considerations for the nutritional assessment of people on genetic potentiator therapy can be inferred from the available literature.

DIET

Complete a comprehensive dietary assessment, ensuring that genetic modulators are being taken per prescribed dosing recommendations, with a fat containing meal or snack (amount and type of fat are not important). Ensure appropriate enzyme dosing for the meal or snack.

CLINICAL

- People with CF-related diabetes on insulin are at risk of experiencing hypoglycemia, especially upon commencement of Ivacaftor – close monitoring of blood glucose levels may be appropriate ⁶⁹³
- Regularly monitor weight gain and trends (including BMI) and consider body composition to prevent excessive increases in fat mass. Other accepted clinical endpoints to measure nutritional status such as body measurements and waist circumferences have limitations when used with the CF population as discussed in Chapter 5 Nutrition Assessment
- Monitor perception of body image.

BIOCHEMICAL AND LABORATORY DATA

A recent descriptive analysis reviewed the clinical relevance, reliability, validity, and feasibility of using gastrointestinal outcome measures to measure CFTR protein function ⁶⁹⁰. To help guide concurrent nutritional related therapies (e.g. PERT and PPIs), practitioners may wish to examine faecal elastase and measure intestinal fat absorption for people with CF of all ages being treated with CFTR modulators ⁶⁹⁰.

Intervention

Working proactively with the person with CF and/or their family, consider discussing the following:

- discuss possible nutritional implications, weight, diet choices and the importance of individualised dietary adaptations
- the potential impact on PERT and sodium
- the potential impact of weight changes and any related concerns

Individuals with CF-related and/or CF-related liver disease may have additional nutrition related concerns (e.g. episodes hypoglycemia, raised liver function test results). These concerns should be reviewed in the context of the individual's CF disease and dietary intake, as well as potential side effect/s of CFTR modulator therapy ⁶⁹³.

Monitoring & Evaluation

Dietitians should aim to engage individuals with CF on CFTR modulator therapies every three months to ensure nutrition status, dietary management and weight gain are monitored proactively, ideally in conjunction / alongside the interdisciplinary team.

If the course of CF lung disease is altered (e.g. change in exacerbations frequency), an individual's nutritional status and/or dietary intake patterns may change if overall nutritional requirements reduce, or appetite and intake become less variable over time. Reduction in overall energy intake may not be a concern if adequate nutritional status is maintained; however attention to diet quality may be required.

Practice Points PICO 14.2.1 and 14.2.2

- Practitioners need to proactively monitor weight gain patterns throughout the first few years of Ivacaftor therapy so that nutritional recommendations can be tailored to the rapidly changing body composition.
- People with CF-related diabetes are at risk of experiencing hypoglycemia, especially upon commencement of Ivacaftor – monitor blood glucose levels closely
- The relationship between sodium intake and sweat chloride levels is currently unknown. There is not yet clear evidence for a change in salt supplementation requirements, but provide advice on sodium requirements based on the person's signs and symptoms of salt depletion.
- Genetic modulators should be taken with a fat containing meal or snack
 - People who are PI should also take their PERT at this time
- Children:
 - After establishment of Ivacaftor ensure that catch up growth is achieved before considering altering a child's diet in terms of energy and/or salt.
- If the course of CF lung disease is altered (e.g. a reduction in exacerbation frequency), an individual's nutritional status or dietary intake pattern may also change if overall nutritional requirements are lowered or appetite/intake becomes more stable. A reduction in overall energy intake may not be a concern if adequate nutritional status is maintained, however attention to diet quality may be required.

Practice Points PICO 14.2.3

Gastrointestinal outcome measures such as faecal elastase and intestinal fat absorption are appropriate to use in this population group. Use of these tests may help guide practitioners in what are appropriate concurrent nutritional therapies (i.e. PERT and protein pump inhibitors).

As genetic modulator therapies are relatively new, it is possible that a range of clinical and symptomatic observations will be made, about which more evidence to guide practice recommendations may emerge in the future in relation to modulation or restoration of physiological functions affected by CFTR. There is limited evidence to date of the impact of other CFTR modulator therapies on gastrointestinal function or nutritional outcome measures. Until such evidence is available, identify and evaluate any changes in gastrointestinal or other symptoms in people taking CFTR modulator therapies.

