NUTRICIA

Fortimel

FortiCare

Sensations

2.4 kcal/ml

Fortimel Forticare Sensations 2,4kcal is a food for special medical purposes.
For the dietary management of patients with or at risk of disease related malnutrition,
due to cancer, chronic catabolic disease, or cachexia and must be used under medical supervision.

EOF Registration No: FORTIMEL FORTICARE SENSATIONS 2,4KCAL (Cool Berry, Cool Mango/ Peach) 67587/06-06-2024

FOR HEALTHCARE PROFESSIONALS ONLY

CONTENTS

1 What is cancer-related malnutrition?

Cancer

Cancer incidence is increasing rapidly throughout the world. GLOBOCAN estimated there were 19.3 million new cases of cancer and 9.9 million deaths from cancer worldwide in 2020[1]. Before reaching the age of 75 years, 21.4% of people will develop cancer and 17.7% will die from this disease. It is estimated that 1 in 5 men and 1 in 6 women will develop cancer and 1 in 8 men and 1 in 10 women will die from cancer[2]. These stark figures do not convey the many challenges that patients face during their cancer journey, including the side effects of treatments and a wide range of potentially serious cancer-related emergencies[3] and chronic complications, such as disease-related malnutrition (DRM) and cachexia, that impact quality of life and survival. For many patients cancer is a chronic disease.

Disease-related malnutrition is common in patients with cancer and is associated with poorer patient outcomes[19].

Overlap exists between the terminology (and the conditions) related to nutritional status in patients with cancer. Therefore it is helpful to consider definitions from the European Society for Clinical Nutrition and Metabolism (ESPEN) expert group for action against cancer-related malnutrition[4] since these address definitions in the specific context of cancer. However, whilst the definitions are important the over-arching principle is that they are intended to help identify and treat the underlying metabolic and nutritional issues that adversely affect outcomes in cancer patients[4].

DISEASE-RELATED MALNUTRITION "is a condition that results from the activation of systemic inflammation by an underlying disease such as cancer[5]. The inflammatory response causes anorexia and tissue breakdown that can, in turn, result in significant loss of body weight, alterations in body composition, and declining physical function[5]."

CACHEXIA "is a multifactorial wasting syndrome characterized by involuntary weight loss with ongoing loss of skeletal muscle mass with or without loss of fat mass; such wasting cannot be reversed by conventional nutrition care and may lead to functional impairment[6-10]."

In **PRE-CACHEXIA** "early clinical and metabolic signs precede extensive involuntary loss of weight and muscle. Risk for cachexia and its worsening depends on factors such as cancer type and stage, extent of systemic inflammation, and degree of response to anticancer therapy[6,8]."

SARCOPENIA "is low lean body mass (LBM) (mostly muscle); fatigue is common, strength may be lessened, and physical function limited[7,8]. As functionality is lost, patients with cancer may no longer be able to live independently, and they often report lower quality of life[11]."

Figure 1. Malnutrition in patients with cancer: anorexia, cachexia and sarcopenia. Anorexia associated with poor food intake leading to weight loss is common in disease-related malnutrition, especially in cancer patients. These harmful changes are driven by pro-inflammatory cytokines and tumor-derived factors. The associated conditions of cachexia and sarcopenia may also be present or may develop as cancer advances-cachexia due to inflammation, and sarcopenia due to fatigue and low physical activity and to other causes of declining muscle mass and function.

Adapted from Arends et al., 2017[4].

ANOREXIA AND LIMITED FOOD INTAKE

Anorexia is associated with poor food intake by:

- Altered CNS* appetite signals with symptoms resulting from cancer or its treatments (nausea, diarrhea, pain)
- Physical limitations to food intake and use (mouth ulcers, GI* obstruction)

**CNS; Central nervous system, GI; gastrointestinal*

PRECACHEXIA AND CACHEXIA

With cachexia, anorexia and weight loss are worsened by:

- Catabolic drivers (inflammatory cytokines) that further reduce nutrient intake and increase metabolic needs

SARCOPENIA

Sarcopenia ensues as:

- Body reserves are depleted
- Lean body mass, mostly muscle, is lost

KEY PRACTICE POINT

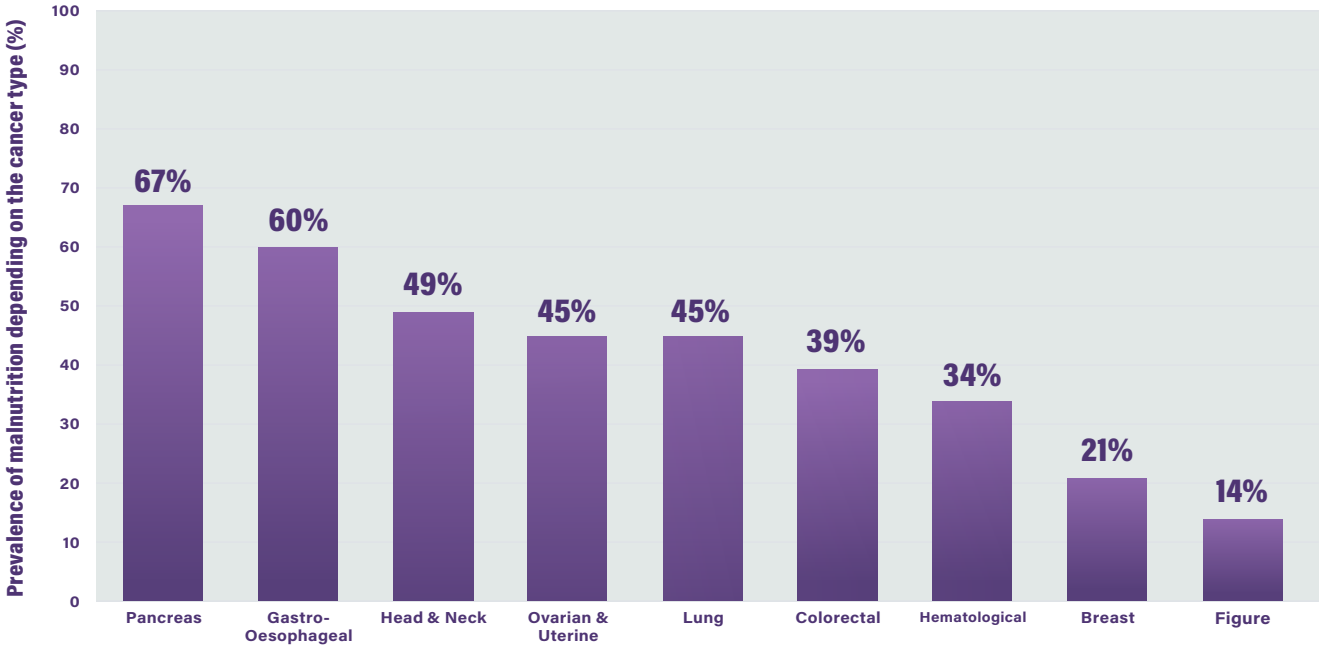
Whilst the definitions for cancer-related malnutrition are important the over-arching principle is that they are intended to help **identify and treat** the underlying **metabolic** and **nutritional** issues that adversely affect outcomes in cancer patients[4].

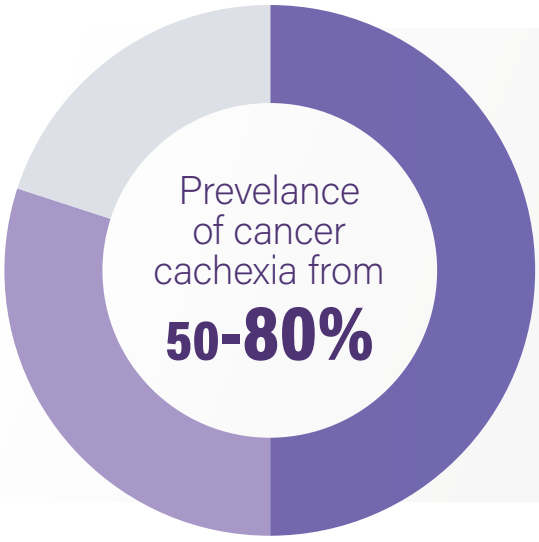
How prevalent is cancer-related malnutrition?

Overall, at least 1 in 3 cancer patients is malnourished[12]. On average, prevalence of malnutrition ranges from 20 to more than 65%, depending on cancer type, stage and patient demographics (Figure 2)[13].

Figure 2. High prevalence of cancer-related malnutrition in various cancer types.

Adapted from Hebuterne et. al., 2014[13].

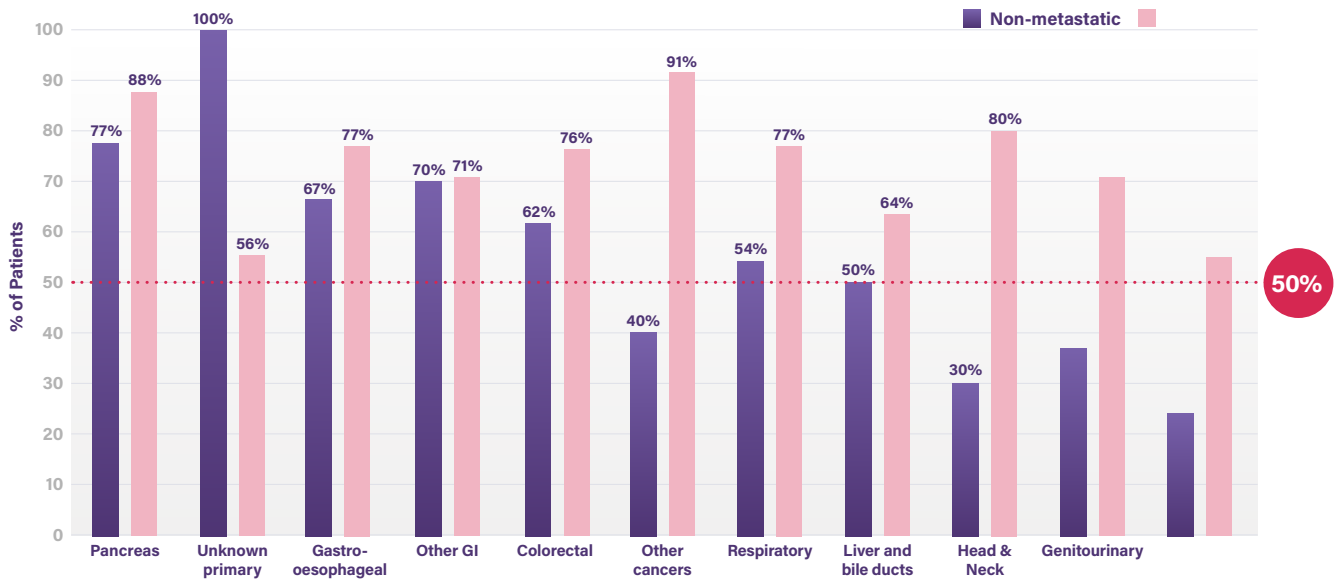




The overall prevalence of **cancer cachexia ranges from 50 to 80%** in patients with advanced cancer[14]. Systemic inflammation, is key hallmark feature of cancer cachexia and is highly prevalent in patients with cancer affecting >50% of patients with cancer (except breast cancer) (Figure 3)[15].

Figure 3. Prevalence of systemic inflammation by cancer site, as determined by % patients with elevated blood levels of C-reactive protein. (N=1087). M0=Stage I-III, M1= Stage IV.

Adapted from Muscaritoli et al., 2017[15].



Loss of muscle mass is a major component of weight loss in cancer-related malnutrition and cachexia, and may represent >70% of total body mass lost by a cancer patient[16]. Studies have shown that patients with cancer have a 24-fold higher rate of muscle loss than observed in healthy aging adults[17,18] and between 38% and 70% of patients are considered to have low muscle mass (sarcopenia)[19]. Table 1 shows the prevalence of low muscle mass across different tumour types as measured by computed tomography (CT) images, which are the gold standard method for measuring body composition and which are routinely obtained for diagnostic and surveillance purposes in oncology care.

Table 1. Prevalence of low muscle mass in patients with cancer according to the primary tumour location in the literature (all stages). Adapted from Ryan et al., 2016[19].

Primary cancer	% with low muscle mass (sarcopenia)	
	Median	Range
Lung	70%	(47-79%)
Head and neck	64%	
Pancreatic	56%	(44-89%)
Liver	54%	(28-76%)
Oesophagus	53%	(16-75%)
Kidney	53%	(29-90%)
Prostate	52%	(47-56%)
Lymphoma	51%	(47-55%)
Colorectal	49%	(20-80%)
Bladder	48%	(33-69%)
Gastric	47%	(23-70%)
Ovarian	47%	(45-50%)
Melanoma	44%	(24-63%)
Mixed	41%	(15-47%)
Breast	38%	(14-67%)

The definitions of low muscle mass are: Prado et al. (2008)[20]: Skeletal muscle index (SMI) <52.4 cm^2/m^2 in men and <38.5 cm^2/m^2 in women. Martin et al. (2013)[21]: SMI <43.0 cm^2/m^2 in men with a BMI <25 kg/m^2 and <53.0 cm^2/m^2 in men with a BMI >25 kg/m^2 and SMI <41.0 cm^2/m^2 in women. Baumgartner et al. (1998)[22] converted dual-energy x-ray absorptiometry (DXA) cut points by Mourtzakis et al. (2008)[23] as SMI <55.4 cm^2/m^2 in men and <38.9 cm^2/m^2 in women.

KEY PRACTICE POINT

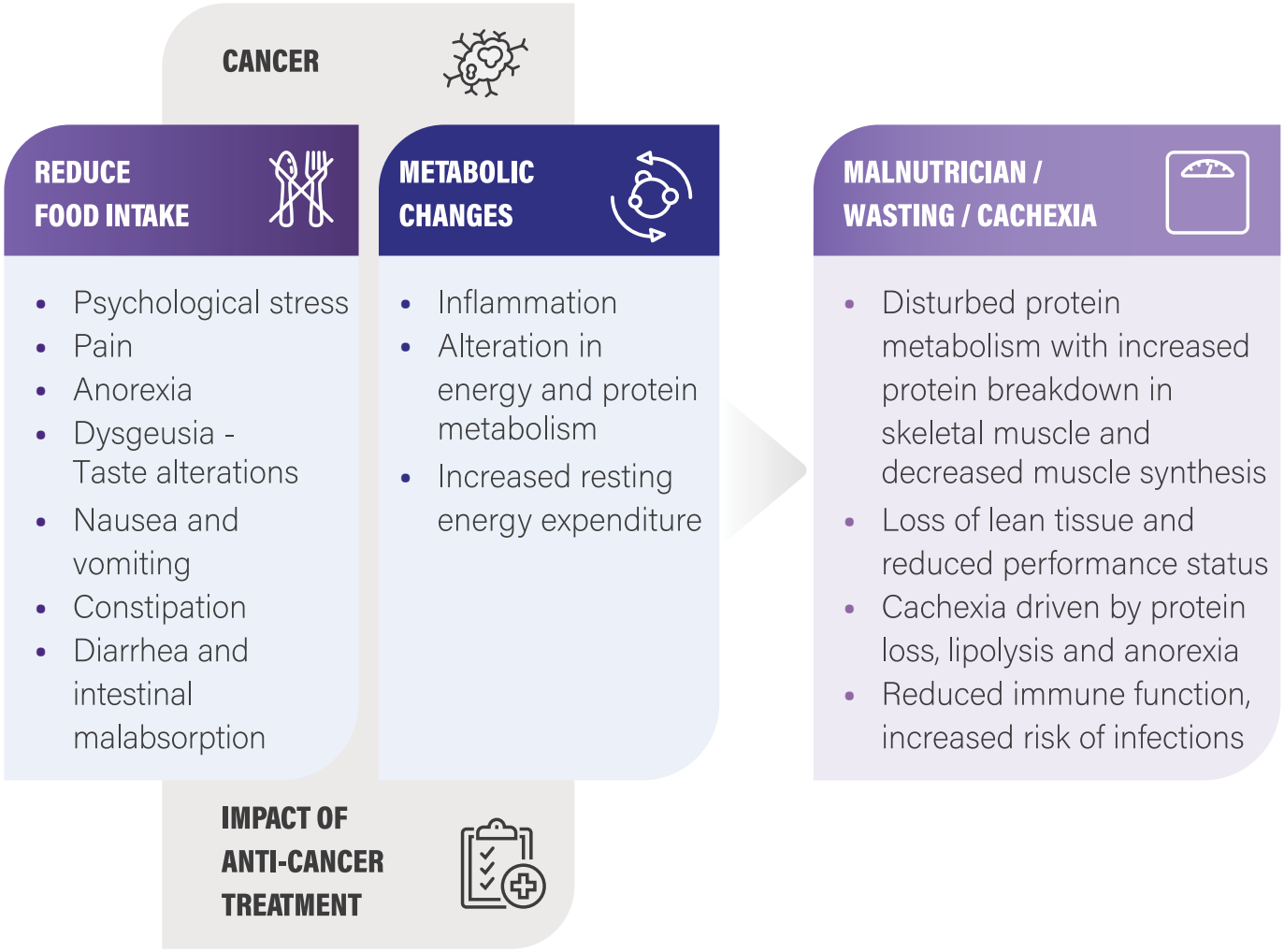
Malnutrition, cachexia and low muscle mass (sarcopenia) are common in cancer patients. **Systemic inflammation** is a key hallmark feature of cancer cachexia.

The causes of cancer-related malnutrition

What causes cancer-related malnutrition?

Malnutrition in patients with cancer is both multi-factorial and complex. Reduced food intake and metabolic alterations driven by both the malignancy and impact of therapeutic treatment are key factors in its development (Figure 4).

Figure 4. Multifactorial aetiologies for malnutrition, wasting and cancer cachexia in patients with cancer. Adapted from Marin Caro et al., 2007[24].



Systemic inflammation

In addition to reduced food intake, cancer is associated with a variety of metabolic changes leading to systemic inflammation, which can result in the development of a 'catabolic state' in which increased catabolic metabolism (as opposed to anabolic metabolism) accelerates weight loss[6,16] and drives further specific nutritional needs of cancer patients. Pro-inflammatory cytokines secreted by either immune cells or tumours play a key role in mediating the metabolic, physiologic and behavioural features of cancer-induced weight and muscle loss.

Adapted from Arends et al., 2017[4].

Figure 5. Systemic inflammation from the host and host-tumour interaction contribute to malnutrition.

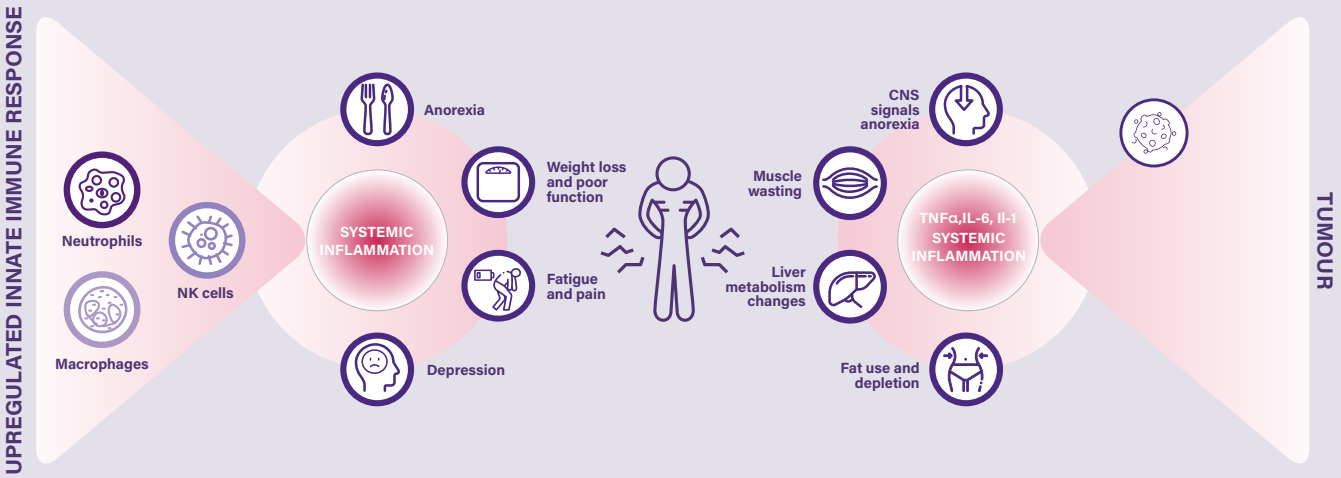


Figure adapted from Arends et al.[2]

Taste and other sensory alterations

Many cancer patients experience taste abnormalities throughout the course of their disease[25]. Taste changes are exacerbated during treatment, with a high prevalence ranging from 16-70% during chemotherapy and 50-70% during radiotherapy[26]. Dysgeusia is most common, including a reduction of the taste threshold as well as the development of bad tastes, such as bitter, chemical, metallic or nauseating tastes[27, 28].

The alterations in taste are an underestimated cause of eating problems and adherence to nutritional interventions in patients with cancer[29-32]. Sensory alterations are associated with a decrease in appetite and a reduction in energy and nutrient intake, adversely affecting patients nutritional status and leading to subsequent weight loss (Figure 7)[33-39].

Figure 6. Sensory alterations are commonly experienced by cancer patients.

Taste and smell alterations may develop throughout the course of the disease, **before, during and up to 1 year after treatment**[26]

Metallic taste has been reported in **32-34%** of patients with various cancer types[40,41]

Up to **70%** of cancer patients experience **taste changes** during chemotherapy and radiotherapy[26]

Prevalence of **dry mouth/xerostomia of 40%** was reported in cancer patients with various tumor types undergoing chemotherapy[42,43]

Figure 7. The impact of sensory alterations on nutritional intake in cancer patients.

KEY PRACTICE POINT

Reduced food intake and **metabolic changes** driven by cancer and it's treatment are key factors in the development of cancer-related malnutrition. **Taste alterations** affect many patients with cancer and are an underestimated cause of reduced energy and nutrient intake.

2 The impact of cancer-related malnutrition

Numerous studies demonstrate the negative impact of weight loss and malnutrition on cancer patients.

Involuntary weight loss and muscle loss reduces the ability of patients to receive, tolerate and respond to therapy. BMI and weight loss independently predicts poor survival[47]. Weight loss is a major source of distress for patients and their caregivers, affecting patients' quality of life and physical function.

Malnutrition and loss of muscle mass in cancer patients are associated with:

- More complications post operatively[48]
- More infections[12,49, 50]
- Longer length of hospital stay[12, 51, 52]
- Increased re-admissions[53, 54]
- More toxicity to systemic anti-cancer therapy[55, 56]
- Reduced quality of life[57-60]
- Increased risk of mortality[12, 61]
- Poorer overall survival[48, 49, 57]

Muscle loss, treatment toxicity and poorer tolerance to anti-cancer treatment

'Tolerability of treatment regimes and outcome of therapy depend on several aspects, one of the most important being the nutritional status of the patient.'

Muscaritoli, Arends and Aapro, 2019[62].

A review of several clinical studies investigating the relationship between muscle loss and dose limiting toxicity in patients summarises data showing that patients who lose muscle mass experience dose limiting toxicities more frequently than patients who maintain muscle mass. These findings are consistently observed across patients with different cancer types and who receive different anti-cancer treatments (Figure 8)[9].

For example, low muscle mass has an impact on the completion of treatment in head and neck cancer. A recent study in patients with head and neck cancer undergoing platinum-based chemo(radio)therapy reported the link between pre-treatment muscle mass and treatment outcomes. Low muscle mass was robustly associated with higher odds of chemotherapy termination due to toxicities[56].

Figure 8. Patients with muscle loss may experience more than a 2-fold increase in different treatment associated toxicities. Adapted from Daly et. al., 2018[63].

Malnutrition, the immune system and increased risk of infection

The immune system is the body's natural defence mechanism which plays an important role in helping to protect the body against disease and infection, modulate inflammation and maintain good health. Malnutrition impairs the immune system, suppressing immune functions that are fundamental to host protection. Calder and Kew (2002) highlight that this 'can be due to insufficient intake of energy and macronutrients and/or due to deficiencies in specific micronutrients. Often these occur in combination[64].

Weakened immune system in patients with cancer has been referred to as cancer-associated immune deficiency, and the integrity of the immune system deteriorates with cancer progression[65]. A weakened immune system can increase cancer patients' risk of poorer disease control, infections and poor outcomes to treatment[65].

Malnutrition is associated with poor immune-related clinical outcomes in patients with cancer

- ↑ Infections (post-surgery and during chemo(radio)therapy)[49, 50, 66]
- ↑ Post-operative complications[48, 51]
- ↑ Hospital length of stay[51, 52, 66]
- ↑ Mortality[61, 66]

KEY PRACTICE POINT

Malnutrition and muscle loss are associated with poorer tolerance to anti-cancer treatment. **Malnutrition impairs the immune system** and leaves patients with cancer vulnerable to infection and poorer clinical outcomes.

Malnutrition & systemic inflammation, the human burden and impact on quality of life

Malnutrition and weight loss are associated with poorer quality of life, depression and anxiety in patients with cancer[67-69] (Table 2). In a systematic review of cancer patients with cachexia, 23 of 27 included studies reported a negative relationship between weight loss and health related quality of life[70].

Systemic inflammation has been associated with both poorer clinical reported performance status and self-reported measures of quality of life in patients with cancer[71]. The reasons why systemic inflammation worsens quality of life in patients with cancer has recently been reviewed[72], and evidence from various preclinical and clinical studies suggest that the systemic inflammatory response has a direct role in the development of cancer associated symptom clusters, including pain, fatigue, mood, anorexia, and physical function[72].

Table 2. Selection of studies demonstrating that malnutrition and weight loss in cancer patients are associated with reduced quality of life

Based on studies included in Value of Medical Nutrition: Evidence Dossier. Medical Nutrition International Industry 2020.

COUNTRY	PATIENT GROUP	KEY fiNDING
Ireland [57]	Cancer patients undergoing chemotherapy	% weight loss biggest predictor of global QoL
Spain [73]	Resected cancer	Risk of malnutrition strongly associated with HRQoL in all three scales: functional, symptom and global
Poland [74]	Non-small-cell lung cancer	Malnutrition significantly correlated with decreased QoL
Spain [60]	Curative gastric cancer resection	Lower scores in functional scales (QoL) in patients with ≥10% body weight loss at 2 years post-surgery
Germany [59]	Patients with cachexia	Lower global health scores than non-cachectic patients

Despite the impact of malnutrition on quality of life in patients with cancer, eating difficulties and weight loss are often overlooked[75]. Figure 9 summaries the key results from a survey carried out in collaboration with the European Cancer Patient Coalition (ECPC) that explored the perspective of patients on cancer-related nutrition issues[75].

Figure 9. Patient perspectives on cancer-related nutritional issues[75].

Answers from **>900** patients in 10 European countries showed a difference in perspective between patients and their physicians. Patients express the need for more information and more focus from clinicians on nutrition-related issues.

- **72.5%** of patients experienced feeding problems during illness
- **60.4%** of patients felt that the topic of food was worrisome
- **53.7%** of patients knew that losing weight can worsen the adverse effects of therapy
- **86%** of patients believed that avoiding weight loss during therapy was important

- **53.9%** of patients reported that their physician did not check their feeding status during therapy
- **35.0%** of patients only reported having their weight recorded at each visit during treatment
- **37.3%** of patients received no advice from their physician/oncologist to improve nutrition
- **7.3%** of patients reported that either they or their relatives received no information about cachexia

KEY PRACTICE POINT

Malnutrition is **associated with poorer quality of life, anxiety and depression** in cancer patients, yet patients' nutritional concerns and needs are often not met.

3 IDENTIFICATION AND MANAGEMENT OF CANCER-RELATED MALNUTRITION

Early nutritional screening, assessment and intervention

In view of the prevalence of pre-existing weight loss at diagnosis[15], nutrition and oncology guidelines consistently emphasise the need to screen for nutritional risk as early as possible, once the diagnosis is made[4,11,76].

Both ESPEN and European Society of Medical Oncology (ESMO) clinical guidelines for malnutrition in cancer and cancer cachexia, respectively, recommend regular nutritional screening in all cancer patients[11, 76]. To detect nutritional disturbances at an early stage, ESPEN recommend to regularly evaluate nutritional intake, weight change and BMI, beginning with cancer diagnosis and repeated depending on the stability of the clinical situation[11]. Validated tools allow rapid and easy nutritional screening of cancer patients in different settings, such as the 'Malnutrition Universal Screening Tool' ('MUST') or Nutrition Risk Screening (NRS-2002).

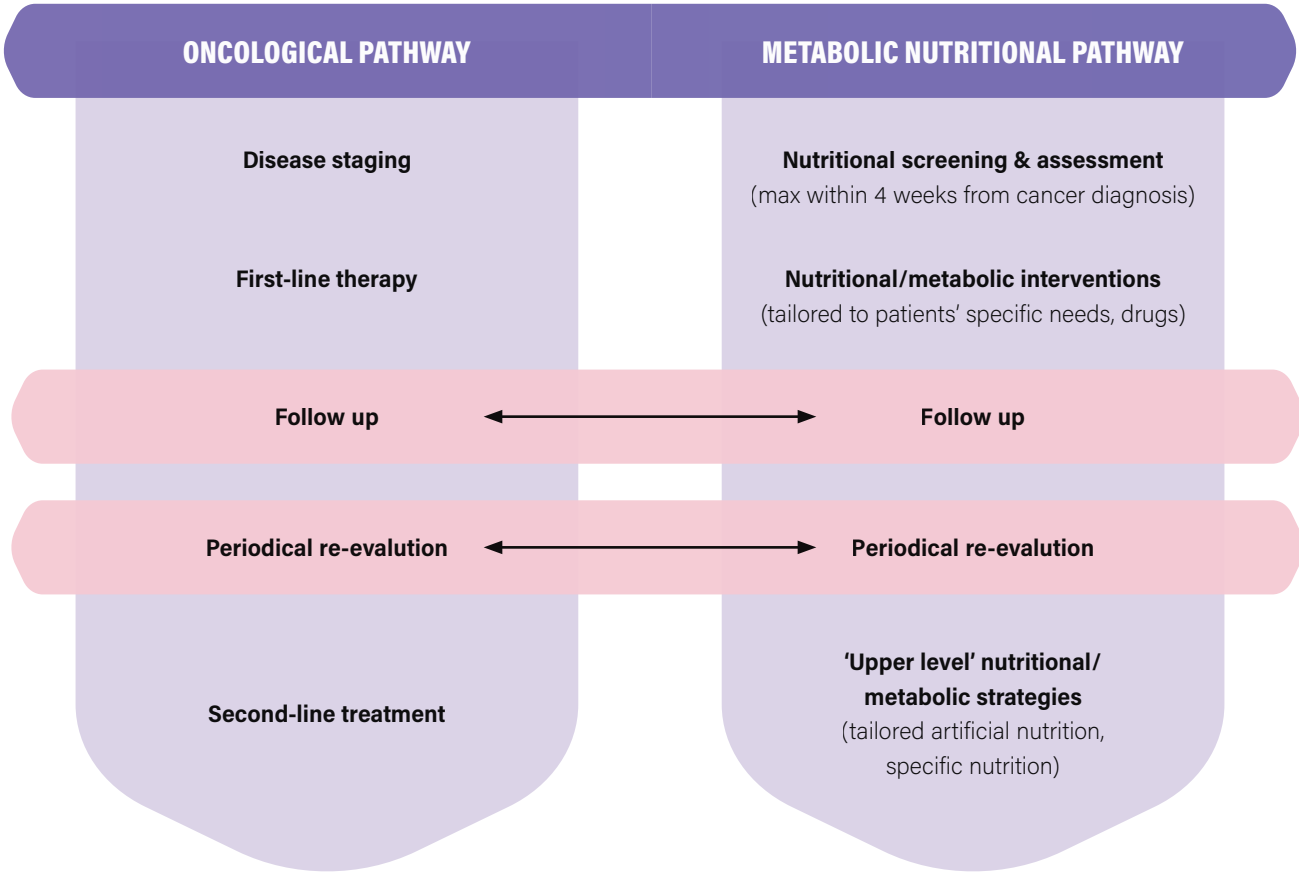
Patients identified as 'at risk' should undergo further assessment to establish the underlying causes and the severity of nutritional and metabolic abnormalities, to help identify those who may benefit from individualised nutritional intervention[11].

Patients found to be at no immediate risk of malnutrition by screening should be re-screened at regular intervals (typically every 3 months or at staging for anti-cancer treatment), or in cases where anti-cancer treatment with a high risk of inducing malnutrition is planned (e.g. combined-modality treatments, high dose chemotherapy, highly emetogenic agents), ESMO cancer cachexia clinical practice guidelines recommend that prophylactic nutritional support should be considered[76].

Attention to nutritional care should be integrated into and managed in parallel to all oncological treatment at every stage of the cancer patients' journey (Figure 10)[62]. The approach of nutritional assessment, nutritional diagnosis, nutritional intervention and follow-up for monitoring and evaluation follows the Nutrition Care Process[5, 77, 78] and can be used to collaborate with patients and carers to individualise nutritional care to help meet their individual preferences and goals and to improve outcomes.

Figure 10. Nutritional care should be instigated at the point of diagnosis and continued in parallel to cancer therapies across the continuum of care.

Adapted from Muscaritoli, Arends and Aapro., 2019[62].

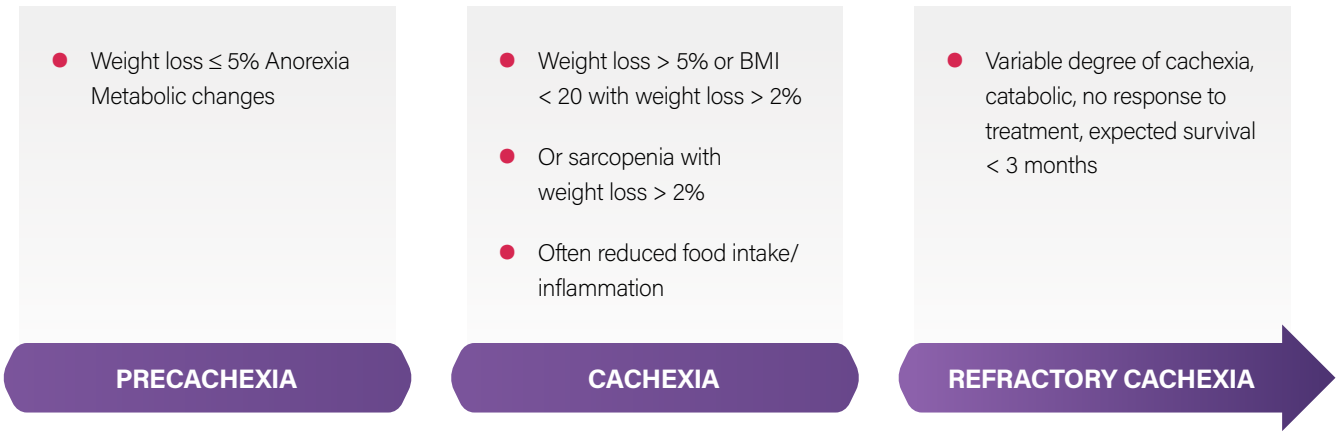


Monitoring nutritional risk needs to be repeated throughout treatment, in order to manage the risk of deterioration of weight and muscle loss, and progression towards more advanced stages of cachexia[4,6,11]. The consensus definitions of cancer cachexia stages are shown in Figure 11.

Ongoing monitoring of nutritional status and adapting nutritional intervention to meet the patients' evolving needs requires the involvement of the multi-disciplinary team including multiple oncology specialities, nurses and nutritional professionals[4].

Figure 11. Patients with cancer may experience cachexia progression as it evolves throughout disease journey. Early screening and assessment are crucial to identify the risk and intervene accordingly.

Adapted from Fearon et al., 2011[6].



'While patients with refractory cachexia are less likely to respond to nutritional therapy[6] the stages of precachexia and cachexia represent unique and unmissable windows of opportunity for nutritional intervention[11, 79]'.

Muscaritoli, Arends and Aapro, 2019[62].

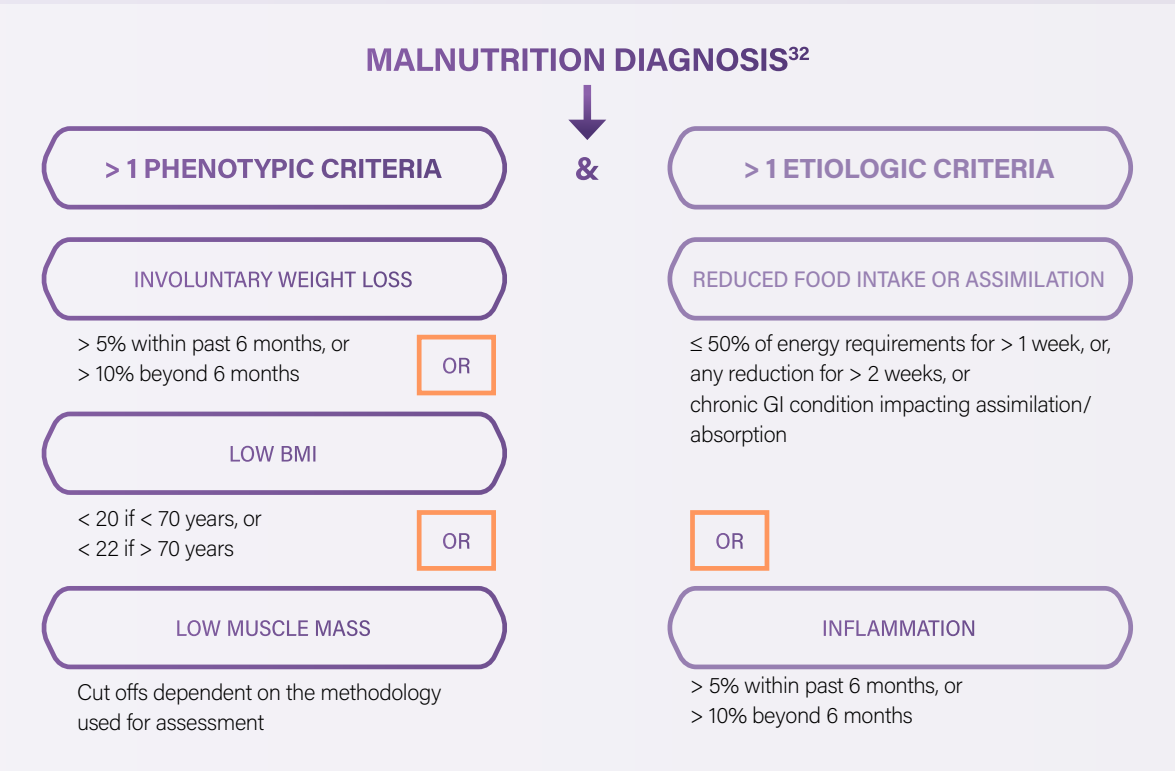
Following screening using a validated nutritional risk screening tool (e.g. 'MUST', NRS-2002 nutritional assessment should be undertaken. Nutritional assessment should be performed in all subjects identified as being at risk by nutritional risk screening, and will give the basis for the diagnosis decision, as well as for further actions including nutritional treatment[5].

ESPEN nutrition in cancer guidelines and ESMO cancer cachexia guidelines recommend that in cancer patients diagnosed as being at risk following malnutrition screening, that objective and quantitative assessment of nutritional intake, nutrition impact symptoms, gastrointestinal function, body weight, muscle mass, physical performance and the degree of systemic inflammation, be performed[11,76]. The assessment of nutritional and metabolic derangements and their origins is necessary to design individualized nutritional intervention strategies[11].

Low muscle mass is independently associated with poor clinical outcomes, and its loss can occur across the BMI spectrum, independent of overall body weight[9] (Figure 13), illustrating why ESPEN recommend that nutritional assessment include measures of body composition.

Healthcare professionals need to be alert to the possible presence of sarcopenic obesity.

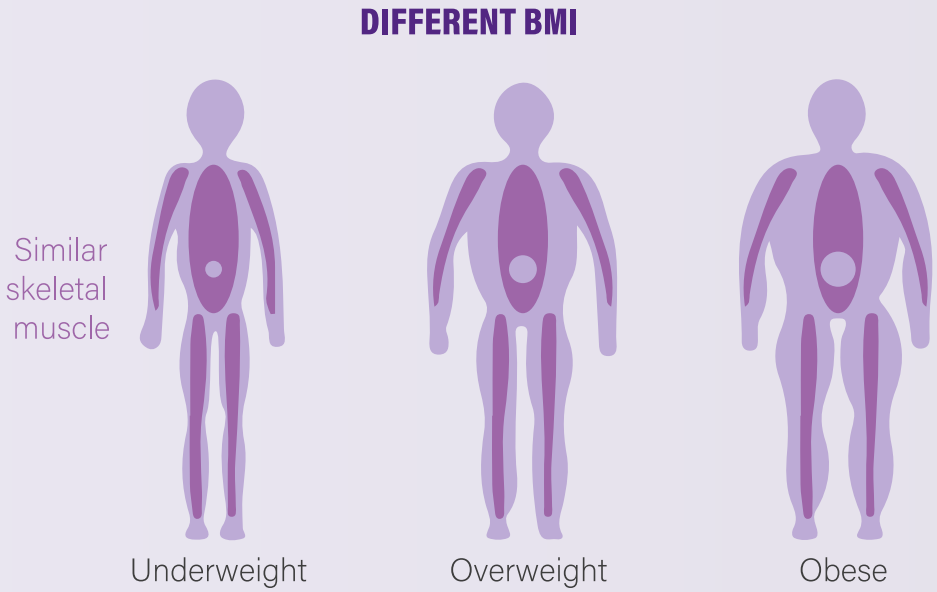
Figure 12. GLIM criteria for diagnosis of malnutrition. Adapted from Cederholm et al., 2019[80].



Experts from the Global Leadership Initiative on Malnutrition (GLIM) recently published consensus diagnostic criteria for malnutrition to be used once nutritional risk is identified after screening and integrating parameters of weight and muscle loss, nutritional intake, and systemic inflammation (Figure 13)[80]. This GLIM criteria for diagnosing malnutrition and cachexia (with the presence of systemic inflammation) is recommended by ESPEN and ESMO[11,76].

Sarcopenic obesity "is low lean body mass in obese individuals[2]. In such patients, clinicians frequently overlook muscle loss due to the presence of excess fat and extracellular water[5]."

Figure 13. Looking beyond body weight: evaluating and monitoring muscle mass loss.



KEY PRACTICE POINT

Expert guidelines recommend **early nutritional screening, assessment and intervention** in cancer patients. Internationally agreed criteria have been agreed for the diagnosis of malnutrition. Nutritional care should be instigated at the point of diagnosis and continued in parallel to cancer therapies across the continuum of care.

Nutritional needs and targets in cancer patients

Due to the impact of cancer and its treatment, it is frequently a challenge for patients undergoing treatment to fulfil their nutritional needs and maintain an adequate nutritional status[81-83].

High energy and protein

Patients with cancer can have a negative energy balance because of the combined effects of reduced food intake and metabolic derangements and therefore require high energy intake to compensate for these needs[11,76].

Energy Recommendation

- The ESPEN and ESMO guidelines on nutritional recommendations in patients with cancer and cancer cachexia recommended energy intakes (if energy expenditure is not measured individually) of 25 and 30 kcal/kg/day[11,76]. For example, for a 70 kg man that equates to 1750 to 2100 kcal/day.

Low Energy Intake in Cancer Patients

- Caloric deficit may reach up to 50% of the usual intake in patients with head and neck cancer receiving chemoradiotherapy[83].
- In lung cancer patients, it was reported that 60% of stage I and II patients, 83% of stage III patients, and 75% of stage IV patients eat less than their nutritional need[84].
- In a study in ovarian cancer patients undergoing chemotherapy, energy intake was consistently insufficient, and was lowest on the day of chemotherapy treatment[82].
- In a cohort of head and neck cancer patients 63% of patients failed to achieve intakes that satisfied the ESPEN energy recommendations, and energy intakes decreased during the course of treatment[85].

Protein is important for numerous structural and functional purposes and is essential for growth and repair of the body. Patients with cancer with weight loss and/or muscle wasting often exhibit an increase in whole body protein turnover, which is linked to reduced muscle protein synthesis, negative nitrogen balance, changes in plasma amino acids and an increase in inflammatory ('acute phase') hepatic protein synthesis[86-88]. Reaching increased protein requirement is a challenge for cancer patients due to the burden of the disease and its treatment[82]. High protein supplementation aims to help patients to close the gap and reach their specific needs.

Protein Recommendation

- The ESPEN guidelines on nutrition in cancer patients 'recommend protein intake should be above 1 g/kg/day and, if possible up to 1.5 g/kg/day'[11]. This is in line with the most recent ESMO cancer cachexia guidelines which recommend that cancer patients should be provided with at least 1.2g protein/kg/d[76]. For example, for a 70kg man that equates to 70 to 105 g/day (1-1.5 g protein/kg/d).

Low Protein Intake in Cancer Patients

- Studies have reported that 49% of lung and colorectal cancer patients and 52% of head and neck patients fail to achieve protein intakes satisfying minimum ESPEN protein requirements (>1.0 g/kg/d)[85, 89].
- In a study in ovarian cancer patients undergoing chemotherapy, protein intake was consistently insufficient, and was lowest on the day of chemotherapy treatment[82].
- Evidence reported that protein intake in lung cancer patients during chemotherapy significantly decreased after two cycles of treatment[90].

Omega 3 PUFAs (EPA & DHA)

Omega 3 PUFA's Eicosapentaenoic acid (EPA), Docosahexaenoic acid (DHA), are known for their anti-inflammatory properties and have been shown to reduce the levels of key pro-inflammatory molecules such as CRP, IL-6 and TNF-α in colorectal and lung cancer patients[91-93]. Omega 3 PUFAs also have immune-modulating actions which can act to reduce inflammation and support immune functioning[86]. Omega 3 PUFA, EPA has been demonstrated to have beneficial effects on inflammation, appetite and performance status[91, 95].

N-3 PUFA Recommendation

- The ESPEN guidelines on nutrition in cancer patients states 'in patients with advanced cancer undergoing chemotherapy and at risk of weight loss or malnourished, we recommend to use supplementation with long-chain N-3 fatty acids or fish oil to stabilise or improve appetite, food intake, lean body mass and body weight'[11]. Data suggest that at least 2 g/day are required for clinical benefit on nutrition-related endpoints[96]. The ESMO cancer cachexia clinical practice guidelines recommend that 'patients receiving chemotherapy, radiotherapy or chemoradiotherapy may be offered n-3 PUFA enriched oral nutritional supplements to increase body weight, attenuate the loss of lean body mass and improve quality of life'[76].

Low Intake of N-3 PUFAs in Cancer Patients

- Several studies in patients with cancer showed a lower intake of EPA & DHA than the mean intake in the general population[97, 98] probably caused by a lower nutritional intake in these patients due to the presence of cachexia and anorexia.
- Significantly lower levels of n-3 PUFA serum phospholipids have been observed in patients with lymphoma receiving chemotherapy compared with healthy subjects[99].

Omega 3 PUFAs (EPA & DHA)

Cancer patients may be at risk of developing micronutrient deficiencies as a result of reduced intake, increased losses (e.g. via stools, urine, blood, vomit), the use of drugs interfering with micronutrient metabolism, and/or increased requirements. In general, a deficient micronutrient supply can be assumed for all cancer patients whose energy intake amounts to <60% of the daily requirements for more than 10 days[100]. Adequate micronutrient intake is essential to support immune function[64].

Vitamin D is well-known for its central role in supporting bone health. By maintaining calcium and phosphate homeostasis and promoting calcium absorption in the gut, it enables normal bone mineralisation, growth and remodelling[101, 102]. Vitamin D is also important for muscle function, as shown by studies reporting an association between low vitamin D status and symptoms such as changes in muscle morphology, muscle weakness and poor physical performance[103-109]. Vitamin D has other important functions which include modulation of the innate and adaptive immune responses, and deficiency of vitamin D is associated with increased susceptibility to infection[110-112]. In cancer patients, poor vitamin D status is associated with poorer prognosis[113-115].

Recommendation

- The ESPEN guidelines on nutrition in cancer patients 'recommend that vitamins and minerals are supplied in amounts approximately equal to the RDA and discourage the use of high-dose micronutrients in the absence of specific deficiencies'[11].

Low Intake of Micronutrients and Vitamin D

- Cancer patients have a high prevalence of inadequacy of micronutrients such as vitamin C, vitamin E, Vitamin D, B-group complex vitamins, folate and magnesium, which can potentially lead to deficiencies[116, 117].
- There is a 50-75% gap between micronutrient intake in cancer patients and the RDA[82].
- Up to 67% of cancer patients have vitamin D inadequacy and up to 31% has a vitamin D deficiency[118].
- The prevalence of vitamin D insufficiency is 2.5-fold higher in patients with cancer than in the general population[118, 119].

KEY PRACTICE POINT

Patients with cancer has **specific nutritional needs,** in particular for energy, protein, micronutrients such as vitamin D and Omega 3 PUFAs. However, **intake of these key nutrients is often low** in cancer patients.

ONS in the management of cancer-related malnutrition

Oral nutritional supplements (ONS) are an effective, non-invasive method of helping patients' meet their nutritional needs, and are recognised within the ESPEN and ESMO guidelines on nutrition in cancer patients and in patients with cancer cachexia as an important part of nutritional care[11].

ESPEN GUIDELINES ON NUTRITION IN CANCER PATIENTS – RECOMMENDATIONS RELATING TO ONS

- 'We recommend nutritional intervention to increase oral intake in **cancer patients** who are able to eat but are malnourished or at risk of malnutrition. This includes dietary advice, the treatment of symptoms and derangements impairing food intake (nutrition impact symptoms), and offering **oral nutritional supplements.**'
- 'In **surgical cancer patients** at risk of malnutrition or who are already malnourished we recommend **appropriate nutritional support** both **during hospital care** and **following discharge** from hospital.'
- 'We recommend that **during radiotherapy** (RT) – with special attention to RT of the head and neck, thorax and gastrointestinal tract – an adequate nutritional intake should be ensured primarily by individualized nutritional counselling and/or with use of **oral nutritional supplements** (ONS), in order to avoid nutritional deterioration, maintain intake and avoid RT interruptions.'

ESMO GUIDELINES ON CANCER CACHEXIA - RECOMMENDATIONS RELATING TO ONS

- 'In patients with inadequate food intake, nutritional interventions are recommended **Low risk interventions (e.g. Counselling and ONS) are preferred**.'
- 'Dietary counselling should be the first choice of nutritional support offered to improve oral intake and possible weight gain in cachectic or at-risk patients who are unable to eat. Dietary counselling should emphasise protein intake, an increased number of meals per day, treatment of nutrition impact symptoms and **offering nutritional supplements** when necessary.'
- **'ONS can be supplied as part of dietary counselling to improve energy intake and induce weight gain.'**

Intervention with ONS in cancer patients helps meet patients' nutritional needs and is associated with improved nutritional and clinical outcomes:

NUTRITIONAL

- Positive effect on appetite and macronutrient (energy and protein) intake[120, 121]
- Increased micronutrient intake[122, 123]
- Improved body weight[81, 124-126]
- Improved muscle mass[127, 128]

CLINICAL

- Fewer post-operative infections[129, 130]
- Fewer post-operative complications[130-132]
- Better tolerance to cancer chemotherapy[126, 133, 134]
- Improved quality of life[81, 126, 132]
- Lower risk of in-hospital vmortality[135]

Importantly, studies have demonstrate that high-protein, Omega 3 PUFA-enriched ONS during chemotherapy were more beneficial on body weight, muscle mass and quality of life than ONS not containing Omega 3 PUFA[81, 94, 136, 137]. High-protein, Omega 3 PUFA-enriched ONS was also shown to improve treatment tolerability during chemoradiotherapy in H&N cancer[126].

KEY PRACTICE POINT

ONS are integral to the management of malnutrition in cancer patients and are recommended in expert guidelines on nutrition in cancer. Intervention with ONS in cancer patients is associated with improved nutritional and clinical outcomes. **Omega 3 PUFAs are known to have antiinflammatory properties** and when given as a key component of ONS demonstrate superiority over standard ONS on body weight, muscle mass and quality of life in cancer patients undergoing chemo(radio)therapy.

Adherence to ONS

Due to disease burden, and its treatment, it may be a challenge for patients to comply with their prescription for the necessary duration[81]. In cancer patients undergoing chemotherapy or radiotherapy taste and appetite alterations can affect adherence to ONS prescription and preferences may change at different time points during treatment[29]. Adherence to ONS prescription needs to be encouraged and monitored in daily practice in order to reach the expected goals and benefits of nutritional intervention[73, 130].

- Patient education and regular follow-up are key factors in supporting adherence to nutritional intervention[4, 29, 138, 139].
- Low volume ONS with high energy/nutrient density may also improve compliance compared to standard ONS[139, 140].
- Taste is an important aspect of compliance to ONS[141]. Providing flavour variety can prevent taste fatigue[138, 141]. Improved and adapted palatability of ONS may also increase compliance -in particular as cancer patients frequently experience changes in taste function. A recent study investigating the impact of taste alterations on overall liking of tailor-made ONS flavours with warming and cooling sensations, reported that patients with taste alterations were more discriminant in liking of ONS flavours. It was reported that sensory-adapted flavours were appreciated by patient with cancer, particularly in patients with taste alterations. Therefore, the presence of taste alterations should be considered when developing new ONS flavours, as well as in clinical practice when offering flavour options to patients with cancer.

KEY PRACTICE POINT

Taste alterations are common in cancer patients affecting their ability to meet their nutritional needs and ability to take ONS as prescribed. Innovative tailor-made ONS flavours have been **designed to address specific sensory needs** of cancer patients.

4 THE SUPPORT: FORTIMEL FORTICARE SENSATIONS 2,4kcal

KEY FEATURES

- Fortimel Forticare Sensations 2,4kcal is a **food for special medical purposes for the dietary management of patients with or at risk of disease related malnutrition due to cancer, chronic catabolic disease or cachexia.** It must be used under medical supervision.
- Fortimel Forticare Sensations 2,4kcal is a **ready-to-use, small volume, high protein, energy dense oral nutritional supplement** in liquid form with the addition of **Omega 3 fatty acids.** It is enriched with minerals, vitamins (including 10 Qg of vitamin D per serving) and trace elements. Each serving provides a 1.1g serving of eicosapentaenoic acid (EPA), 0.73 g of docosahexaenoic acid (DHA).
- Fortimel Forticare Sensations 2,4kcal **designed to provide a similar nutritional value** to that of a 200 ml high energy, high protein ONS in 40% less volume.
- Fortimel Forticare Sensations 2,4kcal is the **only high protein & Omega 3 fatty acids (EPA & DHA) & Vitamin D enriched medical nutrition product for malnourished cancer patients in the market** in a small volume with patient-tailored and patient-validated flavours.

FORTIMEL FORTICARE SENSATIONS 2,4kcal

To help meet increased energy and protein needs of malnourished cancer patients, as recommended by ESPEN/ ESMO guidelines[11,76]

To help address the high prevalence of Vitamin D deficiency in patients with cancer[82,100]

HIGH ENERGY, HIGH PROTEIN

306 kcal and 18 g protein

HIGH IN VtITAMIN D

10 µg Vitamin D

ENRICHED WITH OMEGA 3 FATTY ACIDS FROM FISH OIL

1.1 g EPA and 0.7 g DHA

Small 125ml compact volume

Tailored and validated flavours*

*which refers to the study

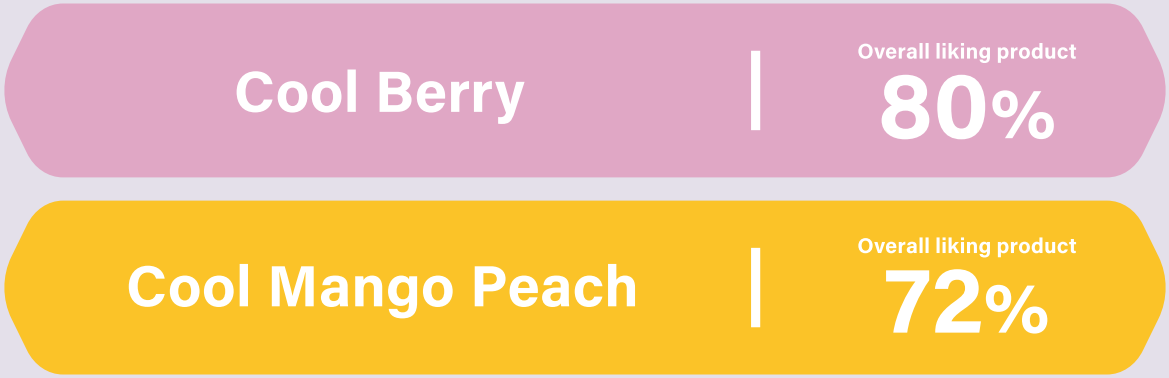
Omega 3 helps to target systemic inflammation Known anti-inflammatory properties, with EPA and DHA from fish oil being the most potent of the fatty acids[64]

To support compliance and patient experience with a patient-centric approach*

*DHA: Docosahexaenoic acid; EPA: Eicosapentaenoic acid; *Patient validation study*
(Kwiecien et al. 2023 *Clin Nutr Espen*, 54, p500).

Fortimel OmegaCare is a food for special medical purposes for the dietary management of patients with or at risk of disease related malnutrition due to cancer, chronic catabolic disease or cachexia. It must be used under medical supervision only.

PATIENT VALIDATION STUDY



Adherence to ONS

The new flavours of Fortimel Forticare Sensations 2,4kcal are tailored and validated with cancer patients. The Cool Berry and Cool Mango Peach flavours are specifically designed to better address the needs of patients experiencing taste alterations.

During product development, a sensory study was performed to evaluate the overall liking of different prototype ONS flavours to select the best flavours with patients undergoing anti-cancer treatment. In total, 50 cancer patients with various cancer types were included to investigate their liking and sensory characteristics of four different prototype flavours, followed by a questionnaire that explored their sensory alterations.

In the study, 56% of the patients reported sensory alterations. The results of the sensory testing by cancer patients showed that the most appreciated flavours were Cool Berry and Cool Mango Peach. Overall, 80% of patients liked Cool Berry and 72% liked Cool Mango Peach. As a result, these flavours were selected for Fortimel Forticare Sensations 2,4kcal.

Recommended intake

Fortimel Forticare Sensations 2,4kcal is intended for use as a supplement to food intake, in order to enhance the protein, energy and micronutrient intake of patients with or at risk of cancer related malnutrition. It is not suitable as a sole source of nutrition. For enteral use only.

The typical dosage for Fortimel Forticare Sensations 2,4kcal is 1-2 bottles per day, unless specified by a clinician or dietitian.

Directions for preparation and/or use

Fortimel Forticare Sensations 2,4kcal is ready to use and has a shelf life of 12 months unopened. It is best served chilled. Store in a cool, dry place at room temperature (5-25°C). Shake well before use. Once opened, close the bottle and store in a refrigerator for a maximum of 24 hours.

Restrictions of use

Precautions and contraindications

Precautions:

Fluid intake should be monitored and corrected to ensure adequate hydration status. The high protein and mineral content of Fortimel Forticare Sensations 2,4kcal are at the origin of a high potential renal solute load of the product. To process this load, a considerable amount of water is needed, while the product itself brings only a small volume of fluid.

Fortimel Forticare Sensations 2,4kcal contains a minor quantity of lactose (<0.35 g/100ml). Patients with lactose intolerance may require lactase depending on their extent of intolerance.

FORTIMEL FORTICARE SENSATIONS 2,4kcal IS NOT SUITABLE FOR:

- patients with cow's milk protein allergy
- patients with galactosaemia
- patients requiring tube feed
- intravenous use
- as sole source of nutrition

THE CONTRAINDICATIONS TO ORAL FEEDING IN GENERAL ARE[143, 144]:

- gastrointestinal failure or suppressed gastrointestinal function
- complete intestinal obstruction
- major intra-abdominal sepsis

AGE RESTRICTIONS

Fortimel Forticare Sensations 2,4kcal has been developed to meet nutritional needs of adults. It is:

- **not suitable** for children under 6 years of age, and;
- **to be used** with caution in children aged 6-10 years.

If used in children, strict medical supervision is warranted.

Note: *Fortimel Forticare Sensations 2,4kcal providing 20 Qg vitamin D with recommended 2 servings a day. Vitamin D is an important mediator of calcium homeostasis. If cancer patients suffer from severe hypercalcemia it is advised to not supplement vitamin D, hence not provide in Fortimel Forticare Sensations 2,4kcal.*

KEY PRACTICE POINT

Fortimel Forticare Sensations 2,4kcal is the only **high protein & Omega 3 fatty acids (EPA & DHA) & Vitamin D enriched medical nutrition product** on the market in a small volume with patienttailored and patient-validated flavours.

5 THE SUPPORT: FORTIMEL FORTICARE SENSATIONS 2,4kcal

Table 3. Macronutrient composition of Fortimel Forticare Sensations 2,4kcal, Cool Berry and Cool Mango Peach flavours, expressed per 100 ml and serving (1 bottle/serving unit).

Nutrient	Unit	Fortimel Compact Protein OmegaCare 100 ml/g	Fortimel Compact Protein OmegaCare 125 ml serving
Energy density	kcal/ml	2,45	-
Energy	kcal	245	306
Protein	g %	14.6 23.8	18.25 23.8
Carbohydrates	g %	25.1 40.9	31.4 40.9
-Polysaccharides	g	11.5	14.4
-Sugars	g	13.4	16.8
-Lactose	g	<0.35	<0.35
Fat	g %	9.6 35.3	12 35.3
- saturates	g	2.2	2.75
- monounsaturated	g	3.8	4.75
- polyunsaturated	g	3.5	4.38
EPA	g	0.88	1.1
DHA	g	0.59	0.73
Dietary fibre	g %	0 0	0 0
Salt	mg	0.10	0.13

Table 4. Micronutrient composition of Fortimel Forticare Sensations 2,4kcal expressed per, 100 ml and serving (1 bottle/serving unit),

Nutrient	Unit	Fortimel Compact Protein OmegaCare/ 100 ml/g	Fortimel Compact Protein OmegaCare/ 125 ml (1 serving)
Na	mg	39,10	48,88
K	mg	98,00	122,50
Cl	mg	46,80	58,50
Ca	mg	336,00	420,00
P	mg	287,00	358,75
Mg	mg	54,00	67,50
Fe	mg	2,25	2,81
Zn	mg	2,30	2,88
Cu	mg	0,34	0,43
Mn	mg	0,24	0,30
F	mg	0,25	0,31
Mo	µg	14,70	18,38
Se	µg	13,40	16,75
Cr	µg	8,48	10,60
I	µg	30,50	38,13
Vitamin A	µg RE	232,00	290,00
Vitamin D	µg	7,85	9,81
Vitamin E	mg αTE	4,09	5,11
Vitamin K	µg	14,00	17,50
Thiamin	mg	0,24	0,30
Riboflavin	mg	0,50	0,63
Niacin	mg NE	4,23	5,29
Pant. Acid	mg	1,55	1,94
Vitamin B6	mg	0,51	0,64
Folic acid	µg	35,40	44,25
Vitamin B12	µg	1,04	1,30
Biotin	µg	10,60	13,25
Vitamin C	mg	31,40	39,25
Choline	mg	99,00	123,75

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