

### TOGETHER YOU & YOUR TEAM CAN MAKE A DIFFERENCE KEEP ON STRENGTHENING THEIR RESILIENCE

#### THIS INFORMATION IS INTENDED FOR HEALTHCARE PROFESSIONALS ONLY

All products mentioned are Foods for Special Medical Purposes for the dietary management of disease related malnutrition and must be used under medical supervision. Information is accurate as of April 2024.

### **EMPOWERING ONCOLOGY CARE: CLINICAL EVIDENCE FOR IMPROVING PATIENT OUTCOMES**

YOUR EXPERT PARTNER IN NUTRITIONAL CANCER CARE

# **EXECUTIVE SUMMARY**

### Cancer affects millions of people around the world each year and has one of the highest mortality rates globally.<sup>1</sup>

Cancer leaves affected patients at very high risk of malnutrition and nutrient deficiencies, as the result of their disease and the treatments they undergo, yet this risk is often missed or insufficiently addressed by clinicians and patients.<sup>2</sup>

It is estimated that up to 80% of cancer patients will experience malnutrition at some stage during their illness.<sup>3</sup>



One of the most prevalent nutrition problems experienced by cancer patients is muscle wasting, which occurs commonly regardless of the patients' cancer stage.<sup>1</sup>



Low muscle mass occurs in more than half of newly diagnosed cancer patients, and is associated with unfavourable clinical outcomes including reduced quality of life and shorter survival times.<sup>1,4</sup>

Early and continuous high protein intervention is essential for both malnourished and non-malnourished patients to help maintain nutritional status and prevent post-surgery complications.<sup>5</sup>

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# THE IMPORTANCE OF PROTEIN IN PATIENTS WITH CANCER

# **PROTEIN IN CANCER**

Some cancer patients may have increased protein requirements due to changes to their protein metabolism, meaning their protein stores are broken down faster and their rate of protein synthesis is slower. Without additional protein intake, this can result in muscle loss.<sup>6</sup>

Nutritional deficits that contribute to this problem are preventable and often reversible, with patients who consume more high-quality protein shown to be able to build up their protein stores again. Low muscle mass can happen at any stage of cancer and is associated with poorer tolerance of treatment, increased risk of complications and infections, and poorer survival rates.<sup>7</sup>

Preserving adequate nutritional status and muscle can support outcomes during cancer treatment. Therefore, prompt nutritional support to address energy and protein needs is recommended along the oncology journey.<sup>2,8</sup>

ESPEN and ESMO recommend protein intake of at least 1.2g/kg/day in all cancer patients, and up to 2g/kg/day when patients are severely depleted.<sup>2,8</sup>

Increased protein requirement +45g/day: Example in a 60kg adult



"ESPEN & ESMO recommend medical nutrition in cancer care"

ESPEN: European Society for Clinical Nutrition and Metabolism; ESMO: European Society for Medical Oncology.



Despite the increased protein requirements, **up to 66%** of cancer patients failed to meet their daily protein recommendations.<sup>9-11</sup>

Low protein intake is associated with:

**The role of oral nutritional supplements (ONS) in cancer** Where intake from food is insufficient, oral nutritional supplements can help patients meet their needs.<sup>2,8</sup>

Specifically, high protein ONS have been demonstrated to:

Length of hospital stay<sup>18</sup>



**HIGH PROTEIN ORAL NUTRITIONAL** SUPPLEMENTS ENABLE THE MAJORITY OF **CANCER PATIENTS TO MEET ESPEN PROTEIN** RECOMMENDATIONS **DURING SYSTEMIC TREATMENT: RESULTS** FROM THE PROTEOS STUDY<sup>19</sup>

Dingemans A, et al. Clinical Nutrition ESPEN. 2023;54:493.

COLORECTAL CANCER LUNG CANCER

**HIGH PROTEIN ONS** 

#### Introduction

This multi-centre, randomised, controlled, open-label, parallel-group study aimed to evaluate whether a low-volume, high-protein oral nutritional supplement (ONS) could make it easier for colorectal and lung cancer patients to meet their recommended protein intake of 1g/kg bodyweight per day while receiving anti-cancer treatment, compared to patients receiving standard nutritional care.

Preliminary analysis initially included 37 patients, but only 29 completed the study.

#### Study design

#### First line systematic anti-cancer treatment



nutritional support according to hospital standard practice. Table 1: Study population.

Subject characteristics at baseline: mean <u>+</u> SD or n (%)	TG (n=26)	CG (n=11)
Sex (male)	<b>11</b> (42.3%)	<b>8</b> (72.7%)
Age (year)	66.1 <u>+</u> 7.8	70.1 <u>+</u> 8.2
Body mass index (kg/m²)	26.2 <u>+</u> 3.7	27.2 <u>+</u> 3.0
Energy intake (kcal/kg/d)	28.0 <u>+</u> 9.1	24.5 <u>+</u> 7.3
Protein intake (g/kg/d)	1.12 ± 0.33	1.04 ± 0.30

T0 = baseline T1 = end of 1st treatment cycle T2 = end of 2nd treatment cycle T3 = end of intervention (week 12).

#### **Study results**

Brotein intake: 1.2-1.5g/kg/day Primary endpoint: protein intake at T1



A higher proportion of subjects in the TG met minimum ESPEN protein recommendations of 1-1.5g/kg bodyweight/day





#### Conclusions

- Without specific nutritional support, cancer patients often fail to meet the minimal protein intakes advised by ESPEN guidelines.
- Twice daily high-protein, low-volume ONS enabled significantly more patients to meet ESPEN protein recommendations.
- Adequate protein intake is important to prevent nutritional deterioration, to support muscle mass/function and improve outcomes during treatment.<sup>2,8</sup>
- In view of the challenges of cancer patients to consume sufficient protein, high protein ONS should be considered early in the patient journey to enable patients to meet recommended intakes.

ESPEN: European Society for Clinical Nutrition and Metabolism; SD: standard deviation.

Protein intake was higher in TG and significantly higher at T1 and T2.



# TARGETED NUTRITIONAL INTERVENTION IMPROVES OUTCOMES

## PREVALENCE AND SURVIVAL IMPACT OF PRE-TREATMENT CANCER-ASSOCIATED WEIGHT LOSS: A TOOL FOR GUIDING EARLY PALLIATIVE CARE<sup>20</sup>

Gannavarapu S, et al. Journal of Oncology Practice. 2018;14(4):e238-e250.

LUNG CANCER GI CANCERS

#### CANCER- ASSOCIATED WEIGHT LOSS

#### Introduction

This was a UK retrospective cohort study of >3000 adult patients with lung or gastrointestinal (GI) cancer. Patients were assessed using a tumour registry of patients treated between January 2006 and December 2013 at a single tertiary centre.

**Study question:** What is the prevalence and survival impact of cancer-associated weight loss at the time of diagnosis and prior to treatment?

#### Method

Survival was calculated from time of cancer diagnosis to death. The prevalence and survival impact of pre-treatment cancer associated weight loss were evaluated using the Kaplan-Meier method and compared with the log rank test.

#### Cancer-associated weight loss was assessed using the validated international consensus for cancer cachexia:

Weight loss	Criteria
Overt weight loss	Unintentional weight loss >5% within 6 months preceding diagnosis in patients with body mass index (BMI) ≥ 20 OR >2% in patients with BMI <20
Minimal weight loss	Unintentional weight loss that doesn't reach the threshold for overt weight loss
No weight loss	Patients with stable weight, weight gain or purposeful weight loss

#### **Population characteristics:**

- 3,180 consecutively treated adult patients with lung or GI (including colorectal, liver and pancreatic) cancer
- Median age: 62 years
- 57.4% men, 42.6% women
- Multiple tumour sites and stages of cancer represented including non-small cell lung cancer (NSCLC; n=1,369), colorectal (n=623) and pancreatic (n=267) primaries

#### **Study results**

Overt weight loss was observed in 34% of patients at cancer diagnosis.

Table 1. Prevalence of overt weight loss by tumour site (n=3,180).

Tumour site	Prevalence (%)
Gastroesophageal	56.5
Pancreatic	53.2
Small-cell lung	38
Non-small cell lung cancer	30.4
Colorectal	27.6
Anal	26.1
Hepatobiliary	24.3

Table 2. Prevalence of overt weight loss by disease stage (n=3,180).

Disease stage	Prevalence (%)
Stage I	17.6
Stage II	25.8
Stage III	36.6
Stage IV	43.3

Across the entire cohort, weight loss at the time of cancer diagnosis was strongly linked to reduced survival time, even after factors including age, sex, comorbidities, tobacco use, stage, size and grade of cancer were controlled.

Median survival time for patients without weight loss at diagnosis was 28.2 months, compared to 17.5 months for those with minimal weight loss, and 13.6 months for those with overt weight loss at diagnosis.



Graph 1. Overall survival rates of all patients with lung or GI malignancies.

**Table 3.** Median survival of patients (months) with no weight loss and with overt weight loss, characterised by tumour site (n=3,180).

	Median survival (months)	
Tumour site	No weight loss	Overt weight loss
NSCLC	20.5	9.9
Gastroesophageal	37.9	13.9
Hepatobiliary	25.1	7.6

The link between cancer-associated weight loss at diagnosis and reduced survival was evident across all types of cancer studied, but was particularly strong in NSCLC, gastroesophageal and hepatobiliary cancers (p<0.001).

#### Discussion

All patients who experienced weight loss at diagnosis had shorter survival times than those who hadn't lost weight at the time of diagnosis. Patients with overt weight loss saw the greatest reduction in survival. This suggests even minimal weight loss associated with cancer needs to be addressed as early as possible to prevent further muscle and fat wastage, and avoid worsening clinical outcomes in patients.

### Conclusions

The presence of early, minimal weight loss alone is predictive of worse survival outcomes across a range of cancer pathologies and even in early-stage disease. These results highlight the need for early detection and intervention for cancer cachexia to improve prognosis.



**NUTRITIONAL SUPPORT DURING THE HOSPITAL STAY REDUCES MORTALITY IN PATIENTS** WITH DIFFERENT **CANCER TYPES: SECONDARY ANALYSIS OF A PROSPECTIVE** RANDOMISED TRIAL<sup>4</sup>

Bargetzi L, et al. Annals of Oncology. 2021;32(8):1025-1033.

LUNG CANCER GI CANCERS HAEMATOLOGICAL CANCERS

ONS

#### Introduction

This study is a secondary analysis of cancer patients included in the EFFORT trial, a prospective, open-label, randomised, controlled multicentre trial conducted across 8 hospitals in Switzerland, which compared the effects of individualised nutritional support to standard hospital food on clinical outcomes in patients with different types of cancer.

#### **Study Design**

**Intervention:** 255 patients received individualised nutritional support to meet energy and protein goals. The plan was based on food fortification, between meal snacks and oral nutritional supplements (ONS). On discharge, patients received dietary counselling and an ONS prescription, if necessary.

**Control**: 251 patients received standard hospital food with no nutritional counselling or recommendation for additional support.

#### **Population Characteristics:**

- 506 adult patients with a main admission diagnosis of cancer, including:
  - Lung cancer (n=113)
  - Haematological malignancies (n=108)
  - Gastrointestinal tumours (n=84)
  - Other types of cancer (n=201)
- Patients with increased nutritional risk and expected hospital stay >4 days
- 60.6% of the control group and 57.3% of the intervention group were male
- Mean age of control group = 71.5 years; mean age of intervention group = 69.2 years

#### **Study results**

Patients in the intervention group receiving nutritional support had a 5% decrease in mortality over time (19.9% to 14.1%, p=0.027), regardless of their cancer type and activity.



Graph 1. Kaplan-Meier estimates of cumulative incidence of all-cause mortality within 30 days according to randomisation group.

#### Patients in the intervention group had:



- Patients had a higher risk of functional decline in activities of daily living in the control group compared to the intervention group (OR-0.59; 95% CI-0.38-0.93; p=0.021).
- Patients receiving indiviualised nutritional support showed significant improvements in their quality of life scores, measured by the EQ-5D Index, compared to the control group.

#### Conclusions

Individualised nutritional support reduces the risk of mortality and improves functional and quality of life outcomes in patients with cancer with an increased nutritional risk. This study supports malnutrition screening on admission followed by an individualised nutrition support strategy to meet energy and protein requirements in this vulnerable patient group.

## A SYSTEMATIC REVIEW AND META-ANALYSIS OF THE EFFECTS OF COMMUNITY USE OF ORAL NUTRITIONAL SUPPLEMENTS ON CLINICAL OUTCOMES<sup>21</sup>

Cawood A L, et al. Ageing Research Reviews. 2023;88:101953.

DISEASES OF ANY NUTRITIONAL STATUS ONCOLOGY, FRAILTY AND DRM

ONS

**30%** OF THE STUDIES IN THIS TRIAL USED A NUTRICIA ONS

**40%** OF THE STUDIES IN THIS TRIAL WERE CONDUCTED IN CANCER PATIENTS

#### Introduction

This systematic review and meta-analysis reviewed evidence from 44 randomised control trials analysing the effects of oral nutritional supplements (ONS) in community settings on the incidence of complications. Complications included infections, pressure ulcers, post-operative complications and poor wound and fracture healing.

#### **Study Design**

44 studies were conducted in a variety of regions; Europe (n=15), UK (n=11), North and South America (n=4), Asia (n=10), multi-country (n=2) and others (n=2).

#### **Study Characteristics:**

- Mean prescribed energy and protein intakes were 588kcal/day and 22g/day, respectively
- Mean energy density of ONS was 1.5kcal/ml with 23% energy from protein
- Mean intervention period was 74 days
- Control groups varied between studies; standard diet (n=25), placebo (n=10) and dietary advice (n=9)

#### **Population characteristics:**

- 5,716 adult patients with disease of any nutritional status in the community (including oncology, frailty and disease related malnutrition)
- Mean age 67 years
- 47% female
- In 64% of studies, patients received intervention in the community only; 36% in both community and hospital settings
- 66% of the studies were conducted on patients undergoing surgery, and 34% on medical patients including head and neck cancer patients

#### **Study Results**

Oral nutritional supplements used in the community, in addition to diet, significantly reduced complications compared with the control (OR-0.68; 95% Cl-0.59-0.79; p<0.001).



A significant reduction in the incidence of complications was only seen when adherence to ONS was good  $\geq$ 80% (p=0.001).



The significant reduction in the incidence of complications was only seen in patients using readyto-drink ONS (p<0.001) and was not evident when using powdered forms of ONS.

Table 1. Subgroup analysis showing that for all ages, settings, patient types and nutritional status, the reduction in complications with ONS was significant.

Reduction in the incidence of complications in the intervention group vs control

		Meta-analysis subgroup results
Age	>65 years	OR, 0.79; 95%, Cl 0.66-0.94; p=0.007
	<65 years	OR, 0.49; 95% Cl, 0.38-0.64; p<0.000
Setting	Community	OR, 0.65; 95% Cl, 0.52-0.80; p<0.001
	Community + hospital	OR, 0.72; 95% Cl, 0.59-0.87; p=0.001
Groups	Surgical	OR, 0.65; 95% Cl, 0.55-0.77; p<0.000
	Medical	OR, 0.76; 95% Cl, 0.59-0.98; p=0.037
Nutritional status	Malnourished	OR, 0.73; 95% Cl, 0.57-0.94; p=0.013
	Well nourished + malnourished	OR, 0.67; 95% Cl, 0.53-0.83; p=0.000
High protein ONS		OR, 0.66; 95% Cl, 0.54-0.80; p<0.001

#### Conclusions

Current research suggests that the use of ONS in community settings can lead to clinically meaningful reductions in complications. We also know from previous research that a reduction in complications can have benefits on the healthcare system<sup>22,23</sup>



# TIMING - EARLY NUTRITIONAL INTERVENTION IMPROVES OUTCOMES

# ESPEN AND ESMO RECOMMEND MEDICAL NUTRITION IN CANCER CARE

Main recommendations for nutritional care are consistent across both guidelines.

Recommendations	ESPEN guideline <sup>2</sup>	ESMO guideline <sup>8</sup>	Notes
Malnutrition risk screening	$\checkmark$	$\checkmark$	In all patients, at regular intervals, using a validated tool
At-risk patients undergo nutritional assessment	$\checkmark$	$\checkmark$	Objective measures very clearly defined in ESPEN and ESMO guidance
In patients with inadequate food intake, <b>personalised</b> <b>nutritional intervention</b> is recommended	$\checkmark$	$\checkmark$	Emphasis on increasing nutritional intake and physical activity, and reducing inflammation, with dietary guidance and counselling as needed
Guidance provided on nutritional <b>requirements</b>	$\checkmark$	$\checkmark$	For energy, protein, micronutrients
ONS recommended as part of nutritional counselling as needed <sup>26</sup> to improve energy intake, bodyweight and quality of life	~	~	ESMO guidance highlights that this advice should be delivered by an adequately trained professional

ESPEN: European Society for Clinical Nutrition and Metabolism; ESMO: European Society for Medical Oncology.

# PREHABILITATION

The necessity for prehabilitation, a component of the continuum to rehabilitation, begins from the moment of diagnosis with the goal of enhancing a patient's health. Prehabilitation helps cancer patients in the lead up to treatment, by encouraging the adoption of healthy habits and prescribing nutrition, exercise and psychological interventions as needed.<sup>24</sup>

Prehabilitation aims to support patients' tolerance of treatment and their long-term health.  $^{\rm 24}$ 

#### Prehabilitation has been shown to:<sup>24</sup>



Reduce time in hospital

 $\bigcirc$ 

Support heart

health

Prevent



Improve posttreatment recovery



Elevate nutritional status



complication after surgery



Support some aspects of brain function

Optimise quality of life

#### The cancer patient journey



Adapted from Macmillan Cancer Support, 2021<sup>24</sup>



# TASTE CHANGES IN PATIENTS WITH CANCER

**SELF-REPORTED TASTE AND SMELL ALTERATIONS** AND THE LIKING OF ORAL **NUTRITIONAL SUPPLEMENTS** WITH SENSORY-ADAPTED **FLAVOURS IN CANCER PATIENTS RECEIVING** SYSTEMIC ANTITUMOUR TREATMENT<sup>25</sup>

De Haan J J, et al. Supportive Care Cancer. 2021;29(10):5691-5699.

VARIOUS CANCERS

FORTISIP COMPACT PROTEIN

#### Introduction

Taste and smell alterations (TAs and SAs) are commonly experienced by cancer patients receiving treatment, which can have consequences on food intake, increasing their risk of malnutrition and cachexia. This exploratory study aimed to assess the prevalence of taste and smell changes in cancer patients receiving anticancer treatment, and determine the impacts on patients' tolerance and enjoyment of oral nutritional supplements (ONS) formulated with warming and cooling sensations.

#### **Study Design**

Patients were randomly selected and approached at the oncology ward or outpatient clinic at the University Medical Center Groningen. Patients were asked to complete a product questionnaire to ascertain their overall preference for 5 different ONS flavours, including questions on flavour, sweetness, texture, warming/cooling sensation and colour.

> **ONS tested:** ONS were a variety of flavours of Fortisip Compact Protein; a low volume, high protein, energy dense ONS. Each bottle contained 125ml, 306kcal and 18g of protein. 5 prototype flavours, designed for patients with TAs were tested:

- 2 warming sensation flavours: hot tropical ginger (HTG) and hot mango (HM)
- 2 cooling sensation flavours: cool red fruits (CRF) and cool lemon (CL)
- 1 neutral flavour (N)

#### **Population characteristics:**

- 50 patients
- 60% male
- 72% >55 years old
- 68% were treated with chemotherapy
- Median duration since the start of treatment was 2 months
- 16% of patients used ONS daily

Cancer type	Proportion of patients (%)
Urogenital	26
Colorectal	20
Sarcoma	10
Oesophageal/gastric	8
Gynaecological	8
Other (brain, breast, hepatobiliary, lung, neuroendocrine etc)	28

#### Study Results



30% and 16% of patients experiencing TAs reported a weaker taste for salty and sweet flavours, respectively. 17% and 10% reported a stronger taste for sweet and sour flavours, respectively.

Of the 5 flavours assessed, 3 were positively received by patients with TAs (with and without SAs), with 93% of patients recording liking scores >6 for cool red fruits, 73% for neutral, and 67% for hot tropical ginger.

(Note: Values are averages of patients with TAs with and without SAs)



**High acceptability** amongst cancer patients for sensory adapted oral nutritional supplements (ONS).

Of all flavours, 3 were rated highly with average scores >6 out of 10:



#### Conclusions

Patients experiencing TAs were more discerning when choosing flavours of ONS they deemed palatable, appearing to prefer sensory-adapted flavours. Patients without TAs were more agreeable to the full flavour range of ONS. This suggests that TAs should be accounted for when developing and selecting ONS flavours for oncology patients.



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