Welcome to the Interactive ProSure® Clinical Trial Compendium. Click on the table of contents above to jump to a specific chapter. You can also use the left and right arrows at the bottom right to navigate through the pages.

EPA - eicosapentaenoic acid
Introduction

This compendium includes a summary of 29 publications based on 21 clinical studies conducted with ProSure, a therapeutic nutritional product scientifically formulated to address the nutritional needs of people with cancer-induced weight loss or who are at risk for developing this complication. These 21 studies have been conducted in patients with a range of cancer types including: pancreatic, lung, head and neck, colorectal, esophageal, and solid tumors and leukemia in children. A supporting publications section is included in this compendium that includes summaries of clinical studies that support the use of fish oil supplements in patients with cancer. Other papers included in this section are an international consensus definition and classification of cancer cachexia and a minireview paper of studies that evaluated the role of eicosapentaenoic acid on lean body mass in cancer cachexia.

People with cancer often experience weight loss along with a loss of quality of life—conditions that reach far beyond the battle against malignant cell growth. Unintended weight loss is sometimes the first sign of cancer a patient notices, but weight loss is just one aspect of a more complicated condition known as cancer cachexia. Cachexia may also lead to anorexia, anemia, muscle loss, decreased strength, and physical and mental fatigue. Such impairments can in turn lead to malnutrition, social isolation, and depression.

Cancer cachexia has recently been defined by an international consensus panel as a multifactorial syndrome defined by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment. The pathophysiology is characterised by a negative protein and energy balance driven by a variable combination of reduced food intake and abnormal metabolism. Cancer cachexia is caused by factors that are released by certain tumors and by the host’s inflammatory response to the presence of the tumor. These factors depress appetite and impair the body’s metabolism of dietary fat, protein, and carbohydrate.

Such changes actually begin before weight loss is evident and can worsen as cancer progresses. Studies have shown that cancer cachexia can be managed in part by specialized nutrition. ProSure is clinically proven to benefit people with cancer. If weight loss due to cancer cachexia is not effectively treated, poor outcomes can result. Such outcomes include decreased response to cancer treatments, increased frequency of complications and infections, and shortened survival. In addition to survival, people with cancer are particularly concerned about restoring and maintaining quality of life.

Clinical studies demonstrate that drinking ProSure daily as part of an overall cancer care plan:

- Promotes weight gain
- Helps build or maintain lean body mass
- Improves physical activity
- Improves quality of life
- Increases strength
- Improves appetite and dietary intake
- Attenuates the proinflammatory response

ProSure is enriched with eicosapentaenoic acid (EPA), which helps decrease the harmful metabolic changes induced by tumor-related factors. Calorically dense with a high amount of protein, ProSure helps build lean body mass. ProSure’s unique combination of EPA with protein- and energy-rich ingredients helps counter the physiological abnormalities that underlie weight loss due to cancer cachexia. For cancer patients, ProSure is recommended as two 240-mL servings per day along with regular food consumption. Studies have shown that adding ProSure to the diet does not inhibit usual meal intake but actually improves appetite so that meal intake improves.
This is a navigatable bookshelf. Click on the books to view each ProSure® publication.
The effect of an oral nutritional supplement enriched with fish oil on weight-loss in patients with pancreatic cancer


In a prospective, single-arm, pilot study conducted by Barber and colleagues, ProSure was given to weight-losing patients with advanced pancreatic cancer who had a median weight loss of 2.9 kg/month (6.4 lb/month) before enrollment. Weight, body composition, and functional status data were collected at baseline, 3 weeks, and 7 weeks. Resting energy expenditure (REE), food intake, and quality of life (QoL) data were collected at baseline and 3 weeks only.

Objective
To assess whether the provision of additional calories and protein in conjunction with fish oil could reverse weight-loss in patients with advanced pancreatic cancer.

Study Design
- **STUDY POPULATION:** Pancreatic (n = 20)
- **LENGTH OF STUDY:** 7 weeks
- **INTERVENTION:** 2 servings ProSure (240 mL/serving)

Outcomes
- Median ProSure consumption: 1.9 servings/day
- **WEIGHT GAIN:**
  - 3 weeks (median 1.0 kg [2.2 lb]) \(P = 0.024\)
  - 7 weeks (median 2.0 kg [4.4 lb]) \(P = 0.033\)
- **Increased lean body mass.** Statistically significant increases in lean body mass at both 3 (median 1.0 kg; \(P = 0.0064\)) and 7 weeks (1.9 kg; \(P = 0.0047\)). Weight gain was predominantly lean body mass (95% of total weight gain), not fat or water.
- **Increased appetite and dietary intake.** Statistically significant improvements in appetite \(P = 0.001\) and dietary intake \(P = 0.0016\) at 3 weeks. Participants consumed a median additional 370 Cal/day at 3 weeks. They did not substitute ProSure for their usual food intake, rather, ProSure supplemented their diet and increased caloric intake.
- **Decreased resting energy expenditure (REE).** Statistically significant reduction in REE or resting metabolic rate (RMR) at 3 weeks.

Study Conclusions
This small pilot study suggests that in contrast to conventional nutritional supplements, a fish-oil enriched supplement may reverse cachexia in patients with advanced pancreatic cancer.
Fish-oil enriched nutritional supplement attenuates progression of the acute-phase response in weight-losing patients with advanced pancreatic cancer


Weight-losing patients with advanced pancreatic cancer were enrolled in this prospective, single-center, open-label study.

Objective
To evaluate the effect of a fish-oil enriched nutritional supplement on the levels of individual acute-phase proteins in patients with advanced pancreatic cancer.

Study Design
• STUDY POPULATION: Pancreatic (n = 36; ProSure 18, Supportive care 18); Healthy controls (n = 6)
• LENGTH OF STUDY: 4 weeks
• INTERVENTION: 2 servings ProSure (240 mL/serving)
  or supportive care

Outcomes
• Significant increase in negative acute phase proteins (albumin, prealbumin, and transferrin) (+1.32 g/L) in patients receiving the fish-oil enriched nutritional supplement (P = 0.048) compared with a significant decrease (-2.44 g/L) in the patients receiving supportive care. The difference between the two groups was highly significant (P = 0.0012)
• Although not a primary outcome, a positive effect on weight was observed after 4 weeks in the patients receiving the fish-oil enriched nutritional supplement (median change in weight = +1.0 kg) compared to the patients receiving supportive care (median change in weight = -2.8 kg)

Study Conclusions
Results from this study suggest that many positive and negative acute-phase proteins are altered in patients with advanced pancreatic cancer. Consuming a fish-oil enriched nutritional supplement may help stabilize the acute-phase protein response which may play a role in reducing wasting in patients with advanced pancreatic cancer.
Barber and colleagues enrolled weight-losing, non-diabetic patients with unresectable pancreatic adenocarcinoma and healthy, weight stable controls in this prospective, single-center, single-arm study. Patients with cancer had a rate of weight loss of 2.9 kg/month prior to enrollment. Resting energy expenditure was measured in the fasting and fed state using indirect calorimetry. Bioimpedence analysis was used to estimate body composition.

Objective
To evaluate the metabolic response to feeding in patients with cancer cachexia compared with healthy controls and to determine the effect on the metabolic response to feeding after consuming a fish-oil enriched nutritional supplement for 3 weeks in patients with advanced pancreatic cancer.

Study Design
- **STUDY POPULATION:** Pancreatic (n = 16); Healthy weight-stable controls (n = 6)
- **LENGTH OF STUDY:** 3 weeks
- **INTERVENTION:** 2 servings ProSure (240 mL/serving)

Outcomes
After 3 weeks of consuming a median 1.9 cans/day (range 1.25-2.0) of the fish-oil enriched nutritional supplement, patients experienced:
- Median weight gain of 1.0 kg (-0.25 to 1.75) (P < 0.05 compared with baseline)
- Median increase in lean body mass of 0.75 kg (0.1-1.6) (P < 0.05)
- No effect on fat mass, 0.0 kg (-0.6 to 0.9)
- Resting energy expenditure rose significantly in response to feeding (9.6%) and was no different from baseline healthy control values.

Study Conclusions
Results suggest that normalization of the metabolic response can be achieved in both the fasted and fed state in weight-losing patients consuming a fish-oil enriched nutritional supplement. Nutritional status also improved.
Effect of a fish-oil enriched nutritional supplement on metabolic mediators in patients with pancreatic cancer cachexia


Barber and colleagues enrolled weight-losing patients with pancreatic cancer in this prospective, single-arm study. Patients had a rate of weight loss of 2.9 kg/month prior to enrollment.

**Objective**

To evaluate the effects of a fish-oil enriched nutritional supplement on cytokine and hormonal mediators thought to play a role in cancer cachexia.

**Study Design**

- **STUDY POPULATION**: Pancreatic (n = 20)
- **LENGTH OF STUDY**: 3 weeks
- **INTERVENTION**: 2 servings ProSure (240 mL/serving)

**Outcomes**

After 3 weeks of consuming a median 1.9 cans/day (range 1.25-2.0) of the fish-oil enriched nutritional supplement, patients experienced:

- **Significant decrease in IL-6** from a median of 16.5 to 13.7 ng/mL; *P* = 0.015
- **Significant increase in serum insulin concentration** from a median of 3.3 to 5.0 mU/L; *P* = 0.0064
- **Significant decrease in the cortisol-to-insulin ratio** (*P* = 0.0084)
- **Significant decrease in the percent of patients excreting proteolysis inducing factor** from 88% to 40%; *P* = 0.008
- Median weight gain of 1.0 kg (interquartile range -0.1 to +2.0, *P* = 0.024 versus baseline)

**Study Conclusions**

Results of this study demonstrate that a number of catabolic mediators of cachexia can be modulated by a fish-oil enriched nutritional supplement in patients with pancreatic cancer. The modulation of these catabolic mediators may explain the reversal of weight loss observed in the patients consuming this supplement.
Weight gain is associated with improved quality of life in patients with cancer cachexia consuming an energy and protein dense, high n-3 fatty acid oral supplement


In a multicenter, randomized, double-blind, controlled trial, cachectic patients with pancreatic cancer were randomized to consume two servings of an energy and protein dense oral supplement enriched with n-3 fatty acids or an isocaloric, isonitrogenous control. Body weight, quality of life, and grip strength were measured at baseline and after 8 weeks.

Objective
To evaluate the effect of an energy and protein dense oral supplement enriched with n-3 fatty acids (ProSure) on body weight and quality of life in cachectic patients with pancreatic cancer.

Study Design
- **STUDY POPULATION**: Pancreatic (n = 200; ProSure = 95, control = 105)
- **LENGTH OF STUDY**: 8 weeks
- **INTERVENTION**: 2 servings/day ProSure (240 mL/serving) or isocaloric, isonitrogenous control

Outcomes
Compared to the control group, weight change in the ProSure group correlated significantly with changes in:
- EQ-5D index, \( r = 0.46, P = 0.001 \)
- EQ-5D vasc, \( r = 0.38, P = 0.01 \)
- Physical functioning domain of QLQ-C30 (\( r = 0.33, P = 0.022 \))
- Grip strength (\( r = 0.38, P = 0.009 \))

Study Conclusions
In patients with advanced pancreatic cancer taking ProSure, weight gain was associated with improvements in quality of life and grip strength.
Effect of a protein and energy dense n-3 fatty acid enriched oral supplement on loss of weight and lean tissue in cancer cachexia: a randomised double blind trial


In a multicenter, randomized, double-blind, controlled trial, 200 cachectic patients with pancreatic cancer were randomized to consume two servings of a protein and energy dense oral supplement enriched with n-3 fatty acids or an isocaloric, isonitrogenous control. Before the study, participants were losing weight at a median rate of 3.3 kg/month (7.3 lb/month). Weight, lean body mass, dietary intake, and quality of life (EORTC QLQ-C30 and EQ-5D) were measured at baseline and after 8 weeks.

**Objective**

To examine the effect of a high-protein, calorically-dense, EPA-containing nutrition supplement on weight, lean body mass (LBM), dietary intake, and quality of life in cachectic patients with advanced pancreatic cancer.

**Study Design**

- **STUDY POPULATION**: Pancreatic (n = 200; ProSure = 95, control = 105)
- **LENGTH OF STUDY**: 8 weeks
- **INTERVENTION**: 2 servings/day ProSure (240 mL/serving) or isocaloric, isonitrogenous control

**Outcomes**

- **Weight**: Weight of people in both groups stabilized at 4 and 8 weeks. **Increased daily intake of ProSure was positively correlated with increased body weight at 8 weeks.** ($P < 0.001$, $r = 0.50$)

- **Lean body mass**: Increased daily intake of ProSure was positively correlated with **increased lean body mass** at 8 weeks. ($r = 0.33$, $P = 0.036$). No such correlation was observed in the control group.

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Effect of a protein and energy dense n-3 fatty acid enriched oral supplement on loss of weight and lean tissue in cancer cachexia: a randomised double blind trial (continued)


Effect of weight change on QOL-C30 physical function score

Study Conclusions

Supplement intake in both groups was below the recommended 2 servings/day (average 1.4 servings/day). Therefore, a post-hoc dose response analysis was undertaken and revealed that when the supplements were taken at the recommended dose, only the patients consuming the n-3 fatty acid enriched energy and protein dense oral supplement experienced net gain of weight, lean tissue, and improved quality of life.

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- **Dietary intake.** People consuming ProSure had a significant increase in total (meal plus supplement) energy and protein intake \((P \leq 0.001)\). There was no increase in the control group.

- **Quality of life (QOL) and grip strength.** ProSure intake positively correlated with QOL measured by the EQ-5D \(_{\text{vase}}\) \((r = 0.37, P = 0.01)\), but there was no correlation in the control group. **Weight gain** in the ProSure group also correlated with improvements in other measures of QOL and with measures of physical function: EQ-5D \(_{\text{vase}}\) \((r = 0.46, P = 0.001)\), EQ-5D \(_{\text{vase}}\) \((r = 0.38, P = 0.01)\), physical functioning domain of QLQ-C30 \((r = 0.33, P = 0.022)\), and grip strength \((r = 0.38, P = 0.009)\). There was no correlation in the control group.

Effect of weight change on EQ5D Score
Reduced total energy expenditure and physical activity in cachectic patients with pancreatic cancer can be modulated by energy and protein dense oral supplement enriched with n-3 fatty acids

*Moses AWG, Slater C, Preston T, Barber MD, Fearon KCH  *Br J Cancer. 2004;90:996-1002

In a prospective, randomized, double-blind, controlled trial, Moses and colleagues evaluated the effect of ProSure on physical activity level (PAL) in 19 weight-losing patients with pancreatic cancer. Study participants were asked to consume 2 cans/day of either an n-3 fatty acid containing oral nutritional supplement or an isocaloric, isonitrogenous control for 8 weeks. Total energy expenditure (TEE) was measured at baseline (within the first 14 days of the study) and again between 6 and 8 weeks using the doubly-labeled water technique. Resting energy expenditure (REE) was measured by indirect calorimetry, and PAL was calculated by the formula PAL = TEE/REE.

**Objective**
To assess the total energy expenditure (TEE), resting energy expenditure (REE) and physical activity level (PAL) in cachectic patients with advanced pancreatic cancer.

**Study Design**
- **STUDY POPULATION:** Pancreatic (n = 19; ProSure = 7, control = 12)
- **LENGTH OF STUDY:** 8 weeks
- **INTERVENTION:** 2 servings/day ProSure (240 mL/serving) or isocaloric, isonitrogenous control

**Outcomes**
- **Physical Activity Level (PAL).** There was a statistically significant ($P = 0.005$) increase from baseline PAL in the ProSure group. There was no significant PAL change in the control group; most patients remained confined to bed. This significant increase in PAL parallels the significantly increased Karnofsky Performance Status previously reported for pancreatic cancer patients who received ProSure nutrition. (Barber, et al. Br J Cancer. 1999).

**Change in PAL for patients treated with ProSure versus control***


**Study Conclusions**
Patients with pancreatic cancer consuming ProSure experienced an increase in PAL; improving from a baseline PAL of 1.2-1.3 (confined to bed) to a near-normal sedentary level (PAL = 1.5).
Weight stabilisation is associated with improved survival duration and quality of life in unresectable pancreatic cancer


Davidson and colleagues performed a post hoc analysis of data from 107 patients who were enrolled in the Fearon 2003 trial. Patients were included in the post hoc analysis if weight data was available for both baseline and week 8.

Objective
To examine whether weight stabilization was associated with improved survival and QoL and to identify determinants of weight stabilization.

Study Design
• STUDY POPULATION: Pancreatic (n = 107)
• LENGTH OF STUDY: 8 weeks
• INTERVENTION: 2 servings/day ProSure (240 mL/serving) or isocaloric, isonitrogenous control

Outcomes
• Patients with weight stabilization survived longer from baseline (log rank test 5.53, \( P = 0.019 \)). They also reported higher QoL scores (\( P = 0.037 \)) and a greater mean energy intake (\( P < 0.001 \)) at week 8 than those who continued to lose weight.

Study Conclusions
Weight stabilization over an 8 week period in weight-losing patients with unresectable pancreatic cancer was associated with improved survival duration and QoL.
EPA enriched nutritional support and fast track surgery for elective periampullary carcinoma


Patients undergoing elective surgery for periampullary carcinoma were enrolled in this prospective, single-center, open-label study.

**Objective:**
To evaluate the role of early enteral feeding and an EPA enriched diet during the postoperative period in patients with periampullary carcinoma.

**Study Design:**
- **STUDY POPULATION:** Patients undergoing elective surgery for periampullary carcinoma (n = 228; fast track rehabilitation after surgery with EPA enriched supplement (ProSure) n = 128; conventional treatment postoperatively n = 100)
- **LENGTH OF STUDY:** 2 months
- **INTERVENTION:** ProSure or conventional treatment

**Outcomes:**
Fast track treated patients experienced:
- Significantly faster resumption of bowel function (4.1 ± 0.3 days vs 6.3 ± 0.7 days)
- Significantly shorter postoperative hospital length of stay (6.7 ± 0.8 days vs 13.1 ± 0.5 days)
- Less postoperative weight loss at 2 months (6.5% vs 13.6%)

**Study Conclusions**
Fast track surgery can benefit high-risk patients undergoing elective surgery for periampullary cancer.
Guarcello and colleagues evaluated weight losing patients with lung cancer who were scheduled to undergo chemotherapy in a prospective, randomized, blinded, controlled study. Patients were included in the study if they had experienced > 10% body weight loss in the previous 6 months.

**Objective:**
To evaluate the influence of an EPA-enriched, energy-dense oral supplement on inflammatory and nutritional status, as well as on the quality of life of lung cancer patients.

**Study Design:**
- **STUDY POPULATION:** Patients with lung cancer eligible for chemotherapy (n = 46; ProSure n = 26, control n = 20)
- **LENGTH OF STUDY:** 60 days
- **INTERVENTION:** 2 servings ProSure (240 mL/serving) or isocaloric, isonitrogenous control

**Outcomes:**
- Over the 2-month study interval when chemotherapy was administered, only patients who received ProSure showed significant increases in body weight (at 30 days, + 0.9 kg, *P* < 0.05), energy and protein intakes, appetite, and quality of life. In addition, levels of markers for nutritional status were significantly increased at 30 days (prealbumin + 3, *P* < 0.05; transferrin + 26, *P* < 0.05), while levels of inflammatory marker C-reactive protein were decreased in patients who consumed ProSure.

**Study Conclusions:**
Intake of ProSure seems effective in improving the quality of life and nutritional status of patients with lung cancer undergoing chemotherapy without decreasing meal intake.
A double blind randomized controlled trial on oral nutritional supplementation of omega-3 fatty acids in non-small cell lung carcinoma


van der Meij and colleagues conducted a double-blind, randomized, placebo-controlled trial in patients with stage III non-small cell lung carcinoma who were randomized to receive either ProSure or a control supplement during 5 weeks of chemo-radiotherapy.

Objective

To assess the effect of an oral nutritional supplement enriched with omega-3 fatty acids on nutritional status in patients with non-small cell lung carcinoma receiving chemo-radiotherapy.

Study Design

- STUDY POPULATION: Patients with stage III non-small cell lung carcinoma receiving chemo-radiotherapy (n = 40; ProSure = 20, control = 20)
- LENGTH OF STUDY: 5 weeks
- INTERVENTION: 2 servings ProSure (240 mL/serving) or isocaloric isonitrogenous control

Outcomes

- Compared to the control group, the ProSure group had better weight maintenance during weeks 1, 2, and 4 (1.2 kg, 1.4 kg, and 1.8 kg, $P < 0.05$) and higher EORTC-QLQC30 physical function scores at week 5 ($P < 0.05$).

Study Conclusions

Results of this study underscore the beneficial effects of a high-protein, calorically-dense, low-fat nutritional supplement enriched with EPA (ProSure) on nutritional status and physical function in patients with non-small cell lung carcinoma undergoing chemo-radiotherapy.
van der Meij and colleagues conducted a double-blind, randomized, placebo-controlled trial in patients with stage III non-small cell lung carcinoma who were randomized to receive either ProSure or a control supplement during 5 weeks of chemo-radiotherapy.

Objective
To compare the effects on nutritional status, quality of life, physical activity and immune parameters of a supplemental drink enriched with omega-3 fatty acids with a placebo supplemenatal drink in patients with non-small cell lung cancer receiving chemo-radiotherapy.

Study Design
• STUDY POPULATION: Patients with stage III non-small cell lung carcinoma receiving chemo-radiotherapy (n = 40; ProSure = 20, control = 20)
• LENGTH OF STUDY: 5 weeks
• INTERVENTION: 2 servings ProSure (240 mL/ serving) or isocaloric isonitrogenous control

Outcomes
• Compared to the control group, the ProSure group had better weight maintenance during weeks 1, 2, and 4 (1.1 kg, 1.4 kg, and 1.7 kg, $P < 0.05$) and higher physical functioning as measured by EORTC-QLQ-C30 and physical activity measured by wearing the Personal Activity Monitor at weeks 3 and 5 ($P < 0.05$).
van der Meij and colleagues conducted a double-blind, randomized, placebo-controlled trial in patients with stage III non-small cell lung carcinoma.

**Objective:**
To assess the effects of an oral nutritional supplement containing n-3 fatty acids on nutritional status and inflammatory markers in patients with non-small cell lung cancer undergoing multimodality treatment.

**Study Design:**
- **STUDY POPULATION:** Patients with stage III non-small cell lung carcinoma receiving chemo-radiotherapy (n = 40; ProSure n = 20, control n = 20)
- **LENGTH OF STUDY:** 5 weeks
- **INTERVENTION:** 2 servings ProSure (240 mL/serving) or isocaloric control

**Outcomes:**
- Compared to the control group, the ProSure group had:
  - Better weight maintenance after weeks 2 and 4 (1.3 kg and 1.7 kg, respectively, \( P < 0.05 \))
  - Better fat free mass maintenance after 3 and 5 weeks (1.5 and 1.9 kg, respectively, \( P < 0.05 \))
  - A trend towards a lower IL-6 production after 5 weeks (-27.9; \( P = 0.08 \))

**Study Conclusions:**
Results of this study underscore the beneficial effects of a protein and energy-dense, oral nutritional supplement containing n-3 fatty acids on nutritional status in patients with stage III non-small cell lung carcinoma undergoing multimodality treatment.
Patients with advanced non-small cell lung cancer (NSCLC) who were naive to treatment with good performance status (ECOG 0-2) were included in this prospective, randomized, single-blind study.

Objective:
To evaluate the influence of nutritional parameters on quality of life and survival in advanced NSCLC patients.

Study Design:
- **STUDY POPULATION**: Patients with advanced NSCLC, n =119
- **LENGTH OF STUDY**: One week before treatment through completion of two courses of chemotherapy – 2 months
- **INTERVENTION**: 2 servings ProSure (240 mL/serving) or isocaloric diet with nutritional assessment

Outcomes:
- Malnutrition measured by Subjective Global Assessment (SGA), weight loss >10%, body mass index (BMI) >24 was associated with a decrease in the majority of quality of life (QoL) domains.
- Patients with ECOG 2 and malnutrition parameters showed lower overall survival (OS); however after multivariate analysis, ECOG 2 (HR 2.7 [95% CI 1.5-4.7] P =0.001), phase angle ≤ 5.8 (3.02 [1.2-7.11] P =0.011) and SGA (2.7 [95% CI 1.31-5.5] P =0.005) were associated with poor survival.
- Patients were divided into low, medium, and high risk groups according to regression coefficients with OS at 1 year of 78.4%, 53% and 13.8%, respectively.
Patients with advanced non-small cell lung cancer (NSCLC) who were naive to treatment were included in this prospective, randomized, study.

**Objective:**
To evaluate the effect of an EPA-containing supplement on body composition, quality of life, and survival in patients with advanced NSCLC.

**Study Design:**
- **STUDY POPULATION:** Patients with advanced NSCLC, n = 92
- **LENGTH OF STUDY:** Two courses of chemotherapy
- **INTERVENTION:** 2 servings ProSure (240 mL/serving) or isocaloric diet

**Outcomes:**
Between baseline and the end of the second cycle of chemotherapy, patients who consumed the EPA-containing supplement had a **significant increase** in:
- calories, protein, and carbohydrates (P <0.001) compared with the control group.
- lean body mass (+1.6 kg) despite a slight decrease in weight, (P = 0.04) compared with the control group (-0.3 kg).

In addition, the patients who consumed the EPA-containing supplement also experienced an improvement in global and physical measures of quality of life with less fatigue, anorexia, and neuropathy compared with the control group.
**A randomized clinical trial with oral immunonutrition (ω3-enhanced formula vs arginine-enhanced formula) in ambulatory head and neck cancer patients**


In a prospective, randomized, controlled, blinded study by de Luis and colleagues, patients with head and neck cancers were randomized to receive either 2 servings a day of a nutritional supplement (ProSure) or an isocaloric, arginine-enriched drink during a 12-week period of recovery from cancer surgery.

**Objective**

To investigate whether oral ambulatory nutrition of head and neck cancer patients, using an ω3 fatty acid-enhanced diet (low ratio ω6/ω3 fatty acids) versus an arginine-enhanced diet, could improve nutritional variables as well as clinical outcome, postoperative infections, and wound complications.

**Study Design**

- **STUDY POPULATION**: Post-surgical head and neck cancer patients (n = 73; ProSure = 38, arginine-enhanced supplement = 35)
- **LENGTH OF STUDY**: 12 weeks
- **INTERVENTION**: 2 servings ProSure (240 mL/serving) or 2 servings (300 mL/serving) arginine-enhanced supplement

**Outcomes**

- From baseline to 3 months, patients consuming ProSure exhibited a statistically significant increase in weight (65.5 ± 11.5 kg vs 70.4 ± 11.1 kg; *P* < 0.05), fat mass (15.4 ± 6.6 vs 18.1 ± 8.4 kg; *P* < 0.05), and tricipital skinfold (10.9 ± 4.7 vs 12.35 ± 6.1 mm; *P* < 0.05).

**Study Conclusions**

Use of ProSure significantly increased weight gain, including both body fat and visceral proteins. The arginine-enriched drink increased only visceral protein.
Patients with otolaryngeal cancer who were undergoing radical radiotherapy were enrolled in this prospective, single-center, open-label study.

Objective:
To evaluate the effect of oral supplementation enriched with omega-3 fatty acids on inflammatory parameters and oxidative stress in patients with otolaryngeal cancer treated with radiotherapy.

Study Design:
- **STUDY POPULATION:** Patients with otolaryngeal cancer (n = 32; omega-3 fatty acids enriched supplement (ProSure) n = 16, control n = 16)
- **LENGTH OF STUDY:** During radiotherapy and 3 months after treatment
- **INTERVENTION:** ProSure or standard supplement

Outcomes:
Oxidative stress and inflammatory parameters were significantly better in the patients supplemented with omega-3 fatty acids compared to the patients who received the standard supplement.

After 3 months of treatment, the patients supplemented with omega-3 fatty acids experienced:
- An increase in total antioxidant capacity ($P < 0.05$)
- An increase in glutathione peroxidase activity ($P < 0.01$)
- A decrease in lipoperoxide levels ($P < 0.05$)
- A decrease in C-reactive protein levels ($P < 0.05$)

Study Conclusions:
Supplementation with omega-3 fatty acids appears to improve oxidative stress in patients with otolaryngeal cancer treated with radiotherapy.
Weed and colleagues conducted a prospective, single-arm, open-label study in patients with head and neck cancer experiencing unintentional weight loss of at least 5% during the preceding 6 months who were scheduled for surgical resection with curative intent.

**Objective:**
To determine the safety and tolerance and the impact of pre- and post-operative consumption of a protein and energy dense nutritional supplement containing omega-3 fatty acid eicosapentaenoic acid (EPA) on weight and body composition in patients with head and neck cancer-related weight loss undergoing treatment with curative intent.

**Study Design:**
- **STUDY POPULATION:** Patients with head and neck squamous cell cancer (n = 38)
- **LENGTH OF STUDY:** 2 weeks prior to surgery and during hospitalization
- **INTERVENTION:** 2 servings ProSure (240 mL/serving)

**Outcomes:**
Mean ProSure consumption before surgery was 1.8 cans/day; in-hospital consumption was 1.5 cans/day.

The following changes in weight were noted:
- 70% of patients maintained or gained weight from study entry to time of hospital admission
  - Weight gain from study entry to hospital admission = + 0.71 kg (n = 27)
- 57% of patients maintained or gained weight from study entry to hospital discharge
  - Weight gain from study entry to hospital discharge = + 0.66 kg (n = 30)
- In 23 patients there was a statistically significant increase in mean lean body mass (LBM) from study entry to hospital discharge: +3.20 kg; +7% ($P < .001$).

**Study Conclusions:**
Data from this pilot study suggests that patients with head and neck cancer can benefit from a protein and energy dense, EPA-containing nutritional supplement before and after surgical treatment.
Patients with previously untreated stage IIb-IV nasopharyngeal cancer (NPC) who were to receive concomitant chemoradiotherapy were enrolled in this open-label, prospective, randomized trial.

Objective:
To evaluate the benefit of an EPA-containing nutrition supplement in NPC patients who are receiving concomitant chemoradiotherapy.

Study Design:
- **STUDY POPULATION**: Patients with previously untreated stage IIb-IV NPC (n = 116; EPA-containing nutrition supplement (ProSure) n = 59, control n = 57)
- **LENGTH OF STUDY**: 3 months
- **INTERVENTION**: EPA-containing nutrition supplement or isotonic balanced nutrition formula

Outcomes:
Significant difference between the groups in infection rates requiring hospitalization:
- 6 patients in the EPA supplement group (10.2%) vs 16 patients in the control group (28.1%), \( P = 0.014 \)

Study Conclusions:
Intake of an EPA-containing supplement was found to decrease the rate of hospital admission due to infection.
Nutrition intervention using an eicosapentaenoic acid (EPA)-containing supplement in patients with advanced colorectal cancer. Effects on nutritional and inflammatory status: a phase II trial


In a prospective, open-label study by Read and colleagues, patients with advanced colorectal cancer were given ProSure 3 weeks before chemotherapy began and for 9 weeks during chemotherapy.

**Objective**

To assess the impact of an eicosapentaenoic acid-containing protein and energy dense oral nutritional supplement (EPA-ONS) on nutritional and inflammatory status, quality of life (QOL), plasma phospholipids, and cytokine profile, tolerance of irinotecan-containing chemotherapy and EPA-ONS in patients with advanced colorectal cancer receiving chemotherapy.

**Study Design**

- **STUDY POPULATION:** Patients with colorectal cancer receiving chemotherapy (n = 23) 20 patients completed 3 weeks; and 15 completed 9 weeks
- **LENGTH OF STUDY:** 3-9 weeks
- **INTERVENTION:** 2 servings ProSure (240 mL/ serving)

<table>
<thead>
<tr>
<th>Marker</th>
<th>Baseline</th>
<th>Pre-chemo End week 3</th>
<th>During or post-chemo End week 9</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, kg</td>
<td>75.9 (17.0)</td>
<td>78.4 (17.5)</td>
<td>78.4 (17.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Lean body mass, kg</td>
<td>50.3 (10.7)</td>
<td>51.4 (10.2)</td>
<td>51.7 (10.6)</td>
<td>NS</td>
</tr>
<tr>
<td>C-reactive protein, mg/L</td>
<td>18.2 (13.9)</td>
<td>33.1 (32.6)</td>
<td>19.4 (17.7)</td>
<td>0.004 (end of week 3)</td>
</tr>
<tr>
<td>QOL—overall well-being</td>
<td>7 (2.2)</td>
<td>7 (1.7)</td>
<td>8 (1.7)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Mean values (SD)

*P values are for baseline vs timepoint value; NS, not significant

**Outcomes**

- ProSure feeding (average daily intake 408 mL) produced a significant increase in mean weight (+2.5 kg, P = 0.03) at 3 weeks and preserved lean body mass during chemotherapy. In addition, there was a significant increase in energy levels (P = 0.03) during the study, while quality of life (QOL) was maintained.

**Study Conclusions**

The researchers concluded that ProSure helped patients with advanced colorectal cancer receiving chemotherapy to maintain weight, and lean body mass, and possibly improved symptom control, nutritional status and QOL. Dietary counseling improved compliance with ProSure. Inflammation, measured by C-reactive protein, was stabilized.
Enteral nutrition enriched with eicosapentaenoic acid (EPA) preserves lean body mass following esophageal cancer surgery: results of a double-blinded randomized controlled trial


In a prospective, randomized, double-blind, controlled trial, Ryan and colleagues studied the effect of consuming an EPA enriched enteral nutrition formula pre- and postoperatively in patients undergoing esophagectomy.

Objective
To evaluate the effects of perioperative EPA enriched enteral nutrition on the metabolic, nutritional, and immuno-inflammatory response to esophagectomy, and on postoperative complications.

Study Design
• **STUDY POPULATION:** Patients with resectable esophageal cancer (n = 53; ProSure = 28, control = 25)

• **LENGTH OF STUDY:** 5 days preoperatively (orally) and 21 days postoperatively (jejunal feeding)

• **INTERVENTION:** 2 servings ProSure (240 mL/serving) or isocaloric isonitrogenous control

Outcomes
• ProSure-fed patients **maintained lean body mass** throughout the study, while patients on standard enteral nutrition lost significant amounts of muscle from the leg (0.3 kg ± 0.6; P = 0.05), arm (0.17 kg ± 0.3; P = 0.01), and trunk (1.44 kg ± 2.7; P = 0.03), for a total loss of 1.9 kg (± 3.7) lean body mass. In the hospital, 39% of standard-fed patients experienced severe weight loss (> 5% total body weight), but only 8% of ProSure-fed patients showed such loss, a difference that was statistically significant (P = 0.03). Compared with the standard enteral nutrition fed group, the ProSure-fed group also had a significantly (P < 0.05) **attenuated stress response to surgery** for IL-8, IL-10, and TNF-α.

• In addition, there was no abnormal intra-operative bleeding and no difference between the ProSure group and the control group in prothrombin time, platelets, or D-Dimer levels.

Significantly fewer patients fed EPA-ONS (ProSure) experienced severe weight loss in comparison with control-fed patients.

Continued on next page.
Enteral nutrition enriched with eicosapentaenoic acid (EPA) preserves lean body mass following esophageal cancer surgery: results of a double-blinded randomized controlled trial (continued)


Continued from previous page.

Study Conclusions
The anti-inflammatory and anabolic properties of protein and energy dense EPA-containing nutrition (ProSure) benefit patients undergoing complex, major surgery for esophageal cancer. Such properties may also benefit patients with other solid tumors such as lung and head and neck cancer.

IL-8 levels were significantly lower on postoperative days 7 and 14 in the EPA-containing nutrition group compared to the control nutrition group ($P = 0.05$).
Complementary effect of ProSure for anticancer chemotherapy

Taniguchi M 2nd International Conference on Cancer Nutrition Therapy, 2011, Edinburgh, Scotland

Case study

Objective:
To evaluate the supportive effect of ProSure to anticancer chemotherapy in advanced gastric cancer.

Study Design:
- STUDY POPULATION: 60-year-old male post-surgical gastric cancer patient
- LENGTH OF STUDY: 7 months
- INTERVENTION: 2 servings ProSure (240 mL/serving)

Outcomes:
With oral ProSure supplementation, patient could take foods gradually and was weaned from parenteral nutrition (PN). His body weight and serum albumin level remained stable. Because of his fair nutritional status, chemotherapy could be continued. Serum CEA and CA19-9 levels were decreasing and became normal. He could live at home with normal food intake and oral supplementation of ProSure for seven months post surgery.

Chemotherapy enabled oral supplementation of ProSure (improved stenosis of stomach allowing oral intake), and ProSure enabled continuation of chemotherapy due to improved nutritional status.

Study Conclusions:
ProSure and chemotherapy have complementary effects in a post-surgical patient with advanced gastric cancer.
Patients with stage IV colorectal cancer who were going to receive first line chemotherapy were enrolled in this prospective, randomized, controlled, open-label pilot study.

**Objective:**
To assess the effectiveness of an oral nutritional supplement enriched with eicosapentaenoic acid on chemotherapy tolerability in patients with advanced colorectal cancer. Chemotherapy tolerability was assessed based on variation of changes in health related quality of life (HRQOL).

**Study Design:**
- **STUDY POPULATION:** Patients with stage IV colorectal cancer (n = 13; EPA enriched supplement (ProSure) n = 6, control n = 7)
- **LENGTH OF STUDY:** 3 months
- **INTERVENTION:** ProSure plus dietary counseling or counseling alone

**Outcomes:**
**At 3 months:**
- Patients in the EPA group gained significantly more weight compared to the control group (4.94 kg vs -1.17 kg; \( P = .045 \)).

An overview of HRQOL showed a trend towards improvement in the supplemented group.

**After 3 months:**
- Statistically significant differences between groups were only found for the Social Function scale (16.67 vs -13.89; \( P = .038 \)).
- Both groups had a decrease in physical function (-4 vs 15.56; \( P = \text{ns} \)); however, only the control had a worsening over 10 points, which is considered clinically meaningful.
- The supplemented group experienced an improvement in role function (13.33 vs 2.78; \( P = \text{ns} \)).
- Changes over 10 points were also found with the control group experiencing more fatigue (-4.44 vs 11.11; \( P = \text{ns} \)) and pain (-10 vs 2.78; \( P = \text{ns} \)).

**Chemotherapy compliance:**
- No significant differences between groups; however, during the intervention period, none of the 5 patients in the supplemented group experienced a delay or stoppage of their chemotherapy regimen compared to 4 of 6 patients in the control group who experienced some type of interruption in their treatment due to toxicity.

**Study Conclusions:**
Although this study included a small sample size, results show a positive effect on weight maintenance, and some domains of HRQOL, and chemotherapy tolerability in advanced colorectal cancer patients taking an EPA enriched supplement plus dietary counseling.
Nutritional support including eicosapentaenoic acid in the prevention of chemoradiotherapy induced acute gastrointestinal complications: a prospective, controlled, clinical evaluation

Kilic D, Pak Y, Oguz M 3rd National Gastrointestinal Oncology Congress, 2011, Antalya, Turkey

Well-nourished patients receiving pelvic chemoradiotherapy for rectal cancer were enrolled in this open-label, prospective, controlled trial.

Objective:
To evaluate the efficacy of oral nutritional support with EPA in preventing acute chemoradiotherapy related gastrointestinal complications in patients with rectal cancer.

Study Design:
- **STUDY POPULATION:** Patients with rectal cancer receiving chemoradiotherapy (n = 47; EPA-containing nutrition supplement (ProSure) n = 27, control n = 20)

Patients received the following chemotherapy regimen: 5FU 425 mg/m² and folinic acid 25 mg/m² during days 1-4 and 31-33 of radiation treatment. After completion of chemoradiotherapy, patients underwent surgery for total mesorectal excision. After surgery, patients received 4 cycles of chemotherapy containing 5FU 425 mg/m² and folinic acid 25 mg/m² FA for 5 days for 3 weeks.

- **LENGTH OF STUDY:** duration of radiation
- **INTERVENTION:** 2 servings ProSure (240 mL/serving)

Outcomes:
Patients in the EPA supplement group experienced:
- Less Grade 2 or more diarrhea than the control group, 55% vs 85%, respectively, \( P = .038 \).
- Less Grade 2 or more GI toxicity than the control group, 40% vs 95%, respectively, \( P < .0001 \).

When chemoradiotherapy began, all patients were well-nourished. However, at the end of treatment, 5% of the patients in the EPA group and 35% of the controls were found to be malnourished, \( P = .044 \).

Post treatment quality of life (QOL) scores showed significant differences between the groups in favor of the EPA group for appetite loss, diarrhea, GI symptoms, weight loss, and defecation problems (\( P < .05 \)).

Study Conclusions:
In patients with rectal cancer receiving chemoradiotherapy, use of an oral nutritional supplement with EPA was effective in preventing chemoradiotherapy induced GI complications while maintaining pretreatment QOL.
Patients who started primary chemotherapy for advanced recurrent gastric cancer were enrolled in this open-label trial.

**Objective:**
To investigate the usefulness of Glasgow prognostic score (GPS) in patients undergoing chemotherapy for gastric cancer and to investigate, in an exploratory manner, the efficacy of ProSure in “cachexia group”, i.e., patients with increased CRP level and decreased albumin level.

**Study Design:**
- **STUDY POPULATION:** Patients with gastric cancer (n = 94)
- **LENGTH OF STUDY:** non-interventional
- **INTERVENTION:** Patients were classified into 4 groups based on CRP level of 0.5 mg/dL and albumin level of 3.5 g/dL
  
  - **Group A** (normal group) normal CRP and normal albumin
  - **Group B** (malnutrition group) normal CRP and decreased albumin
  - **Group C** (inflammation group) increased CRP and normal albumin
  - **Group D** (cachexia group), increased CRP and decreased albumin

Prognosis was compared among the groups.

Additionally, 6 patients in Group D were able to take 240 mL/day or more of ProSure while receiving chemotherapy

**Outcomes:**
The 94 patients were classified as follows:

- **Group A**, 39 patients (41%)
- **Group B**, 14 patients (15%)
- **Group C**, 14 patients (15%)
- **Group D**, 27 patients (29%)

One-year survival rate was 72% in group A, 63% in group B, 62% in group C, and 36% in group D, demonstrating a significantly poor prognosis in group D ($P = 0.0026$). Of the 6 patients who could take ProSure continuously, 1 improved to group A, and 2 to group B. All three patients who remained in group D showed improvement in CRP or albumin, or both.

**Study Conclusions:**
GPS is considered a prognostic factor for patients undergoing chemotherapy for gastric cancer. Results suggest that patients in the cachexia group can benefit from taking an EN formula (ProSure) enriched with EPA.
Nutrition intervention improves outcomes in patients with cancer cachexia receiving chemotherapy—a pilot study

*Bauer JD, Capra S Support Care Cancer. 2005;13:270-274*

In this prospective, single-arm, pilot study, patients with pancreatic or non-small cell lung cancer received weekly nutritional counseling by a dietitian and were asked to consume a protein- and energy-dense oral nutritional supplement containing EPA (ProSure).

**Objective**

To examine the effect of nutrition intervention with nutrition counseling by a dietitian and the intake of a protein- and energy-dense oral nutritional supplement containing EPA on outcomes of dietary intake, body composition, nutritional status, functional capacity and quality of life in patients with cancer cachexia receiving chemotherapy.

**Study Design**

- **STUDY POPULATION**: Patients with pancreatic or non-small cell lung cancer receiving chemotherapy (*n* = 7)
- **LENGTH OF STUDY**: 8 weeks
- **INTERVENTION**: Weekly nutrition counseling by a dietitian and one can per day of a protein and energy-dense, n-3 fatty acid-enriched oral nutritional supplement between meals.

**Outcomes**

- Nutritional intervention (weekly counseling and use of ProSure) together with chemotherapy provided significant benefits that included *improvements in quality of life* (EORTC QLQ-C30 global scale), *performance status* (Karnofsky score), *mean dietary and energy intake*, as well as *clinically significant improvements in weight gain and increases in lean body mass*.

**Study Conclusions**

Nutritional intervention (weekly counseling and use of ProSure) for 8 weeks in addition to chemotherapy improved outcomes in patients with pancreatic or non-small cell lung cancer.
An eicosapentaenoic acid supplement versus megestrol acetate versus both for patients with cancer-associated wasting: a North Central Cancer Treatment Group and National Cancer Institute of Canada collaborative effort


In this prospective, randomized, double-blind, controlled trial patients with incurable cancer and weight loss greater than 5 pounds (2.3 kg) within 2 months (or physician-estimated caloric intake < 20 kcal/kg body weight/day) were randomly assigned to receive either an EPA containing nutritional supplement (ProSure) plus placebo megestrol acetate, megestrol acetate plus an isocaloric, isonitrogenous control nutritional supplement, or an EPA containing nutritional supplement plus megestrol acetate. The primary endpoint was a 10% weight gain from baseline between each of the EPA groups and the megestrol acetate plus control group.

Objective
To determine whether an EPA-containing nutritional supplement—either alone or in combination with megestrol acetate (MA)—improves weight, appetite, quality of life, and survival in advanced cancer patients with cancer-associated wasting, compared with MA alone.

Study Design
• STUDY POPULATION: Incurable malignancies, excluding brain, breast, ovarian, prostate, or endometrial cancer (n = 421; n = 141 EPA + placebo megestrol acetate group, n = 140 megestrol acetate + control group, n = 140 EPA + megestrol acetate group)
• LENGTH OF STUDY: 4 weeks
• INTERVENTION: 2 servings/day ProSure (240 mL/serving) or isocaloric, isonitrogenous control

Outcomes
• Weight gain. Both ProSure- and megestrol acetate-treated groups had more than one-third of patients gaining weight over the 4-week course. ProSure was as effective as megestrol acetate, and there were fewer side effects with ProSure.

• The megestrol acetate + control group had a greater percentage of patients with ≥ 10% weight gain (18%) compared to the EPA + megestrol acetate group (11%) and the EPA + placebo megestrol acetate group. This was statistically significant. However, when comparing % of patients with ANY weight gain, there were no statistically significant differences among the groups.
• No difference among groups in the QoL assessment.
• No difference among groups for length of survival.
• A greater incidence of impotence was noted in the megestrol acetate + control group.

Study Conclusions
The authors conclude that ProSure alone or with megestrol acetate was no better than megestrol acetate alone.
Critical considerations on the use of a protein and energy dense omega-3 enriched sip feed in cancer patients

Rivista Italiana di Nutrizione Parenterale ed Enterale. 2005;23:43-46

Capuano and colleagues conducted a prospective, single-arm study in patients with cancer cachexia.

Objective

To determine the compliance and effects of ProSure on body mass index (BMI), body weight, ECOG performance status, prealbumin, and retinol binding protein in cancer patients.

Study Design

- **STUDY POPULATION**: Ambulatory patients with a variety of cancer types (n = 22)
- **LENGTH OF STUDY**: 4 weeks
- **INTERVENTION**: 2 servings ProSure (240 mL/serving)

Outcomes

- A positive correlation was observed with supplement intake and both weight gain, 3 kg ± 1 (range 2-4 kg) and improvement in performance status.

Study Conclusions

The researchers concluded that patients’ adherence to the recommended dose of supplements such as ProSure is critical to the prevention and treatment of cancer cachexia. Alterations or loss of taste, preference for foods or nutritional supplements may affect intake of supplements. Improvements in acceptability and palatability may help the treatment of cancer-related weight loss.
In a prospective, randomized, open-label study, Bayram and colleagues evaluated the effect of ProSure on cancer-related weight loss in children with leukemia or solid tumors who were undergoing chemotherapy. Weight changes, body mass index (BMI), and tolerance were monitored for 3 months, with a subset of patients followed an additional 6 months.

Objective
To evaluate the clinical effects of a protein and energy dense EPA containing oral supplement in pediatric cancer patients receiving active chemotherapy treatment.

Study Design
- **STUDY POPULATION:** The mean age of the children was 7.5 years. Pediatric patients with malignant disease (leukemia or solid tumors) receiving intensive chemotherapy ($n = 52$; ProSure = 33, control = 19)
- **LENGTH OF STUDY:** 3 months
- **INTERVENTION:** 2 servings ProSure (240 mL/serving) or usual dietary care

Outcomes
- After 3 months, only 6.1% of children in the ProSure group lost weight, compared to 47.4% of children in the control group ($P = 0.001$). Similarly, 12.1% of the children in the ProSure group had a lowered BMI, compared to 52.6% of children in the control group ($P = 0.002$). These differences were associated with a higher rate of cancer remission in the ProSure group compared to the control group (87.9% vs 63.2%, $P = 0.036$).

Study Conclusions
Children with malignant disease fed a protein and energy dense EPA containing oral supplement experienced a decrease in cancer-induced weight loss.
This section includes summaries of 5 studies and 2 papers that support the use of fish oil in patients with cancer.

Summaries of three early studies that demonstrate the clinical benefits of using fish oil in patients with pancreatic cancer and generalized tumors are included. In addition, 2 recently published studies using supplemental fish oil in patients with lung cancer are summarized.

Two publications that are not clinical studies are also included: A summary of a recently published international consensus statement on the definition and classification of cancer cachexia and a minireview of studies that evaluated the role of eicosapentaenoic acid (EPA) on lean body mass (LBM) in cancer cachexia.
The effect of polyunsaturated fatty acids on the progress of cachexia in patients with pancreatic cancer


Patients with unresectable adenocarcinoma of the pancreas (stage II-IV) and a history of weight loss were enrolled in this prospective, single-arm pilot study.

**Objective:**
To evaluate the effect of fish oil capsules, containing eicosapentaenoic acid (EPA), on nutritional parameters and acute phase response (APR) in cachectic patients with pancreatic cancer.

**Study Design:**
- **STUDY POPULATION:** Patients with unresectable adenocarcinoma of the pancreas (n = 18)
- **LENGTH OF STUDY:** 3 months
- **INTERVENTION:** 2 g/day fish oil capsules increased at weekly intervals by 2 g to a maximum dose of 16 g/day

**Outcomes:**
- Patients tolerated a median maximum dose of 12 g/day of fish oil.
  All patients were losing weight before the study (median 2.9 kg/month).
- After 3 months of supplementation, weight loss had been stopped or reversed in 14 of 18 patients (median weight change 0.3 kg/month).
- After 1 month of supplementation, CRP levels significantly decreased from 15 mg/L to 10 mg/L (P < 0.002); although following 3 months of supplementation, CRP levels had returned to presupplementation levels.
- One month of supplementation increased plasma EPA (from undetectable levels to a median of 5.3% total fatty acids) and DHA (from 3.5% to a median of 6.6% total fatty acids).
- There was no significant change in body water and body composition, and resting energy expenditure was stabilized.

**Study Conclusions:**
Supplementation with fish oil (2 g/day EPA) significantly altered the progression of cachexia in patients with pancreatic cancer. Following supplementation with fish oil, patients became weight stable (median 0.3 kg/month) compared with pre-study when they were losing weight at a median rate of 0.2 kg/month.

EPA - eicosapentaenoic acid
Patients with generalized solid tumors were enrolled in this prospective, randomized, controlled study.

**Objective:**
To evaluate the effect of dietary omega-3 polyunsaturated fatty acids from fish oil plus vitamin E on the immune status and survival of well-nourished and malnourished patients with generalized malignancy.

**Study Design:**
- **STUDY POPULATION:** Patients with generalized solid tumors (n = 64)
- **LENGTH OF STUDY:** 40 days
- **INTERVENTION:** 18 g of fish oil capsules 3 times daily

**Outcomes:**
No effect of omega-3 polyunsaturated fatty acids on body weight, serum albumin, or serum transferrin in either the well-nourished or malnourished group.
- A significant increase in the T helper/T suppressor lymphocyte ratio in the malnourished group.
- No significant differences in the production of IL-1 and IL-6 between the well-nourished and malnourished groups.
- Karnofsky Performance Status was significantly improved (P < 0.01) in the malnourished-treated group.

**Study Conclusions:**
Supplementation with fish oil (18 g/day omega-3 polyunsaturated fatty acids) had a significant immunomodulating effect and seemed to help prolong survival in malnourished patients with generalized malignancy.

- Survival was significantly prolonged (P < 0.001) in the well-nourished group compared with the malnourished group. The best survival rates were found in the well-nourished supplemented group, and the worst survival rates were found in the malnourished placebo group.
- Supplementation with omega-3 fatty acids and vitamin E resulted in a significantly increased survival rate (P < 0.025) for all patients compared with placebo.
Patients with unresectable adenocarcinoma of the pancreas were enrolled in this prospective, single-arm study.

Objective:
To evaluate the acceptability and effects of oral supplementation with high-purity eicosapentaenoic acid (EPA) in weight-losing patients with advanced pancreatic cancer.

Study Design:
- **STUDY POPULATION**: Patients with unresectable adenocarcinoma of the pancreas (n = 26)
- **LENGTH OF STUDY**: 12 weeks
- **INTERVENTION**: Daily EPA supplementation starting at 1 g/day for the 1st week and increasing to a maximum of 6 g/day from week 4 to the end of the study

Outcomes:
- Before supplementation, all patients had been losing weight at a median rate of 2.0 kg/month and had lost a median of 13% of their usual body weight.
- A median weight gain of 0.5 kg/month ($P = 0.0009$) was observed after 4 weeks of supplementation.
- There were no significant changes in total body water, and the percentage of people with an elevated CRP did not increase.

Study Conclusions:
As observed in the 1998 study conducted by Wigmore et al, highly purified EPA stabilized weight in people with pancreatic cancer and tempered the progression of weight loss. However, increasing the maximum daily dose of EPA from 2 g to 6 g did not appear to enhance the anticachectic effects.

*Effect of oral eicosapentaenoic acid on weight loss in patients with pancreatic cancer*

Nutritional intervention with fish oil provides a benefit over standard of care for weight and skeletal muscle mass in patients with nonsmall cell lung cancer receiving chemotherapy

Murphy RA, Mourtzakis M, Chu QSC, Baracos VE, Reiman T, Mazurak VC Cancer. 2011;117:1775-1782

Patients with nonsmall cell lung cancer (NSCLC) who were naïve to chemotherapy were enrolled in this open-label trial.

Objective:
To evaluate the effect of nutritional intervention with fish oil on weight and body composition against standard of care (SOC) during the course of chemotherapy.

Study Design:
• STUDY POPULATION: Patients with NSCLC (n = 40; fish oil group n = 16, standard of care group n = 24)
• LENGTH OF STUDY: 1st day of chemotherapy and continuing for the duration of chemotherapy
• INTERVENTION: 1-g gelatin capsules containing 2.2 g EPA 4 times per day or 7.5 mL liquid fish oil containing 2.2 g EPA once per day

Outcomes:
Fish oil was well tolerated with no serious adverse events reported.
• Patients in the fish oil supplement group maintained their weight (0.5 ± 1.0 kg) whereas patients in the SOC group lost an average of -2.3 ± 0.9 kg; P = .05.
• Approximately 69% of patients in the fish oil supplement group gained or maintained muscle mass compared with only 29% of patients in the SOC group who maintained muscle mass.

Study Conclusions:
Nutritional intervention with 2.2 g fish oil per day appears to provide a benefit over SOC by maintaining weight and muscle mass during chemotherapy.
Supplementation with fish oil increases first-line chemotherapy efficacy in patients with advanced nonsmall cell lung cancer


Patients with stage IIIB or IV nonsmall cell lung cancer (NSCLC) who were chemotherapy-naïve were enrolled in this open-label trial.

**Objective:**
To evaluate the effect of fish oil on response rate and clinical benefit from chemotherapy.

**Study Design:**
- **STUDY POPULATION:** Patients with NSCLC (n = 46; fish oil group n = 15, standard of care group n = 31)
- **LENGTH OF STUDY:** 1st day of chemotherapy and continuing for the duration of chemotherapy
- **INTERVENTION:** 1-g gelatin capsules containing 2.2 g EPA and 240 mg DHA 4 times per day or 7.5 mL liquid fish oil containing 2.2 g EPA and 500 mg DHA once per day

**Outcomes:**
Fish oil supplementation was well tolerated with no reported adverse events.
- The patients who received fish oil experienced an increased response rate and greater clinical benefit compared with the patients who received standard of care, (60.0% vs 25.8%, \( P = .008 \); 80.0% vs 41.9%, \( P = .02 \), respectively).
- The incidence of dose limiting toxicity did not differ between the groups (\( P = .46 \)).
- There was a trend towards greater one-year survival in the fish oil group (60.0% vs 38.7%; \( P = .15 \)).

**Study Conclusions:**
Compared with standard of care, supplementation of fish oil in patients with NSCLC undergoing chemotherapy resulted in increased chemotherapy efficacy without affecting toxicity and may contribute to increased survival.
A group of experts in clinical cancer cachexia (medical and surgical oncologists, palliative medicine specialists, and nutritionists) participated in a formal consensus process to develop a definition and classification of cancer cachexia.

Definition:
Cancer cachexia is a multifactorial syndrome defined by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment. The pathophysiology is characterised by a negative protein and energy balance driven by a variable combination of reduced food intake and abnormal metabolism.

Diagnosis of cancer cachexia:
- Weight loss >5% over 6 months, or
- BMI <20 and weight loss >2%, or
- Appendicular skeletal muscle index consistent with sarcopenia (males <7.26 kg/m²; females <5.45 kg/m²) and weight loss >2%

Classification
STAGE
Precachexia
- Weight loss ≤ 5%
- Anorexia
- Metabolic changes

Cachexia
- Weight loss > 5%
- BMI <20 and weight loss > 2% or sarcopenia and weight loss > 2%
- Reduced food intake/systemic inflammation

Refractory cachexia
- Varying degrees of cachexia
- Procatabolic cancer disease not responsive to treatment
- Low performance score
- < 3 months life expectancy

Definition and classification of cancer cachexia: an international consensus
Lancet Oncol. 2011 May;12(5):489-95
A minireview was conducted of studies that evaluated the role of eicosapentaenoic acid (EPA) on lean body mass (LBM) in cancer cachexia. Initial study results suggested improvements in LBM with EPA supplementation. However, results from subsequent larger, phase III clinical trials showed minimal benefit with supplementation. This review discussed potential reasons for discrepancies in these study results with recommendations for future study designs to reduce discrepancies in outcomes.

The potential mechanism of action of EPA on LBM involves the effect of EPA directly and indirectly on muscle wasting and muscle anabolism. EPA's role in muscle anabolism appears to occur through its effect on sensitizing skeletal muscle to insulin. Muscle breakdown may be decreased by EPA's role in downregulating the acute-phase response and decreasing the expression of proteosome subunits. In an animal model of colorectal cancer, EPA and docosahexaenoic acid (DHA) were shown to reduce the side effects of chemotherapy. EPA and DHA have been shown to enhance tumor response to chemotherapy and to improve protein and calorie intake.

Early studies have shown benefits of EPA supplementation on LBM. However, subsequent phase III clinical trials did not show a benefit of EPA supplementation over placebo on LBM. More recent clinical trials have reported a benefit of EPA supplementation over control. Discrepancies in EPA study results during the last decade, may, in part, be explained by differences in study designs. In reviewing these studies, the authors looked at study compliance, measures of phospholipid (PL) EPA levels, assessment of LBM, and timing of intervention.

**Compliance**

Poor compliance to EPA supplementation and contamination between treatment arms have been noted in several studies.
Influence of eicosapentaenoic acid supplementation on lean body mass in cancer cachexia (continued)

Murphy RA, Yeung E, Mazurak VC, Mourtzakis M Br J Cancer. 2011;105:1469-73

Timing of intervention with EPA

In accordance with the recently published cachexia classification system, in order to minimize muscle loss, interventions should be initiated during the pre-cachexia stage. In previous EPA studies, patients may have been enrolled when they were in the refractory cachexia stage. Patients in this stage often have significant disease progression and shorter median survival, such that EPA supplementation may be less effective.

In conclusion, the authors noted that positive results from previous studies may have been due to features of the study designs. For the design of future EPA supplementation trials, the authors made the following recommendations:

- To improve study compliance, offer patients a choice in the format of the supplement (capsules or liquid, parenteral or enteral)
- When analyzing data, consider stratifying outcomes based on PL EPA levels to allow for differences in incorporation of EPA into PL
- Utilize CT image analysis whenever possible to precisely quantify skeletal muscle
- In order to see a beneficial effect, provide EPA supplementation earlier in the disease process, rather than later when muscle loss is accelerated
Click here to return to page 1.