<u>Oncology</u>
<u>Oncology</u> (ONC) Guideline (2013)

Oncology

ONC: Major Recommendations (2013)

Oncology (ONC) Major Recommendations

Below you will find a list of Oncology Recommendations organized by Topic.

To see the Recommendation Summary, just **click** on the Recommendation title. Click on each link to view how recommendations are <u>developed</u>, <u>Executive Summary of Recommendations</u> or print the guideline in <u>PDF</u> format.

Topics Listed by Subject

<u>ONC: Nutrition Status and Outcomes of Adult Oncology Patients</u> (hospital admissions or re-admissions, length of hospital stay (LOS), quality of life (QoL), tolerance to chemotherapy and radiation treatment and mortality)

Nutrition Screening and Referral

For more information on screening for malnutrition risk for adult oncology patients, click here.

ONC: Screening for Malnutrition Risk and Referral of Adult Oncology Patients

ONC: Screening for Malnutrition Risk and Rescreening of Adult Oncology Patients

ONC: Referral of Adult Oncology Patients Identified at Malnutrition Risk to the RDN

ONC: Malnutrition Screening Tools for Adult Oncology Patients

Medical Nutrition Therapy

ONC: Medical Nutrition Therapy in Adult Oncology Patients Undergoing Chemotherapy and Radiation Therapy

ONC: MNT in Adult Oncology Patients Undergoing Chemotherapy and Radiation Treatment

ONC: MNT as Part of Multi-modal Therapy in Adult Oncology Patients Undergoing Chemotherapy and Radiation Treatment

Nutrition Assessment

For more information on nutrition assessment of adult oncology patients, click here.

ONC: Nutrition Assessment Tools for Adult Oncology Patients

ONC: Nutrition Assessment Criteria in Adult Oncology Patients

ONC: Assessment of Food/Nutrition-Related History of Adult Oncology Patients

ONC: Assessment of Anthropometric Measurements in Adult Oncology Patients

ONC: Assessment of Biochemical Data, Medical Tests and Procedures of Adult Oncology Patients

ONC: Assessment of Nutrition-Focused Physical Findings and Client History of Adult Oncology Patients

ONC: Nutrition Assessment for the Stages of Cancer Cachexia in Adult Oncology Patients

For more information on cancer cachexia, click here.

Nutrition Diagnosis

ONC: Nutrition Diagnosis of Malnutrition in Adult Oncology Patients

Nutrition Intervention

ONC: Nutrition Intervention for Adult Oncology Patients with Cancer Cachexia

ONC: Fish Oil, Weight and Lean Body Mass in Adult Oncology Patients

ONC: Dietary Supplements Containing Fish Oil for the Adult Oncology Patient

ONC: Medical Food Supplements Containing Fish Oil for the Adult Oncology Patient

ONC: Glutamine and Oral Mucositis in Adult Oncology Patients

ONC: Parenteral Glutamine and Hematopoietic Cell Transplant (HCT) in Adult Oncology Patients

ONC: Nutrition Substances and Chemotherapy-Induced Peripheral Neuropathy in Adult Oncology Patients

ONC: Neutropenic Dietary Precautions for Adult Oncology Patients

ONC: Neutropenic Dietary Precautions for Adult Oncology Patients with Neutropenia (non-Bone Marrow Transplant) ONC: Neutropenic Dietary Precautions for Adult Oncology Patients Undergoing Bone Marrow Transplant

Nutrition Monitoring and Evaluation

ONC: Monitoring and Evaluation in Adult Oncology Patients

ONC: Monitoring and Evaluation of Adult Oncology Patients

ONC: Monitoring and Evaluation of Adult Oncology Patients with Cancer Cachexia

ADDITIONAL RESOURCES

In addition, the Academy of Nutrition and Dietetics (A.N.D.) and the Oncology Expert Work Group concurs with the **Clinical Oncological Society of Australia (COSA) Evidence Based Practice Guidelines for the Nutritional Management of Patients with Head and Neck Cancer** and approved the following equivalency scale: <u>External Guideline EAL</u> Equivalency Rating

- Click here for the <u>Table of Contents</u>.
 Click here for the <u>Summary of Recommendations</u>

These guidelines are periodically updated as new data becomes available.

- Oncology
- Oncology (ONC) Guideline (2013)

Quick Links

Recommendations Summary

ONC: Nutrition Status and Outcomes of Adult Oncology Patients 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

<u>Recommendation(s)</u>

ONC: Nutrition Status and Outcomes in Adult Oncology Patients

The registered dietitian nutritionist (RDN) should collaborate with other health care professionals, administrators and public policy decision-makers to ensure that the evaluation of nutrition status is a key component of the adult oncology patient care process. Research indicates that poor nutrition status is associated with higher rates of hospital admissions or per-admissions, increased length of hospital stay (LOS), lower quality of life (QoL) and mortality in adult oncology patients. Poor nutrition status is also associated with decreased tolerance to chemotherapy and radiation treatment in adult oncology patients undergoing these therapies.

Rating: Strong

Imperative

• Risks/Harms of Implementing This Recommendation

There are no potential risks or harms associated with the application of this recommendation.

Conditions of Application

There are no conditions which may limit the application of this recommendation.

Potential Costs Associated with Application

Although costs of medical nutrition therapy (MNT) sessions and reimbursement vary, MNT sessions including collaboration with other healthcare professionals, are essential for improved outcomes.

Recommendation Narrative

A total of 45 studies were included in the evidence analysis for this recommendation:

- Six positive-quality <u>randomized controlled trials</u> (RCT) [Barlow et al, 2011; Braga et al, 1998; Hyltander et al, 2005; Ionescu et al, 2009; Ravasco et al, 2005 (*Head and Neck*); Ravasco et al, 2005 (*J Clin* Oncology.)
- Six positive-quality prospective <u>cohort studies</u> (Fearon et al, 2006; Hill et al, 2011; Laky et al, 2010; Ross et al, 2004; Sorensen et al, 2008; Tan et al, 2009)
 Three positive-quality diagnostic, validity or reliability studies (Amaral et al, 2008; Correia et al, 2007;
- Gioulbasanis et al, 2011)

- Gioulbasanis et al, 2011)
 Three positive-quality case-control studies (Alexandre et al, 2003; Carey et al, 2011; Horsley et al, 2005)
 Two postive-quality retrospective cohort studies (Gupta et al, 2010; Yoon et al, 2011)
 Two postive-quality prospective cohort studies (Pressior et al, 2010; Prado et al, 2007)
 Two postive-quality prospective before-and-after study (Ravasco et al, 2003)
 One positive-quality prospective cohort studies (Martin et al, 2010; Martin and Lagergren, 2009; Prado et al, 2008; Prado et al, 2009; Prado et al, 2011)
 Two neutral-quality prospective cohort studies (Martin et al, 2010; Martin and Lagergren, 2009; Prado et al, 2008; Prado et al, 2009; Prado et al, 2011)
 Two neutral-quality non-controlled trials (Bauer et al, 2005; Capuano et al, 2008)
 Two neutral-quality prospective cohort studies (Antoun et al, 2009; Iversen et al, 2010)
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 Two neutral-quality retrospective cohort studies (Laguer et al, 1980; Shahmoradi et al, 2009)
 Two neutral-quality retrospective cohort studies (Eriksson et al, 1998; Kathiresan et al, 2011)

- One neutral-quality descriptive study (Hammerlid et al, 1998)
- One neutral-quality retrospective chart review (Odelli et al, 2005)
- One neutral-quality non-randomized controlled trial (Piquet et al, 2002).

For an overview of the relationship between nutrition status and outcomes, click here.

Nutrition Status and Hospital Admissions or Re-admissions

- Five studies provide evidence that poor nutrition status is associated with higher rates of hospital admissions or re-admissions in adult oncology patients. Four of the five included studies found that a decreased nutrition status is associated with greater numbers of hospital admissions. The fifth study showed the same effect, but was not statistically significant.
- Evidence is based on the following studies: Barlów et al, 2011; Capuano et al, 2008; Hill et al, 2011; Kathiresan et al, 2011; and Piquet et al, 2002

Nutrition Status and Hospital LOS

- Ten studies provide evidence that poor nutrition status is associated with increased length of hospital stay (LOS) in adult oncology patients. Nine of the ten included studies found that a decreased nutrition status
- Evidence is based on the following studies: Amral et al, 2008; Antoun et al, 2009; Barlow et al, 2010; Pressoir et al, 2010; and Sorensen et al, 2008 2011:

Nutrition Status and QOL

- Sixteen studies provide evidence that poor nutrition status is associated with lower quality of life (QoL) in adult oncology patients. Fifteen of the sixteen included studies found that a decreased nutrition status is associated with a lower QoL. Only one study found minimal correlation between nutrition status and QoL. All eight of the studies utilizing the Patient-Generated Subjective Global Assessment (PG-SGA) found that a higher score (higher nutrition risk) was associated with a lower QoL in oncology patients.
 Evidence is based on the following studies: Bauer et al, 2005; Carey et al, 2011; Correia et al, 2007; Fearon et al, 2006; Hammerlid et al, 1998; Hyltander et al, 2005; Isenring et al, 2003; Iversen et al, 2010; Laky et al, 2010; Nourissat et al, 2008; Ollenschlager et al, 1992; Persson et al, 1999; Ravasco et al, 2003; Ravasco et al, 2005 (*J Clin Oncology*); Ravasco et al, 2005 (*Head and Neck*); and Shahmoradi et al, 2009

Nutrition Status and Radiation Treatment Tolerance

- Six studies provide evidence that poor nutrition status is associated with increased radiation treatment intolerance in adult oncology patients undergoing radiotherapy. All included studies found positive associations between nutrition status and two or more of the following: Reduced treatment interruptions, unplanned hospital admissions, treatment toxicity, Patient-Generated Subjective Global Assessment (PG-SGA) score over time and quality of life (Ocl.)
- (PG-SGA) score over time and quality of life (QoL).
 Evidence is based on the following studies: Capuano et al, 2008; Hill et al, 2011; Odelli et al, 2005; Ravasco et al, 2003; Ravasco et al, 2005 (*J Clin Oncology*); Ravasco et al, 2005 (*Head and Neck*)

Nutrition Status and Chemotherapy Treatment Tolerance

- Ten studies provide evidence that poor nutrition status is associated with increased chemotherapy treatment intolerance in adult oncology patients undergoing chemotherapy. All ten included studies found positive associations in one or more of the following: Treatment interruptions, infections, unplanned hospital admissions, treatment toxicity, including dose-limiting treatment toxicity, neutropenic fever, fatigue and severe thrombocytopenia.
- Evidence is based on the following studies: Alexandre et al, 2003; Capuano et al, 2008; Eriksson et al, 1998; Hill et al, 2011; Phippen et al, 2011; Prado et al, 2007; Prado et al, 2009; Prado et al, 2011; Robinson et al, 2008; and Ross et al, 2004

Nutrition Status and Mortality

- Sixteen studies provide evidence that poor nutrition status is associated with mortality in adult oncology patients. All sixteen included studies found positive associations among one or more of the following and mortality: weight loss, malnutrition, poor scores on validated malnutrition and quality of life screening trademost is a statement of the following and mortality.
- Evidence is based on the following studies: Capuano et al, 2008; Dewys et al, 1980; Fearon et al, 2006; Gioulbasanis et al 2011; Gupta et al, 2010; Hammerlid et al, 1998; Martin and Lagergren, 2009; Martin et al, 2010; Persson et al, 1999; Prado et al, 2008; Pressoir et al, 2010; Robinson et al, 2008; Ross et al, 2004; Sorensen et al, 2008; Tan et al, 2009; Yoon et al, 2011

• Recommendation Strength Rationale

- The conclusion statement for the relationship between nutrition status and hospital admissions or re-admissions is Grade II
- The conclusion statement for the relationship between nutrition status and hospital LOS is Grade I
- The conclusion statement for the relationship between nutrition status and <u>Ool</u> is Grade I • The conclusion statement for the relationship between nutrition status and radiation treatment tolerance
- is Grade I • The conclusion statement for the relationship between nutrition status and chemotherapy treatment
- tolerance is Grade I
- The conclusion statement for the relationship between nutrition status and mortality is Grade I

Minority Opinions

None.

Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence

analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked). What is the relationship between nutrition status and hospital admissions or re-admissions in adult oncology patients? What is the relationship between nutrition status and hospital length of stay (LOS) in oncology patients? What is the relationship between nutrition status and quality of life (OOL) in oncology patients? What is the relationship between nutrition status and radiation treatment tolerance in oncology patients? What is the relationship between nutrition status and chemotherapy treatment tolerance in oncology patients? What is the relationship between nutrition status and mortality in oncology patients? References Barlow R, Price P, Reid TD, Hunt S, Clark GW, Havard TJ, Puntis MC, Lewis WG. Prospective multicentre randomised controlled trial of early enteral nutrition for patients undergoing major upper gastrointestinal surgical resection. *Clin Nutr.* 2011 Oct; 30(5): 560-566. Capuano G, Grosso A, Gentile PC, Battista M, Bianciardi F, Di Palma A, Pavese I, Satta F, Tosti M, Palladino A, Coiro G, Di Palma M. Influence of weight loss on outcomes in patients with head and neck cancer undergoing concomitant chemoradiotherapy. *Head Neck.* 2008 Apr; 30(4): 503-508. Hill A, Kiss N, Hodgson B, Crowe TC, Walsh AD. Associations between nutritional status, weight loss, radiotherapy treatment toxicity and treatment outcomes in gastrointestinal cancer patients. *Clin Nutr.* 2011; 30: 92-98. Kathiresan AS, Brookfield KF, Schuman SI, Lucci JA 3rd. Malnutrition as a predictor of poor postoperative outcomes in gynecologic cancer patients. Arch Gynecol Obstet. 2011 Aug; 284(2): 445-451. Piquet MA, Ozsahin M, Larpin I, Zouhair A, Coti P, Monney M, Monnier P, Mirimanoff RO, Roulet M. Early nutritional intervention in oropharyngeal cancer patients undergoing radiotherapy. *Support Care Cancer*. 2002 Sep; 10(6): 502-504. Epub 2002 Aug 2. Amaral TF, Antunes A, Cabral S, Alves P, Kent-Smith L. An evaluation of three nutritional screening tools in a Portuguese oncology centre. J Hum Nutr Diet. 2008; 21: 575-583. Antoun S, Rey A, Béal J, Montange F, Pressoir M, Vasson MP, Dupoiron D, Gourdiat-Borye A, Guillaume A, Maget B, Nitenberg G, Raynard B, Bachmann P. Nutritional risk factors in planned oncologic surgery: What clinical and biological parameters should be routinely used? *World J Surg.* 2009 Aug; 33(8): 1,633-1,640. Braga M, Gianotti L, Vignali A, Cestari A, Bisagni P, Di Carlo V. Artificial nutrition after major abdominal surgery: Impact of route of administration and composition of the diet. *Crit Care Med*.1998; 26(1): 24-30. Horsley P, Bauer J, Gallagher B. Poor nutritional status prior to peripheral blood stem cell transplantation is associated with increased length of hospital stay. Bone Marrow Transplantation, 2005; 35: 1.113-1.116. Ionescu D, Iancu C, Ion D, Al-Hajjar N, Margarit S, Mocan L, Mocan T, Deac D, Bodea R, Vasian H. Implementing fast-track protocol for colorectal surgery: A prospective randomized clinical trial. *World J Surg*. 2009 Nov; 33(11): 2,433-2,438. Laky B, Janda M, Kondalsamy-Chennakesavan S, Cleghorn G, Obermair, A. Pretreatment malnutrition and quality of life-association with prolonged length of hospital stay among patients with gynecological cancer: A cohort study. BMC Cancer. 2010; 10: 232. Pressoir M, Desne S, Berchery D, Rossignol G, Poiree B, Meslier M, Traversier S, Vittot M, Simon M, Gekiere JP, Meuric J, Serot F, Falewee MN, Rodriquez I, Senesse P, Vasson MP, Chelle F, Maget B, Antoun S, Bachmann P. Prevalence, risk factors and clinical implications of malnutrition in French comprehensive cancer centers. *British Journal of Cancer.* 2010: 102, 966-971. Sorensen J. Kondrup J. Prokopowicz J. Schiesser M. Krähenbühl L. Meier R. Liberda M; EuroOOPS study group. EuroOOPS: An international, multicentre study to implement nutritional risk screening and evaluate clinical outcome. *Clin Nutr.* 2008 Jun; 27(3): 340-349. Bauer JD, Capra S. Nutrition intervention improves outcomes in patients with cancer cachexia receiving chemotherapy-a pilot study. *Support Care Cancer*. 2005; 13: 270-274. Carey S, Storey D, Biankin AV, Martin D, Young J, Allman-Farinelli M.Long-term nutritional status and quality of life following major upper gastrointestinal surgery: A cross-sectional study. Clin Nutr. 2011 Dec; 30(6): 774-779. Correia M, Cravo M, Marques-Vidal P, Grimble R, Dias-Pereira A, Faias S, Nobre-Leitão C. Serum concentrations of TNF-alpha as a surrogate marker for malnutrition and worse quality of life in patients with gastric cancer. *Clin*

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<u>Gupta D, Lis CG, Vashi PG, Lammersfeld CA. Impact of improved nutritional status on survival in ovarian</u> cancer. *Support Care Cancer*. 2010 Mar; 18(3): 373-381.

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Tan BH, Birdsell LA, Martin L, Baracos VE, Fearon KC. Sarcopenia in an overweight or obese patient is an adverse prognostic factor in pancreatic cancer. *Clin Cancer Res.* 2009 Nov 15; 15(22): 6,973-6,979.

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 Oncology Oncology (ONC) Guideline (2013)

Quick Links

Recommendations Summary

ONC: Nutrition Status and Outcomes of Adult Oncology Patients 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

Recommendation(s)

ONC: Nutrition Status and Outcomes in Adult Oncology Patients

The registered dietitian nutritionist (RDN) should collaborate with other health care professionals, administrators and public policy decision-makers to ensure that the evaluation of nutrition status is a key component of the <u>adult</u> oncology patient care process. Research indicates that poor nutrition status is associated with higher rates of hospital admissions or re-admissions, increased length of hospital stay (LOS), lower quality of life (QoL) and mortality in adult oncology patients. Poor nutrition status is also associated with decreased tolerance to chemotherapy and radiation treatment in adult oncology patients undergoing these therapies.

Rating: Strong

Imperative

<u>Risks/Harms of Implementing This Recommendation</u>

There are no potential risks or harms associated with the application of this recommendation.

Conditions of Application

There are no conditions which may limit the application of this recommendation.

Potential Costs Associated with Application

Although costs of medical nutrition therapy (MNT) sessions and reimbursement vary, MNT sessions including collaboration with other healthcare professionals, are essential for improved outcomes.

Recommendation Narrative

A total of 45 studies were included in the evidence analysis for this recommendation:

- Six positive-quality <u>randomized controlled trials</u> (RCT) [Barlow et al, 2011; Braga et al, 1998; Hyltander et al, 2005; Ionescu et al, 2009; Ravasco et al, 2005 (*Head and Neck*); Ravasco et al, 2005 (*J Clin Oncology*.)]
- Six positive-quality prospective <u>cohort studies</u> (Fearon et al, 2006; Hill et al, 2011; Laky et al, 2010; Ross et al, 2004; Sorensen et al, 2008; Tan et al, 2009)
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 One positive-quality prospective before-and-after study (Ravasco et al, 2003)
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 Two neutral-quality diagnostic, validity or reliability studies (Phippen et al 2011; Persson et al, 1999)
 Two neutral-quality prospective cohort studies (Antoun et al, 2009; Iversen et al, 2010)
 Two neutral-quality RCTs (Ollenschlager et al, 1992; Robinson et al, 2008)
 Two neutral-quality retrospective cohort studies (Dewys et al, 1980; Shahmoradi et al, 2009)
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- Two neutral-quality retrospective cohort studies (Eriksson et al, 1998; Kathiresan et al, 2011)
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For an overview of the relationship between nutrition status and outcomes, click here.

Nutrition Status and Hospital Admissions or Re-admissions

• Five studies provide evidence that poor nutrition status is associated with higher rates of hospital admissions or re-admissions in adult oncology patients. Four of the five included studies found that a decreased nutrition status is associated with greater numbers of hospital admissions. The fifth study

showed the same effect, but was not statistically significant.

• Evidence is based on the following studies: Barlow et al, 2011; Capuano et al, 2008; Hill et al, 2011; Kathiresan et al, 2011; and Piquet et al, 2002

Nutrition Status and Hospital LOS

- Ten studies provide evidence that poor nutrition status is associated with increased length of hospital stay
- (LOS) in adult oncology patients. Nine of the ten included studies found that a decreased nutrition status is associated with longer LOS, while one study found no statistical difference between groups.
 Evidence is based on the following studies: Amaral et al, 2008; Antoun et al, 2009; Barlow et al, 2011; Braga et al, 1998; Horsley et al, 2005; Hyltander et al, 2005; Ionescu et al, 2009; Laky et al, 2010; Pressoir et al, 2010; and Sorensen et al, 2008

Nutrition Status and QOL

- Sixteen studies provide evidence that poor nutrition status is associated with lower quality of life (QoL) in adult oncology patients. Fifteen of the sixteen included studies found that a decreased nutrition status is associated with a lower QoL. Only one study found minimal correlation between nutrition status and QoL. All eight of the studies utilizing the Patient-Generated Subjective Global Assessment (PG-SGA) found that a higher score (higher nutrition risk) was associated with a lower QoL in oncology patients.
 Evidence is based on the following studies: Bauer et al, 2005; Carey et al, 2011; Correia et al, 2007; Fearon et al, 2006; Hammerlid et al, 1998; Hyltander et al, 2005; Isenring et al, 2003; Iversen et al, 2010; Laky et al, 2010; Nourissat et al, 2008; Ollenschlager et al, 1992; Persson et al, 1999; Ravasco et al, 2003; Ravasco et al, 2005 (*J Clin Oncology*); Ravasco et al, 2005 (*Head and Neck*); and Shahmoradi et al, 2009

Nutrition Status and Radiation Treatment Tolerance

- Six studies provide evidence that poor nutrition status is associated with increased radiation treatment Six studies provide evidence that poor nutrition status is associated with increased radiation treatment intolerance in adult oncology patients undergoing radiotherapy. All included studies found positive associations between nutrition status and two or more of the following: Reduced treatment interruptions, unplanned hospital admissions, treatment toxicity, Patient-Generated Subjective Global Assessment (PG-SGA) score over time and quality of life (QoL).
 Evidence is based on the following studies: Capuano et al, 2008; Hill et al, 2011; Odelli et al, 2005; Ravasco et al, 2003; Ravasco et al, 2005 (*J Clin Oncology*); Ravasco et al, 2005 (*Head and Neck*)

Nutrition Status and Chemotherapy Treatment Tolerance

- Ten studies provide evidence that poor nutrition status is associated with increased chemotherapy treatment incolerance in adult oncology patients undergoing chemotherapy. All ten included studies found positive associations in one or more of the following: Treatment interruptions, infections, unplanned hospital admissions, treatment toxicity, including dose-limiting treatment toxicity, neutropenic fever, fatigue and severe thrombocytopenia.
- Evidence is based on the following studies: Alexandre et al, 2003; Capuano et al, 2008; Eriksson et al, 1998; Hill et al, 2011; Phippen et al, 2011; Prado et al, 2007; Prado et al, 2009; Prado et al, 2011; Robinson et al, 2008; and Ross et al, 2004

Nutrition Status and Mortality

- Sixteen studies provide evidence that poor nutrition status is associated with mortality in adult oncology patients. All sixteen included studies found positive associations among one or more of the following and mortality: weight loss, malnutrition, poor scores on validated malnutrition and quality of life screening tools, sarcopenia, cachexia, and fatigue. Grade I
 Evidence is based on the following studies: Capuano et al, 2008; Dewys et al, 1980; Fearon et al, 2006; Gioulbasanis et al 2011; Gupta et al, 2010; Hammerlid et al, 1998; Martin and Lagergren, 2009; Martin et al, 2010; Persson et al, 1999; Prado et al, 2008; Pressoir et al, 2010; Robinson et al, 2008; Ross et al, 2004; Sorensen et al, 2008; Tan et al, 2009; Yoon et al, 2011

Recommendation Strength Rationale

- The conclusion statement for the relationship between nutrition status and hospital admissions or re-admissions is Grade II
- The conclusion statement for the relationship between nutrition status and hospital <u>LOS</u> is Grade I
- The conclusion statement for the relationship between nutrition status and <u>OoL</u> is Grade I
 The conclusion statement for the relationship between nutrition status and radiation treatment tolerance is Grade I
- The conclusion statement for the relationship between nutrition status and chemotherapy treatment tolerance is Grade I
- The conclusion statement for the relationship between nutrition status and mortality is Grade I

Minority Opinions

None.

• Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked). What is the relationship between nutrition status and hospital admissions or re-admissions in adult oncology patients? What is the relationship between nutrition status and hospital length of stay (LOS) in oncology patients? What is the relationship between nutrition status and quality of life (QOL) in oncology patients?

What is the relationship between nutrition status and radiation treatment tolerance in oncology patients?

What is the relationship between nutrition status and chemotherapy treatment tolerance in oncology patients?

What is the relationship between nutrition status and mortality in oncology patients?

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None.

Oncology
Oncology (ONC) Guideline (2013)

Recommendations Summary

ONC: Screening for Malnutrition Risk and Referral of Adult Oncology Patients 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

Recommendation(s)

ONC: Screening for Malnutrition Risk and Re-Screening of Adult Oncology Patients

All <u>adult</u> patients should be screened for malnutrition risk on entry into oncology services. Early identification and management of malnutrition risk improves and protects nutrition status and quality of life (QoL), which leads to improved outcomes. Re-screening should be repeated routinely throughout treatment to facilitate referral as needed.

Rating: Consensus Imperative

ONC: Referral of Adult Oncology Patients Identified at Malnutrition Risk to the RDN

If an adult oncology patient has been identified at screening to be at risk for malnutrition, the patient should be referred to a registered dietitian nutritionist (<u>RDN</u>) for evaluation. If indicated, the RDN conducts a <u>nutrition assessment</u> and provides <u>medical nutrition therapy</u> (<u>MNT</u>) including the nutrition care process: Nutrition assessment, nutrition diagnosis, nutrition intervention, nutrition monitoring and evaluation. Management of malnutrition risk improves and protects nutrition status and quality of life (QoL), which leads to improved outcomes.

Rating: Consensus

Conditional

• Risks/Harms of Implementing This Recommendation

There are no potential risks or harms associated with the application of this recommendation.

• Conditions of Application

The recommendation ON: Referral of Adult Oncology Patients Identified at Malnutrition Risk to an RDN applies to all adult oncology patients identified at screening to be at risk for malnutrition.

Potential Costs Associated with Application

Costs include staff time to complete screening and referral.

<u>Recommendation Narrative</u>

Screening Adult Oncology Patients for Malnutrition Risk

Timely screening for nutrition impact symptoms and identification of malnutrition can facilitate referral for nutrition management and lead to improved outcomes (Kruizenga et al, 2005). Screening tools should be quick, easy to use, valid and reliable for the patient population or setting. Screening and re-screening should occur within an appropriate time-frame for the setting(Skipper et al, 2012).

The screening tool should be a valid identifier of malnutrition risk in adult oncology patients who would benefit from nutrition assessment and intervention by an RDN.

This tool should be able to detect a measurable adverse effect on body composition, function or clinical outcome (Todorovic et al, 2011).

Screening and assessment in the oncology population has been shown to improve outcomes in oncology patients. Nutrition intervention enables these patients to complete treatment regimens intended to give the best control of disease with fewer treatment interruptions [Ravasco et al, 2005(*J Clin Oncol*); Ravasco et al, 2005 (*Head Neck*) 2005; Isenring et al, 2006, 2007].

For more information about screening tools found to be effective in identifying oncology patients at malnutrition risk, <u>click here</u>.

<u>Recommendation Strength Rationale</u>

Consensus.

Minority Opinions

None.

<u>Supporting Evidence</u>

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

<u>References</u>
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<u>Oncology</u>
<u>Oncology</u> (ONC) Guideline (2013)

Quick Links

Recommendations Summary

ONC: Malnutrition Screening Tools for Adult Oncology Patients 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

Recommendation(s)

ONC: Malnutrition Screening Tools for Adult Oncology Patients

Adult oncology patients should be screened using a malnutrition screening tool validated in the setting (inpatient or ambulatory/outpatient) in which the tool is intended for use. Research indicates that the following tools are valid and reliable for identifying malnutrition risk in oncology patients.

The following have been shown to be valid and reliable for identifying malnutrition risk in adult oncology patients in the inpatient setting:

- <u>Patient-generated Subjective Global Assessment</u> (PG-SGA)
 <u>Malnutrition Screening Tool</u> (MST)
 <u>Malnutrition Screening Tool for Cancer Patients</u> (MSTC)
 <u>Malnutrition Universal Screening Tool</u> (MUST)

The following have been shown to be valid and reliable for identifying malnutrition risk in adult oncology patients in the ambulatory/outpatient setting:

- <u>Patient-generated Subjective Global Assessment</u> (PG-SGA)
 <u>Malnutrition Screening Tool</u> (MST).

Rating: Strong

Imperative

Risks/Harms of Implementing This Recommendation

There are no potential risks or harms associated with the application of this recommendation.

Conditions of Application

There are no conditions which may limit the application of this recommendation.

Potential Costs Associated with Application

Costs include staff time to complete screening.

<u>Recommendation Narrative</u>

A total of 11 studies were included in the evidence analysis for this recommendation:

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- Four positive-quality diagnostic, validity or reliability studies (Amaral et al, 2008; Ferguson, Capra et al, 1999; Laky et al, 2008; Kim et al, 2011)
 Four positive-quality cross-sectional studies (Bauer et al, 2002; Ferguson, Bauer et al, 1999; Isenring et al, 2003; Isenring et al, 2006)
 Two neutral-quality diagnostic, validity or reliability studies (Kirsh et al, 2003; Persson et al, 1999)
 One neutral-quality cross-sectional study (Bauer et al, 2003).

11 validation studies provide evidence that the following tools were found to be valid and reliable for identifying malnutrition in adult oncology patients.

- Ambulatory and acute caresettings: <u>PG-SGA</u> (Bauer, Capra et al, 2002; Isenring et al, 2003; Laky et al, 2008; Persson et al, 2009) and <u>MST</u> (Amaral et al, 2008; Ferguson et al, 1999; Ferguson, Capra et al, 1999; Isenring et al, 2006)
- Acute care setting only: <u>MSTC</u> (Kim et al, 2011) and <u>MUST</u> (Amaral et al, 2008)
 The <u>MAG-MST</u> (Bauer, Capra et al, 2003) and the <u>two-item nutrition screen from the ZSDS</u> (Kirsh et al, 2003) were not found to be valid and reliable for identifying malnutrition in adult oncology patients in acute care settings
- Validity and reliability of the MSTC, MUST, MAG-MST and two-item nutrition screen from the ZSDS tools were not evaluated in adult oncology patients in the ambulatory setting
 Criteria for effective malnutrition screening tools in clinical settings include validity and reliability, the speed and ease with which the tool can be administered and the tool's ability to be used by a variety of members of the Interdisciplinary Team. Tools included in the evidence analysis for this question met the additional criteria of being validated in ambulatory or inpatient oncology settings. additional criteria of being validated in ambulatory or inpatient oncology settings. • For more details on the above tools, see: <u>Comparison of Screening Tools to Determine Malnutrition Risk</u>
- for Adult Oncology Patients
- For further information regarding nutrition screening in other non-cancer populations within the EAL, see Nutrition Screening.
- Recommendation Strength Rationale

Conclusion statement for the validity and reliability of malnutrition screening tools to assess nutritional status of adult oncology patients in ambulatory and acute care settings is Grade I.

Minority Opinions

None.

Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

Which malnutrition screening tools have been found to be valid and reliable for identifying malnutrition risk in adult oncology patients in ambulatory and acute care settings?

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Amaral TF, Antunes A, Cabral S, Alves P, Kent-Smith L. An evaluation of three nutritional screening tools in a Portuguese oncology centre. J Hum Nutr Diet. 2008; 21: 575-583.

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Persson C, Sjoden PO, Glimellius B. The Swedish version of the patient-generated subjective global assessment of nutritional status: gastrointestinal vs urological cancers. *Clin Nutr.* 1999; 18 (2): 71-77.

<u>References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process</u>

None.

Quick Links

Recommendations Summary

ONC: Medical Nutrition Therapy in Adult Oncology Patients Undergoing Chemotherapy or Radiation Therapy 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

Recommendation(s)

ONC: Medical Nutrition Therapy (MNT) in Adult Oncology Patients Undergoing Chemotherapy or Radiation Treatment

If an <u>adult</u> oncology patient is undergoing chemotherapy or radiation treatment, the registered dietitian nutritionist (RDN) should provide medical nutrition therapy (MNT). <u>MNT</u> has been shown to be effective in improving multiple treatment outcomes in patients undergoing chemotherapy, radiation or chemoradiotherapy in ambulatory or outpatient and inpatient oncology settings.

Rating: Strong Conditional

ONC: Medical Nutrition Therapy (MNT) As Part of Multi-modal Therapy in Adult Oncology Patients Undergoing Chemotherapy or Radiation Treatment

The <u>RDN</u> should be a member of the interdisciplinary team providing <u>multi-modal therapy</u> to <u>adult</u> oncology patients undergoing chemotherapy or radiation treatment. Multi-modal therapy includes coordinated interventions from a variety of health care disciplines. Multi-modal therapy that includes <u>MNT</u> demonstrates positive outcomes.

Rating: Fair

Conditional

Risks/Harms of Implementing This Recommendation

There are no potential risks or harms associated with the application of this recommendation.

• Conditions of Application

Recommendations apply to adult oncology patients receiving chemotherapy or radiation treatment.

Potential Costs Associated with Application

Although costs of MNT sessions and reimbursement vary, MNT sessions including collaboration with other healthcare professionals are essential for improved outcomes.

<u>Recommendation Narrative</u>

A total of 20 studies were included in the evidence analysis for this recommendation:

- Seven positive-quality <u>randomized controlled trials</u> (RCTs): Chlebowski et al, 1993; Isenring et al, 2007; Isenring et al, 2004 (*Brit J Cancer*); Ovesen et al, 1993; Ravasco et al, 2005 (*J Clin Oncology*); Ravasco et al, 2005 (*Head and Neck*)
 One positive-quality before and after study: Ravasco et al, 2003
 Four neutral-quality non-randomized controlled trials: Danielson and Fairchild, 2011; Dawson et al, 2001; Goncalves et al, 2005; van den Berg et al, 2010
 Three neutral-quality prospective cohorts: Dintinjana et al, 2008; Glare et al, 2011; Pituskin et al, 2010
 Thwo neutral-quality <u>RCTs</u>: Isenring et al, 2004 (*J Hum Nutr Diet*); Ollenschläger et al, 1992
 One neutral-quality case control: Glimelius et al, 1992
 One neutral-quality case study or case series: Block et al, 2009.

- One neutral-qualitý case study or case series: Block et al, 2009.

MNT and Chemotherapy

- Six studies provided evidence that MNT provided by a nutrition professional was effective in improving multiple treatment outcomes in adult oncology patients receiving chemotherapy
 The studies, mostly international, examined patients with a variety of cancers (breast, ovary, lung,
- leukemias, colorectal, upper GI) prior to receiving chemotherapy in ambulatory and inpatient oncology centers
- Evidence is based on the following studies: Chlebowski et al, 1993; Dintinjana et al, 2008; Glare et al, 2011; Glimelius et al, 1992; Ollenschläger et al, 1992; Ovesen et al, 1993.

MNT as Part of Multi-modal Therapy and Chemotherapy

- One study provided evidence that MNT provided by an RDN as part of multi-modal therapy was effective in improving outcomes in adult oncology patients receiving chemotherapy treatment • Evidence is based on the following study: Block et al, 2009.

MNT and Radiation Therapy

- 11 studies provided evidence that MNT provided by a nutrition professional was effective in improving multiple treatment outcomes. These studies, mostly international, examined patients with a variety of high-risk cancers (head and neck, gastrointestinal) prior to receiving radiotherapy or combined
- radiotherapy in ambulatory and inpatient oncology centers. Evidence is based on the following studies: Chlebowski et al, 1993; Goncalves et al, 2005; Isenring et al, 2007; Isenring et al, 2004 (*Brit J Cancer.*); Isenring et al, 2004 (*J Hum Nutr Diet.*); Isenring et al, 2003; Odelli et al, 2005; Ravasco et al, 2005 (*J Clin Oncology.*); Ravasco et al, 2005 (*Head and Neck*); Ravasco et al, 2003; van den Berg et al, 2010.

MNT as Part of Multi-Modal Therapy and Radiation Therapy

- Three studies provided evidence that MNT provided by an RDN as part of multi-modal therapy was
- effective in improving outcomes in adult oncology patients receiving radiation treatment Evidence is based on the following studies: Danielson and Fairchild, 2011; Dawson et al, 2001; and Pituskin et al, 2010.

Recommendation Strength Rationale

- Conclusion statement regarding MNT provided by a nutrition professional in adult oncology patients receiving **chemotherapy** is a Grade II
- Conclusion statement regarding *MNT* provided by a *nutrition professional* in adult oncology patients receiving *radiotherapy or combined radiotherapy* is a Grade I
 Conclusion statement regarding *MNT* provided by an *RDN* as part of *multi-modal therapy* in adult
- oncology patients receiving radiation treatment is Grade II
 Conclusion statement regarding MNT provided by an RDN as part of multi-modal therapy in adult oncology patients receiving chemotherapy treatment is Grade III.

Minority Opinions

None.

• Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

Is medical nutrition therapy (MNT) provided by a nutrition professional effective in adult oncology patients receiving radiation treatment?

Is medical nutrition therapy (MNT) provided by a nutrition professional as part of multi-modal therapy effective in adult oncology patients receiving radiation treatment?

Is medical nutrition therapy (MNT) provided by a nutrition professional effective in adult oncology patients receiving chemotherapy treatment?

Is medical nutrition therapy (MNT) provided by a nutrition professional as part of multi-modal therapy effective in adult oncology patients receiving chemotherapy treatment?

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 References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process
None.

- <u>Oncology</u>
 <u>Oncology (ONC) Guideline (2013)</u>

Quick Links

Recommendations Summary

ONC: Nutrition Assessment Tools for Adult Oncology Patients 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

<u>Recommendation(s)</u>

ONC: Nutrition Assesssment Tools for Adult Oncology Patients

The registered dietitian nutritionist (RDN) should use an assessment tool validated in the setting (inpatient or ambulatory/outpatient) in which the tool is intended for use as part of the complete <u>nutrition assessment</u>. Research indicates that the following tools have been shown to elicit valid and reliable data as part of a comprehensive nutrition assessment of <u>adult</u> oncology patients in ambulatory and acute care settings:

- Patient-Generated Subjective Global Assessment (PG-SGA)
- Subjective Global Assessment (SGA).

Rating: Strong Imperative

• Risks/Harms of Implementing This Recommendation

There are no potential risks or harms associated with the application of this recommendation.

• Conditions of Application

There are no conditions which may limit the application of this recommendation.

Potential Costs Associated with Application

Although costs of medical nutrition therapy (MNT) sessions and reimbursement vary, MNT is essential for improved outcomes.

Recommendation Narrative

A total of four studies were included in the evidence analysis for this recommendation:

- Two positive-quality diagnostic, validity or reliability studies (Laky et al, 2008; Read et al, 2005)
 One positive-quality <u>cross-sectional study</u> (Kwang and Kandiah, 2010)
 One neutral-quality descriptive study (Li et al, 2010).

Four studies provide evidence that the <u>PG-SGA</u> and the <u>SGA</u> tools have been found to be valid and reliable in assessing the nutritional status of adult oncology patients in ambulatory and acute care settings:

- The <u>MNA</u> was found to have the <u>sensitivity</u> to diagnose oncology patients with malnutrition in the ambulatory setting, but was only moderately specific in identifying malnutrition when compared with the PG-SGA. The MNA was not evaluated in the acute care setting.
- Criteria for effective nutrition assessment tools in clinical settings include validity and reliability and the speed and ease with which the tool can be administered. Tools included in the evidence analysis for this question met the additional criteria of being validated in ambulatory or inpatient oncology settings.
- <u>Recommendation Strength Rationale</u>

Conclusion statement for the validity and reliability of nutrition assessment tools to assess nutritional status of adult oncology patients in ambulatory and acute care settings is Grade I.

Minority Opinions

None.

Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations' rated consensus will not have supporting evidence linked).

Which nutrition assessment tools have been found to be valid and reliable to assess nutritional status of adult oncology patients in ambulatory and acute care settings?

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<u>References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process</u>

None.

Oncology

Oncology (ONC) Guideline (2013)

Recommendations Summary

ONC: Nutrition Assessment Criteria for Adult Oncology Patients 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

Recommendation(s)

ONC: Assessment of Food/Nutrition-related History of Adult Oncology Patients

The registered dietitian nutritionist (RDN) should assess the food, beverage and nutrient intake and related history of

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adult oncology patients including, but not limited to the following:

- Energy and protein intake
- Changes in food and fluid/beverage intake
- Changes in rood and fluid/beverage intake
 Adequacy and appropriateness of nutrient intake or nutrient administration
 Actual daily intake from <u>enteral nutrition</u> (EN) and <u>parenteral nutrition</u> (PN) and other nutrient sources
 Changes in type, texture, or temperature of food and liquids
 Use of <u>medical food supplements</u> (MFS)
 Food avoidance and intolerances
 Meal or snack pattern changes
 Preservitions endors the source backward parenter medications, backal preservitions and sources are consistent on the sources of the source backage in the source of th

- Prescription medications, over-the-counter medications, herbal preparations and complementary or alternative medicine productsFactors affecting access to food.

Assessment of the above factors is needed to effectively determine nutrition diagnoses and plan the nutrition interventions. Inability to achieve optimal nutrient intake may contribute to poor outcomes.

Rating: Consensus

Imperative

ONC: Assessment of Anthropometric Measurement in Adult Oncology Patients

The RDN should assess the following anthropometric measurements in adult oncology patients:

- Height and weight
- Weight change
- Body Mass Index (BMI).

Any <u>weight loss that is unintended</u> in adult oncology patients has potential significance, as oncology patients often experience weight loss prior to admission to oncology services. Low muscle mass is a common and independent predictor of immobility and mortality, is a particularly adverse prognostic indicator in <u>obese</u> patients and is associated with greater toxicities of chemotherapy leading to treatment interruptions including dose reductions, treatment delays and treatment termination.

Assessment of the above factors is needed to effectively determine nutrition diagnoses and plan the nutrition interventions.

Rating: Consensus

Imperative

ONC: Assessment of Biochemical Data, Medical Tests, and Procedures on Adult Oncology Patients

The <u>RDN</u> should evaluate available data and recommend as indicated: Biochemical data, medical tests and procedures of adult oncology patients. Examples include:

- Glucose
- White blood cell (WBC)
- Nutritional anemia profile (hemoglobin, hematocrit, folate, B₁₂, iron)
- Electrolyte and renal profile
- Liver function
- Inflammatory profile, including <u>C-reactive protein</u> (CRP)
 Gastrointestinal (GI) function tests (i.e., swallowing study, abdominal films, gastric emptying, transit time).

Assessment of these factors is needed to effectively determine nutrition diagnoses and plan the nutrition interventions.

Rating: Consensus Imperative

ONC: Assessment of Nutrition-Focused Physical Findings and Client History of Adult Oncology Patients

The RDN should evaluate available data regarding the nutrition-focused physical findings and client history of adult oncology patients including, but not limited to:

Nutrition-focused physical findings:

- Age greater than 65 years
- Loss of muscle mass
 Loss of subcutaneous fat

- <u>Nutrition impact symptoms</u> including but not limited to: Nausea, vomiting, diarrhea, constipation, <u>stomatitis</u>, <u>mucositis</u>, alterations in taste and smell and anxiety
 Changes in appetite
 Vital signs

- Functional indicators (i.e., <u>Karnofsky score</u>, grip strength)
 <u>Localized or generalized fluid accumulation</u>.

Client history:

- Patient/Family/Client Medical/Health history:
 - Nutrition impact symptoms including but not limited to: Dysphagia, depression and pain fatigue
 - Medical treatment or therapy
 - Other diseases, conditions and illnesses including cancer cachexia.

Social history: Psychological/socioeconomic factors (e.g., social support).

Assessment of the above factors is needed to effectively determine nutrition diagnoses and plan the nutrition interventions.

Rating: Consensus

Risks/Harms of Implementing This Recommendation

There are no potential risks or harms associated with the application of this recommendation.

- Conditions of Application

 - The <u>RDN</u> should consider use of an <u>assessment tool</u> validated in the setting (inpatient or ambulatory/outpatient) in which the tool intended for use as part of the complete nutrition assessment
 RDNs should be appropriately trained to conduct a nutrition-focused physical exam
 - If necessary data are not available, the RDN should use professional judgment to request or obtain addition data.
- Potential Costs Associated with Application

Accessibility and costs of additional testing should be considered.

Recommendation Narrative

Nutrition Assessment for Adult Oncology Patients

An adult oncology nutrition assessment should characterize and document the presence of (or expected potential for) altered nutrition status and nutrition impact symptoms that may result in a measurable adverse effect on body composition, function, <u>OoL</u> or clinical outcome and may also include indicators of malnutrition.

The RDN's assessment should include the five domains of the Nutrition Care Process (NCP) and consider the six indicators of malnutrition (energy intake, interpretation of weight loss, body fat, muscle mass, fluid accumulation and reduced grip strength). See <u>Clinical Characteristics to Document Malnutrition</u> (White et al, 2012).

The five domains of the NCP include the following. The Oncology expert work group has provided additional interpretations specific to the assessment of malnutrition in oncology patients:

Food- or Nutrition-Related History

Insufficient energy intake.

Anthropometric Measurements

Weight loss in elderly patients may have additional impact. The usual adult cutoff is <u>BMI</u> of 18.5kg/m², however studies of the elderly support an association between increased mortality and underweight (BMI under 20kg/m² or current weight compared with usual or desired body weight) or <u>unintended weight loss</u> (5% in 30 days or any further weight loss after meeting this criteria) (Grabowski et al, 2001; Fearon et al, 2013; Tan et al, 2009).

- Because weight loss is demonstrated to lead to poor outcomes, it is important to accurately determine a Baseline weight. Weight loss or change should be defined as current weight compared to baseline weight. Baseline weight (include presence of under- or over-hydration) is defined as:
 - Usual body weight from medical records
 - Weight taken when admitted to oncology service or, if not available:
 Self-report of recent healthy weight

 - Consider rate of weight loss over specified time frame (Jensen et al, 2012)
 - Include presence of under- or over-hydration.

Biochemical Data, Medical Tests and Procedures

- Careful interpretation may be required in oncology patients, as they can experience wide variations in glucose and <u>WBC</u> values due to type and timing of treatment
 Other lab values determined to be outside of normal may indicate a need for diet modification of nutrients
 The etiology-based malnutrition definitions are located at this link: <u>Etiology-Based Malnutrition Definitions</u> (Jensen et al, 2012). <u>CRP</u> should be used to evaluate the presence of inflammation (elevated* CRP may be indicative of inflammation). It is also important to differentiate between chronic disease-related malnutrition (lung, pancreatic and <u>GI</u> cancer, sarcopenic obesity and organ failure) and acute disease and injury-related malnutrition (major infection and surgery). Determining the presence and degree of inflammation determines the significance of any patient weight loss (Jensen et al, 2012; and White et al, 2012).

*Past interpretation of >10mg/L CRP has been used to indicate inflammation (Fearon et al, 2006). However, further research will elucidate more specific markers for use.

Nutrition-Focused Physical Findings and Client History

- Loss of muscle mass [White et al, 2012; Prado et al, 2009 (*Clin Cancer Res.*)]
 Patients with loss of muscle mass experience greater treatment toxicity and shorter survival
 Low muscle mass is a common and independent predictor of immobility and mortality, is a particularly adverse prognostic indicator in obese patients and is associated with greater toxicities

 - bit in distribution of the analysis (BIA), dual-energy X-ray absorptiometry (DXA) and anthropometry. Patients with loss of muscle mass experience greater treatment toxicity and shorter survival [Cruz-Jentoft et al, 2010; Prado et al, 2009 (*Curr Opin Support Palliat Care*.)].

- Loss of <u>subcutaneous fat</u> (White et al, 2012; Tan et al, 2009; Fearon, 2011)
 With the increase in obesity in Western society and patients with cancer in particular, reducing fat tissue should not be a priority
- The important problem remains low muscle mass, since up to 50% of patients with advanced cancer have frank sarcopenia. The shortest survival times are among obese patients with Sarcopenia (Tan et al, 2009).
 Localized or generalized fluid accumulation (that may mask weight loss) (White et al, 2012)
 Nutrition impact symptoms that impede intake, digestion or absorption such as anorexia, nausea,

- Nutrition impact symptoms that impede intake, digestion or absorption such as anorexia, nausea, vomiting, diarrhea, constipation, stomatitis, mucositis, <u>dysphagia</u>, alterations in taste and smell, pain, depression and anxiety, can be caused by the cancer itself or the oncology treatment (American Cancer Society, 2000; Kubrak, 2010; Wojtaszek et al, 2002)
 Reduced grip strength** or diminished functional status, as measured by Karnofsky score

 **Consult normative standards per device manufacturer.

 Presence of <u>pre-cachexia</u> or <u>cancer cachexia</u>. Further nutrition assessment is needed for patients with lung, pancreatic or head and neck and gastrointestinal (GI) cancers or those who are at high risk for weight loss or have experienced <u>unintentional weight loss</u>. See recommendation for <u>Nutrition Assessment</u> for the Stages of Cancer cachexia in Adult Oncology Patients.
- Type of oncology treatment.

For recommended tools for use in assessing the nutritional status of <u>adult</u> oncology patients in ambulatory and acute care settings, click here.

Recommendation Strength Rationale

Consensus.

Minority Opinions

None.

Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

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Oncology

Oncology (ONC) Guideline (2013)

Recommendations Summary

ONC: Nutrition Assessment for the Stages of Cancer Cachexia in Adult Oncology Patients 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

Recommendation(s)

ONC: Nutrition Assessment for the Stages of Cancer Cachexia in Adult Oncology Patients

As part of the nutrition assessment, in patients with lung, pancreatic or head and neck and gastrointestinal (GI) cancers or those who are at high risk for weight loss or have experienced <u>unintended weight loss</u>, the registered dietitian nutritionist (RDN) should assess for <u>nutrition impact symptoms</u>, <u>markers of inflammation</u> [e.g., elevated <u>C-reactive</u> <u>protein</u> (CRP)] and other signs of wasting, which may indicate <u>pre-cachexia</u> or <u>cancer cachexia</u>.

The presence of cachexia does not always indicate end of life or need for hospice. Therefore, the identification of cachexia leading to intervention can positively impact clinical outcomes.

Rating: Consensus

- Conditional
 - Risks/Harms of Implementing This Recommendation

Failure to assess for the stages of cancer cachexia may lead to lack of nutrition intervention and increased risk of mortality.

Conditions of Application

- This recommendation applies to patients with lung, pancreatic or head and neck and GI cancers or those
- who are at high risk for weight loss or have experienced <u>unintended weight loss</u> For some individuals, unintended weight loss may be irreversible due to underlying medical conditions If necessary data are not available, the <u>RDN</u> should use professional judgment to request or obtain
- addition data, such as markers of inflammation (CRP).
- Potential Costs Associated with Application
 - Although medical nutrition therapy (MNT) costs and reimbursement vary, MNT is essential for improved outcomes
 - Accessibility and costs of additional laboratory testing should be considered.

Recommendation Narrative

The metabolic response to cancer is heterogeneous, so it is important to intervene and manipulate the factors that are behavior-related, to address the direct causes of decreased intake (obstruction, <u>dysphagia</u>) and address the secondary causes (depression, fatigue, pain, gastrointestinal function) because "symptom management alone can improve survival in patients with advanced cancer (Fearon, 2011).

In cancer-specific pre-cachexia, early clinical and metabolic signs such as loss of appetite and impaired glucose tolerance can precede substantial involuntary weight loss (i.e., up to 5%). The risk of progression is variable and depends on cancer type, stage, presence of systemic inflammation, low food intake and lack of response to anti-cancer therapy (Fearon et al, 2011).

Definitions of Cachexia

There are several stages of cancer cachexia: Pre-cachexia, cachexia and refractory cachexia.

Cancer cachexia: A multi-factorial syndrome characterized 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 <u>protein</u> and energy balance, driven by a variable combination of reduced food intake and abnormal metabolism (Fearon et al, 2011).

Pre-cachexia (in general): Defined by the presence of all of the following criteria:

- Underlying chronic disease
- Unintended weight loss of up to 5% usual body weight during the last six months
 Chronic or recurrent systemic inflammatory response
 Anorexia or anorexia-related symptoms (Muscaritoli et al, 2010).

Pre-cachexia (in cancer): Characterized by early clinical and metabolic signs such as loss of appetite and impaired glucose tolerance; can precede substantial involuntary weight loss (i.e., up to 5%). The risk of progression is variable and depends on cancer type, stage, presence of systemic inflammation, low food intake and lack of response to anti-cancer therapy (Fearon et al, 2011).

Refractory cachexia: May be a result of very advanced cancer (pre-terminal) or the presence of rapidly progressive cancer unresponsive to anti-cancer therapy. This stage is associated with active catabolism or the presence of factors that make active management of weight loss no longer possible or appropriate. Refractory cachexia is characterized by a low performance score (e.g., <u>WHO</u> grade 3 or 4) and a life expectancy of less than three months (Fearon et al, 2011).

- Nutrition impact symptoms that impede intake, digestion or absorption (such as anorexia, nausea, vomiting, diarrhea, constipation, <u>stomatitis</u>, <u>mucositis</u>, dysphagia, alterations in taste and smell, pain, depression and anxiety) can be caused by the cancer itself or the oncology treatment. (American Cancer Society, 2000; Kubrak et al, 2010; Wojtaszek et al, 2002)
 Request a <u>CRP</u> lab value if one is not available in order to assess for presence of inflammation. The presence of inflammation supports a diagnosis of pre-cachexia. If CRP is elevated*, it may be indicative of the presence of inflammation and this value determines the severity of any weight loss (Jensen et al, 2012; White et al, 2012). The metabolic response to cancer is heterogeneous, so it is important to intervene and manipulate the factors that are behavior-related, to address the direct causes of decreased intake (obstruction, dysphagia) and address the secondary causes (depression, fatigue, pain, gastrointestinal function) because "symptom management alone can improve survival in patients with advanced cancer (Fearon 2011)." advanced cancer (Fearon 2011).

*Past interpretation of >10mg/L <u>CRP</u> has been used to indicate inflammation. However, further research will elucidate more specific markers for use.

- Wasting in cancer cachexia may be assessed through the following:

 - Loss of <u>subcutaneous fat</u> (e.g., orbital, triceps, fat overlying the ribs) (White et al, 2012; Tan et al, 2009; Fearon et al, 2011)
 As 50% of patients with advanced cancer have frank <u>sarcopenia</u> (Fearon, 2011) and the shortest survival times are among <u>obese</u> patients with sarcopenia (Tan et al, 2009), reducing weight at the possible expense of lean muscle mass in obese cancer patients should not be a priority.
 - Muscle loss [e.g., wasting of the temples (temporalis muscle); clavicles (pectoralis and deltoids); shoulders (deltoids); interosseous muscles]; scapula [latissimus dorsi, trapezious, deltoids; thigh (quadriceps) and calf (gastrocnemius)] [White et al, 2012; Prado et al, 2009 (*Clin Cancer Res.*)]

 - and calf (gastrocnemius)] [White et al, 2012; Prado et al, 2009 (*Clin Cancer Res.*)]
 Patients with loss of muscle mass experience greater treatment toxicity and shorter survival
 Low muscle mass is a common and independent predictor of immobility and mortality (Prado et al, 2008), is a particularly adverse prognostic indicator in obese patients and is associated with greater toxicities of chemotherapy, leading to treatment interruptions including dose reductions, treatment delays and treatment termination [Fearon et al, 2013; Prado et al, 2009 (*Clin Cancer Res.*), Prado et al, 2009 (*Curr Opin Support Palliat Care.*), Prado et al, 2011; Antoun et al, 2010; Fearon, 2011].
 Body weight has been used as an outcome in clinical trials in cancer-induced weight loss and only recently has research begun to focus on lean body mass as a primary outcome. Existing computerized tomography (CT) images used to diagnose and monitor disease progression are readily available and provide an opportunistic means for body composition analysis. Although this type of analysis is relatively new, its use will be common in the near future and offers the<u>RDN</u> the ability to demonstrate value. Other methods of measuring muscle mass are bioelectrical impedence analysis (BIA), dual-energy X-ray absorptiometry (DXA) and anthropometry. Patients with loss of muscle mass experience greater treatment toxicity and shorter survival. [Prado et al, 2009 (*Curr Opin Support Palliat Care.*); Cruz-Jentoft et al, 2010].
- Recommendation Strength Rationale

Consensus.

Minority Opinions

None.

Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

- <u>References</u>
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Oncology

Oncology (ONC) Guideline (2013)

Recommendations Summary

ONC: Nutrition Diagnosis of Malnutrition in Adult Oncology Patients 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

Recommendation(s)

ONC: Nutrition Diagnosis of Malnutrition in Adult Oncology Patients

The registered dietitian nutritionist (RDN) should use clinical judgment in interpreting nutrition assessment data to diagnose malnutrition in <u>adult</u> oncology patients. Early identification and diagnosis of malnutrition leading to intervention can positively impact body composition, function, quality of life (QoL), treatment tolerance and clinical outcomes.

The presence of two or more of the following criteria or characteristics supports a nutrition diagnosis of malnutrition in the adult oncology patient (See Clinical Characteristics to Document Malnutrition).

- Insufficient energy intake
- <u>Unintended weight los</u>
- Loss of <u>subcutaneous fat</u>
- Loss of muscle mass
- <u>Localized or generalized fluid accumulation</u> (that may mask weight loss)
- Reduced grip strength.

Rating: Consensus

Imperative

• Risks/Harms of Implementing This Recommendation

Failure to make a malnutrition diagnosis may lead to lack of nutrition intervention and increased risk of mortality.

- Conditions of Application

 - Consider advance directives when planning nutrition intervention
 For some individuals, <u>unintended weight loss</u> may be irreversible due to underlying medical conditions
 If necessary data are not available, the <u>RDN</u> should use professional judgment to request or obtain
 - addition data.
- Potential Costs Associated with Application

- Although medical nutrition therapy (MNT) costs and reimbursement vary, MNT is essential for improved outcomes
- Accessibility and costs of additional laboratory testing should be considered.

Recommendation Narrative

Nutrition Assessment for Adult Oncology Patients

An adult oncology nutrition assessment should characterize and document the presence of (or expected potential for) altered nutrition status and <u>nutrition impact symptoms</u> that may result in a measurable adverse effect on body composition, function, <u>OoL</u> or clinical outcome and may also include indicators of malnutrition.

The RDN's assessment should include the five domains of the Nutrition Care Process (NCP) and consider the six indicators of malnutrition (energy intake, interpretation of weight loss, body fat, muscle mass, fluid accumulation and reduced grip strength). See <u>Clinical Characteristics to Document Malnutrition</u> (White et al, 2012).

The five domains of the NCP include the following. The Oncology expert work group has provided additional interpretations specific to the diagnosis of malnutrition in oncology patients:

Food- or Nutrition-Related History

Insufficient energy intake.

Anthropometric Measurements

Weight loss in elderly patients may have additional impact. The usual adult cutoff is <u>BMI</u> of 18.5kg/m², however studies of the elderly support an association between increased mortality and underweight (BMI under 20kg/m² or current weight compared with usual or desired body weight) or <u>unintended weight loss</u> (5% in 30 days or any further weight loss after meeting this criteria) (Grabowski et al, 2001; Fearon et al, 2013; Tan et al, 2009)

- Because weight loss is demonstrated to lead to poor outcomes, it is important to accurately determine a baseline weight. Weight loss or change should be defined as current weight compared to baseline weight. Baseline weight (include presence of under- or over-hydration) is defined as:
 - Usual body weight from medical records. • Weight taken when admitted to oncology service or, if not available:
 - Self-report of recent healthy weight
 - Consider rate of weight loss over specified time frame (Jensen et al, 2012)
 Include presence of under- or over-hydration

Biochemical Data, Medical Tests and Procedures

- Careful interpretation may be required in oncology patients, as they can experience wide variations in glucose and <u>WBC</u> values due to type and timing of treatment
 Other lab values determined to be outside of normal may indicate a need for diet modification of nutrients
- Other had values determined to be obtisite of normal may indicate a need for diet modification of indifience of indication of indifience of inflammation definitions are located at this link: <u>Etiology-Based Malnutrition</u> <u>Definitions</u> (Jensen et al, 2012). <u>CRP</u> should be used to evaluate the presence of inflammation (elevated* CRP may be indicative of inflammation). It is also important to differentiate between chronic disease-related malnutrition (lung, pancreatic and <u>GI</u> cancer, sarcopenic obesity and organ failure) and acute disease and injury-related malnutrition (major infection and surgery). Determining the presence and degree of inflammation determines the significance of any patient weight loss (Jensen et al, 2012; White to be 2012) White et al, 2012).

*Past interpretation of >10mg/L CRP has been used to indicate inflammation (Fearon et al, 2006). However, further research will elucidate more specific markers for use

Nutrition-Focused Physical Findings and Client History

- Loss of muscle mass [White et al, 2012; Prado et al, 2009 (*Clin Cancer Res.*)]
 Patients with loss of muscle mass experience greater treatment toxicity and shorter survival
 As 50% of patients with advanced cancer have frank <u>sarcopenia</u> (Fearon, 2011) and the shortest survival times are among <u>obese</u> patients with sarcopenia (Tan et al, 2009), reducing weight at the possible expense of lean muscle mass in obese cancer patients should not be a priority
 Low muscle mass is a common and independent predictor of immobility and mortality, is a particularly adverse prognostic indicator in obese patients and is associated with greater toxicities of chemotherapy leading to treatment interruptions including dose reductions, treatment delays and treatment termination [Fearon et al, 2013; Prado et al, 2009 (*Clin Cancer Res.*); Prado et al, 2009 (*Curr Opin Support Palliat Care.*); Prado et al, 2011; Antoun et al, 2010; Fearon, 2011]
 Body weight has been used as an outcome in clinical trials in cancer-induced weight loss and only recently has research begun to focus on lean body mass as a primary outcome. Existing
- Body weight has been used as an outcome in clinical trials in cancer-induced weight loss and only recently has research begun to focus on lean body mass as a primary outcome. Existing computerized tomography (CT) images used to diagnose and monitor disease progression are readily available and provide an opportunistic means for body composition analysis. Although this type of analysis is relatively new, its use will be common in the near future and offers the dietitian the ability to demonstrate value. Other methods of measuring muscle mass are bioelectrical impedence analysis (BIA), dual-energy X-ray absorptiometry (DXA) and anthropometry. Patients with loss of muscle mass experience greater treatment toxicity and shorter survival [Cruz-Jentoft et al, 2010; Prado et al, 2009 (*Curr Opin Support Palliat Care.*)].
 Loss of subcutaneous fat (White et al, 2012; Tan et al, 2009; Fearon, 2011)
 With the increase in <u>obesity</u> in Western society and patients with cancer in particular, reducing fat tissue should not be a priority
- - tissue should not be a priority
 - The important problem remains low muscle mass, since up to 50% of patients with advanced cancer have frank sarcopenia. The shortest survival times are among obese patients with
- sarcopenia (Tan et al, 2009).
 Nutrition impact symptoms that impede intake, digestion or absorption such as anorexia, nausea, vomiting, diarrhea, constipation, <u>stomatitis</u>, <u>mucositis</u>, <u>dysphagia</u>, alterations in taste and smell, pain, depression and anxiety, can be caused by the cancer itself or the oncology treatment (American Cancer Society 2000; Kubrak, 2010; Wojtaszek et al, 2002)
 Presence of <u>pre-cachexia</u> or <u>cancer cachexia</u>. Further nutrition assessment is needed for patients with
- lung, pancreatic or head and neck and gastrointestinal (GI) cancers or those who are at high risk for weight loss or have experienced <u>unintentional weight loss</u>.
 See recommendation for <u>Nutrition Assessment for the Stages of Cancer cachexia in Adult Oncology</u>
 - Patients

- <u>Localized or generalized fluid accumulation</u> (that may mask weight loss) (White et al, 2012)
 Reduced grip strength** or diminished functional status, as measured by <u>Karnofsky score</u>
 Type of cancer therapy o treatment (medical or surgical).
- - **Consult normative standards per device manufacturer.

For recommended tools for use in assessing the nutritional status of adult oncology patients in ambulatory and acute care settings, click here.

<u>Recommendation Strength Rationale</u>

Consensus.

Minority Opinions

None.

• Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

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Prado CM, Lima IS, Baracos VE, Bies RR, McCargar LJ, Reiman T, Mackey JR, Kuzma M, Damaraju VL, Sawyer MB. An exploratory study of body composition as a determinant of epirubicin pharmacokinetics and toxicity. *Cancer Chemother Pharmacol.* 2011 Jan; 67 (1): 93-101. Epub 2010 Mar 5. PMID: 20204364.

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Oncology

Oncology (ONC) Guideline (2013)

Quick Links

Recommendations Summary

ONC: Fish Oil, Lean Body Mass and Weight in Adult Oncology Patients 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

Recommendation(s)

ONC: Dietary Supplements Containing Fish Oil for the Adult Oncology Patient

If sub-optimal symptom control or inadequate <u>dietary intake</u> has been addressed and the <u>adult</u> oncology patient is still experiencing loss of weight and <u>lean body mass</u> (LBM), the registered dietitian nutritionist (RDN) may consider use of dietary supplements containing <u>eicosapentaenoic acid</u> (EPA) as a component of nutrition intervention. Research indicates that <u>dietary supplements containing fish oil</u> (actual consumption, 0.26g to 6.0g of <u>EPA</u> per day), resulted in a significant effect on preservation or improvement of weight and <u>LBM</u> in adult oncology patients with weight loss.

Rating: Strong Imperative

ONC: Medical Food Supplements Containing Fish Oil for the Adult Oncology Patient

If sub-optimal symptom control or inadequate dietary intake has been addressed and the <u>adult</u> oncology patient is still experiencing loss of weight and <u>LBM</u>, the <u>RDN</u> may consider use of a <u>medical food supplement</u> (MFS) containing <u>EPA</u> as a component of nutrition intervention. Research indicates that <u>MFS containing fish oil</u> (actual consumption, 1.1<u>a</u> to 2.2g of EPA per day) resulted in significant weight stabilization or weight gain and preservation or improvement of LBM in adult oncology pátients with weight loss.

Rating: Strong Imperative

- <u>Risks/Harms of Implementing This Recommendation</u>
 - Caution patients who are intolerant or allergic to fish about the potential for allergic reactions to fish oil
 The <u>RDN</u> should evaluate for potential drug interactions.

Conditions of Application

- Availability of MFS containing fish oil in the US is limited
- Consideration of <u>dietary supplements containing fish oil</u> should be raised with the physician
 Consideration should be given to the total intake of <u>omega-3 fatty acids</u> from all sources
- Consider advance directives when planning nutrition intervention.
- Potential Costs Associated with Application

There may be an increased cost for intake of dietary supplements and MFS containing fish oil.

Recommendation Narrative

A total of 24 studies were included in the evidence analysis for this recommendation:

- Eight positive-quality <u>randomized controlled trials</u> (RCT) (Bauer et al, 2005; de Luis et al, 2005; Fearon et al, 2006; Fearon et al, 2003; Finocchiaro et al, 2012; Jatoi et al, 2004; Silva et al, 2012; van der Meij et al, 2010)

- der Meij et al, 2010)
 Two positive-quality non-randomized trials (de Luis et al, 2008; Murphy et al, 2011)
 One positive-quality before-and-after study (Burns et al, 2004)
 One positive-quality randomized, non-placebo controlled trial (Persson et al, 2005)
 Three neutral-quality time studies (Barber et al, 1999; Taylor et al, 2010; Wigmore et al, 2000)
 Three neutral-quality <u>RCT</u>s (Bonatto et al, 2012; Guarcello et al, 2007; Ryan et al, 2009)
 Two neutral-quality prospective <u>cohort studies</u> (Read et al, 2007; Weed et al, 2011)
 One neutral-quality non-randomized trial (Barber et al, 2000)
 One negative-quality non-randomized controlled trial (Gogos et al, 1995)
 One negative-quality time study (Wigmore et al, 1996)

- One negative-quality time study (Wigmore et al, 1996)
 One negative-quality RCT (Pratt et al, 2002).

Evidence

Dietary Supplements Containing Fish Oil and Lean Body Mass

- Four of five included studies provide evidence that <u>dietary supplements containing fish oil</u> (actual consumption 0.27g to 6.0g of <u>EPA</u> per day) resulted in a significant effect on preservation or improvement of lean body mass in adult oncology patients with weight loss
 The fifth study (Fearon, 2006) showed the same effect, but was not statistically significant
 More research is needed to determine the optimal dose.

- For a comparison of fish oil dosing in the studies, <u>click here</u>.
 Evidence is based on the following studies: Fearon et al, 2006; Murphy et al, 2011; Taylor et al, 2010; Wigmore et al, 2000; and Wigmore et al, 1996.

Dietary Supplements Containing Fish Oil and Weight

- Eight of 12 studies provide evidence that dietary supplements containing fish oil (actual consumption 0.27g to 6.0g of EPA per day), resulted in preservation or improvement of weight in adult oncology patients with weight loss
- Three studies (Burns et al, 2004; Gogos et al, 1995; Persson et al, 2005) showed the same effect, but
- One study (Fearon et al, 2006) showed a positive effect for a sub-group of the population (gastrointestinal cancer patients), but not for the total population
 For a comparison of fish oil dosing in the studies, <u>click here</u>
- Evidence is based on the following studies: Bonatto et al, 2012; Burns et al, 2004; Fearon et al, 2006; Finocchiaro et al, 2012; Gogos et al, 1995; Murphy et al, 2011; Persson et al, 2005; Pratt et al, 2002; Taylor et al, 2010; Wigmore et al, 2000; Wigmore et al, 1996.

Medical Food Supplements (MFS) Containing Fish Oil and Lean Body Mass

- Seven of nine studies provide evidence that MFS containing fish oil (actual consumption, 1.1g to 2.2 g of EPA per day), resulted in a significant preservation or improvement of lean body mass in adult oncology patients with weight loss
- Two studies (Bauer 2005; de Luis 2008) showed the same effect, but were not statistically significant For a comparison of fish oil dosing in the studies, <u>click here</u>
- Evidence is based on the following studies: Barber et al, 1999; Barber et al, 2000; Bauer et al, 2005; de Luis 2008; Fearon et al, 2003; Read et al, 2007; Ryan et al, 2009; van der Meij et al, 2010; Weed et al, 2011.

Medical Food Supplement Containing Fish Oil and Weight

- Nine of 11 studies provide evidence that <u>MFS containing fish oil</u> (actual consumption 1.1g to 2.2g of EPA per day), resulted in weight stabilization or weight gain in adult oncology patients with weight loss
 Two studies (Fearon, 2003; Jatoi, 2004) showed the same effect, but were not statistically significant
 For a comparison of fish oil dosing in the studies, <u>click here</u>
 Evidence is based on the following studies: Barber et al, 1999; Barber et al, 2000, Bauer et al, 2005; de Luis 2008; de Luis 2005; Fearon 2003; Guarcello 2007; Jatoi 2004; Read et al, 2007; van der Meij et al, 2011 2005; de 2010; Weed et al, 2011.

Recommendation Strength Rationale

- The conclusion statement for the Effect of a Dietary Supplement Containing Fish Oil on LBM is Grade II
 The conclusion statement for the Effect of a Dietary Supplement Containing Fish Oil on Weight is Grade I
 The conclusion statement for the Effect of a MFS Containing Fish Oil on LBM is Grade I
- The conclusion statement for the Effect of a MFS Containing Fish Oil on Weight is Grade I.

Minority Opinions

None.

Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

What is the effect of a dietary supplement containing fish oil on lean body mass (LBM) in adult oncology patients?

What is the effect of a dietary supplement containing fish oil on weight in adult oncology patients?

What is the effect of medical food supplements (MFS) containing fish oil on lean body mass (LBM) in adult oncology patients?

What is the effect of medical food supplements (MFS) containing fish oil on weight in adult oncology patients?

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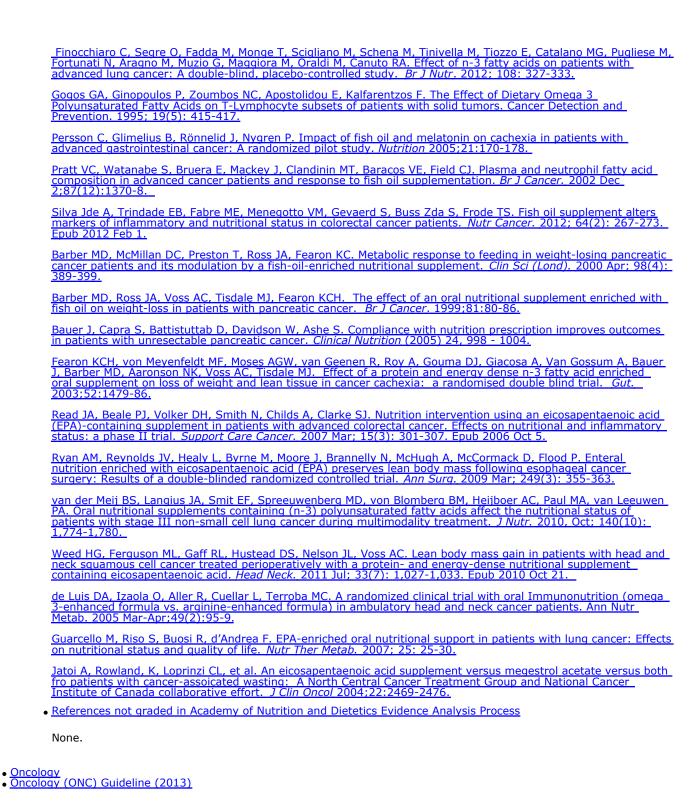
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Recommendations Summary

ONC: Glutamine and Oral Mucositis in Adult Oncology Patients 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

<u>Recommendation(s)</u>

ONC: Glutamine and Oral Mucositis in Adult Oncology Patients with Solid Tumors and Hematological Malignancies

If use of parenteral <u>glutamine</u> is proposed to prevent or treat oral mucositis in oncology patients with solid tumors, the registered dietitian nutritionist (RDN) should advise that its use may or may not be beneficial. Limited research in head

and neck and stem cell transplantation patients receiving parenteral glutamine has not established the effectiveness of L-Alanyl-L-Glutamine in treating or preventing oral mucositis.

Enteral or oral provision of glutamine was not evaluated.

Rating: Weak Conditional

- - Risks/Harms of Implementing This Recommendation

Risks associated with parenteral glutamine administration are similar to those of parenteral nutrition (i.e., increased risk of infection).

- Conditions of Application
 - This recommendation is limited to the use of IV glutamine in patients with head and neck cancer receiving chemoradiation therapy
 - Availability and access to supplemental IV glutamine
 - Consider ádvance directives when planning nutrition intervention.
- Potential Costs Associated with Application

Additional cost of supplemental IV glutamine.

Recommendation Narrative

The evidence summary below is based on research from searches completed through May 2008 (Harris et al, 2008) and Oncology Nursing Society Putting Evidence into Practice (ONS PEP) Mucositis Research Evidence Table, with searches completed through June 2011.

L-Alanyl-L-Glutamine

- The effectiveness of treating of oral mucositis with glutamine has not been established. One small study (N=29), in which patients were given a standard <u>MFS</u> in addition to IV glutamine, showed a moderate effect over mucositis intensity (P=0.044). In another study (N=32 <u>allogeneic stem cell transplantation</u> patients), in which patients were given parenteral (PN) supplemented with 0.57g/kg glutamine-dipeptide, the daily oral mucositis score (DMS) in the Glutamine Group vs. the Placebo Group results were <u>NS</u> and there was no difference in mean daily dose of morphine to alleviate the pain of mucositis. Prevention of mucositis using glutamine has not been demonstrated.
 As of June 2011, ONS PEP included a third study (N=326), in which glutamine was administered orally to breast cancer patients. Glutamine was shown to significantly reduce the incidence of <u>WHO</u> grade 2 or higher and grade 3 or higher oral mucositis, compared to placebo. However, the rating (weight of evidence)
- higher and grade 3 or higher oral mucositis, compared to placebo. However, the rating (weight of evidence category) remained the same. Weight of Evidence Category: **Effectiveness Not Established**.
- Recommendation Strength Rationale
 - The Academy of Nutrition and Dietetics (AND) and the Oncology Expert Work Group concurs with the ONS Putting Evidence Into Practice (PEP) guideline on Evidence-based Interventions for the Management of Oral Mucositis and approved the following equivalency scale External Guideline EAL Equivalency Rating.
 - Evidence to support the recommendation: Effectiveness not established (EAL Rating Equivalent: Weak).
- Minority Opinions

None.

Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

References

References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

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ONS PEP Mucositis Research Evidence Table 5-13: http://www.ons.org/Research/PEP/media/ons/docs/research/outcomes/mucositis/table-of-evidence.pdf. Searches through June 2011. Oncology Nursing Society (ONS), 50-53.

<u>Oncology</u>

Oncology (ONC) Guideline (2013)

Recommendations Summary

ONC: Parenteral Glutamine and Hematopoietic Cell Transplantation (HCT) in Adult Oncology Patients

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2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the Supporting Evidence Section below.

<u>Recommendation(s)</u>

ONC: Parenteral Glutamine and Hematopoietic Cell Transplantation (HCT) in Adult Oncology Patients

When <u>parenteral nutrition</u> (PN) is required for patients undergoing <u>hematopoietic cell transplantation</u> (HCT), the registered dietitian nutritionist (RDN) may or may not recommend parenteral <u>glutamine</u> (GLN) in doses ranging from 0.2g to 0.5g per kg per day. Research indicates parenteral GLN should be initiated early in the treatment course. Parenteral <u>GLN</u> is associated with improved nitrogen balance and decreased morbidity. However, decreased hospital length of stay (LOS) was found only when data from <u>allogeneic and autologous transplants</u> were combined.

Rating: Fair

Conditional

- Risks/Harms of Implementing This Recommendation
 - Use caution when considering provision of parenteral glutamine to oncology patients who have hepatic failure or insufficiency
 - Recommend monitoring liver function tests
 - Risks associated with parenteral glutamine administration are similar to those of parenteral nutrition (i.e., increased risk of infection).

• Conditions of Application

- Recommendation is applicable to <u>adult</u> oncology patients undergoing <u>HCT</u>, who require <u>PN</u>
 Availability and access to supplemental IV glutamine
 Consider advance directives when planning nutrition intervention.

- Potential Costs Associated with Application

Additional costs may be incurred with use of parenteral glutamine.

Recommendation Narrative

Guideline B4

Parenteral GLN in pharmacologic doses may be beneficial in patients undergoing HCT (August et al, 2009).

- Rationale: Studies evaluating the impact of enterally administered GLN show no reduction in morbidity or mortality. Studies evaluating parenterally administered GLN show an improvement in nitrogen balance and decreased morbidity.
- When data from allogeneic and autologous transplants were combined, there was a shorter hospital LOS, compared to no effect from GLN-supplemented PN, when given post transplant to patients undergoing In one small study of prophylactic PN vs. PN initiated after a decrease in oral intake, patients had a
- In one small study of prophylactic PN vs. PN Initiated after a decrease in oral intake, patients had a shorter disease-free survival, with no impact on morbidity or overall survival when they received supplemental GLN. These patients had a reduction in the incidence of severe <u>mucositis</u> after receiving supplemental GLN parenterally. These positive results were not duplicated with orally supplemented GLN.
 A Cochrane Review concluded that while PN-supplemented GLN may not be associated with reduced hospital LOS, patients may have fewer bloodstream infections
 More research is needed to determine appropriate dose and timing. However, use of parenteral GLN continues to be complicated or explored and the properties of the available as a proscription propared by a supplemented.
- GLN continues to be complicated, since parenteral GLN is only available as a prescription prepared by a compounding pharmacy in the US.
- Recommendation Strength Rationale

The Academy of Nutrition and Dietetics (AND) and the Oncology Expert Work Group concurs with the American Society of Parenteral and Enteral Nutrition (ASPEN) Clinical Guidelines: Nutrition Support Therapy During Adult Anticancer Treatment and in Hematopoietic Cell Transplantation and approved the following equivalency scale: External Guideline EAL Equivalency Rating

Evidence to support the recommendation is Grade C (EAL Rating Equivalent: Fair).

Minority Opinions

None.

• Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

 References References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

August DA, Huhmann MB; American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors.

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A.S.P.E.N. clinical guidelines: nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation. *JPEN J Parenter Enteral Nutr.* 2009 Sep-Oct; 33 (5): 472-500. doi: 10.1177/0148607109341804. No abstract available. PMID: 19713551.

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<u>Oncology</u>
<u>Oncology</u> (ONC) Guideline (2013)

Recommendations Summary

ONC: Nutrition Substances and Chemotherapy-Induced Peripheral Neuropathy 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

Recommendation(s)

ONC: Nutrition Substances and Chemotherapy-Induced Peripheral Neuropathy

If an <u>adult</u> oncology patient is at risk for or has <u>chemotherapy-induced peripheral neuropathy</u> (CIPN), the registered dietitian nutritionist (RDN) should advise the patient that the use of nutrition substances (vitamin E, <u>calcium</u> and magnesium infusions, acetyl-L-carnitine, <u>alutamine</u>, glutathione) may or may not be beneficial as a means of preventing or improving CIPN. Research indicates that these substances have had only limited success in preventing or improving <u>CIPN</u> in oncology patients receiving specific chemotherapeutic agents.

Rating: Weak Conditional

Risks/Harms of Implementing This Recommendation

As with all supplements, there is a potential for interaction with treatment that is unknown.

- Conditions of Application
 - This recommendation applies to adult oncology patients who are at risk for or have CIPN Consider advance directives when planning nutrition intervention.
- Potential Costs Associated with Application

Additional costs may be incurred with use of nutrition substances.

<u>Recommendation Narrative</u>

CIPN is a significant debilitating symptom directly related to the administration of neurotoxic chemotherapy for the treatment of cancer. The evidence summary below is based on research from searches completed through May 2008 and the ONS PEP Research Evidence Table for Peripheral Neuropathy with searches completed through June 2011.

- A total of 15 studies using Vitamin E (three studies), Calcium and Magnesium (four studies), acetyl-L-carnitine (two studies), glutamine (three studies) and glutathione (three studies) in various combinations with cisplatin, paclitaxel, oxaliplatin, 5-FU or leucovorin were reviewed. The effectiveness regarding use of these substances in the prevention or improvement of peripheral neuropathy from chemotherapy.
- Weight of the Evidence Category: Effectiveness was not established.
- <u>Recommendation Strength Rationale</u>

The Academy of Nutrition and Dietetics (AND) and the Oncology Expert Work Group concur with the Oncology Nursing Society Putting Evidence Into Practice (ONS PEP) guideline on Evidence-Based Interventions for Chemotherapy-Induced Peripheral Neuropathy and approved the following equivalency scale: External Guideline EAL Equivalency Rating.

- Evidence to support the recommendation on vitamin E, calcium and magnesium infusions, established (EAL Rating Equivalent: **Weak**).
- Minority Opinions

None.

Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

 References References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

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ONS PEP Research Evidence Table for Peripheral Neuropathy: arch/PEP/media/ons/docs/research/outcomes/peripheral/table-of-evidence.pdf. Searches .ons.org completed through June 2011. Oncology Nursing Society.

Oncology
 Oncology (ONC) Guideline (2013)

Recommendations Summary

ONC: Neutropenic Dietary Precautions for Adult Oncology Patients 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

<u>Recommendation(s)</u>

ONC: Neutropenic Dietary Precautions for Adult Oncology Patients with Neutropenia (non-Bone Marrow Transplant)

If an <u>adult</u> oncology patient has <u>neutropenia</u>, the registered dietitian nutritionist (RDN) should provide dietary counseling on safe food handling and foods which may pose infectious risks during the period of neutropenia. A neutropenic diet is not necessary, but safe food counseling is recommended as a prudent precaution. Research has not demonstrated the effectiveness of low-microbial diets.

Rating: Fair

Conditional

ONC: Neutropenic Dietary Precautions for Adult Oncology Patients Undergoing Bone Marrow Transplant

If an adult oncology patient is undergoing bone marrow transplant, the <u>RDN</u> should provide dietary counseling on safe food handling and foods which may pose infectious risks during the period of <u>neutropenia</u>. A neutropenic diet is not necessary, but safe food counseling is recommended as a prudent precaution. There is conflicting research regarding the effectiveness of neutropenic diets in the bone marrow transplant population.

Rating: Weak

Conditional

Risks/Harms of Implementing This Recommendation

There are no potential risks or harms associated with the application of this recommendation.

- Conditions of Application
 - The recommendation ONC: Neutropenic Dietary Precautions for Adult Oncology Patients with Neutropenia
 - (non-Bone Marrow Transplant) applies to oncology patients with neutropenia
 The recommendation ONC: Neutropenic Dietary Precautions for Adult Oncology Patients Undergoing Bone Marrow Transplant applies to oncology patients undergoing bone marrow transplant
 - Consider advance directives when planning nutrition intervention.
- Potential Costs Associated with Application

Although costs of <u>medical nutrition therapy</u> (MNT) sessions and reimbursement vary, MNT sessions including collaboration with other healthcare professional are essential for improved outcomes.

Recommendation Narrative

Infectious complications are a major cause of morbidity and mortality. Therefore, it is important to measure the prevention of infection as an outcome in oncology patients (Zitella et al, 2006).

The following evidence excerpts support the recommendations.

ONC: Neutropenic Dietary Precautions for Adult Oncology Patients with Neutropenia (non-Bone Marrow Transplant)

Guideline B5. Patients should receive dietary counseling regarding foods which may pose infectious risks and safe food handling during the period of neutropenia. Grade C. (August et al, 2009).

Rationale

Although the effect of low-microbial or sterile diets on infection risk is unknown, neutropenic HCT patients

should avoid foods that may contribute to an increased risk for infection

- A descriptive survey of 120 institutions found that 78% utilized low microbial diets, but there were wide
- variations in the triggers used to order low microbial diets (e.g., white blood cell and neutrophil counts)
 Eight studies of both pediatric and adult patients were included in the analysis of the role of diet and infectious risk in combination with other interventions such as isolator units and laminar airflow rooms
- Some studies suggested a reduced incidence of infection in patients who received a sterile diet, while
 other studies indicated no difference or no additional benefit
- It is difficult to make comparisons between the study groups because the dietary restrictions were not
- An adequately described and because of variations in practice
 More definitive research is needed on this topic. Until further research is available, it seems prudent to continue to provide dietary restrictions on high-risk foods during the period of neutropenia. Palatability of food choices in these anorectic patients should be considered.

ONC: Neutropenic Dietary Precautions for Adult Oncology Patients Undergoing Bone Marrow Transplant

Guideline: Low Microbial Diet for Neutropenic Patients Grade: EFFECTIVENESS UNLIKELY. (Zitella et al, 2006).

- Most institutions recommend dietary restrictions to their patients with neutropenia, even though there is eggs and unwashed fruits and vegetables are most commonly recommended
- Inconsistencies in the literature and practice complicate and impact the result. Many of the studies related to diet include confounders, such as protected environments and differences in restrictions.
 Further research is needed on the effectiveness of the neutropenic diet in preventing infection and what
- role diet plays in the institutional environment.
- <u>Recommendation Strength Rationale</u>

The Academy of Nutrition and Dietetics (AND) and the Oncology Expert Work Group concur with the American Society of Parenteral and Enteral Nutrition (ASPEN) Clinical Guidelines: Nutrition Support Therapy During Adult Anticancer Treatment and in Hematopoietic Cell Transplantation and the ONS Putting Evidence Into Practice (PEP) guideline on Prevention of Infection and approved the following equivalency scale External Guideline EAL <u>Equivalency Rating</u>

Evidence to support the recommendation is as follows:

- Grade C (EAL Rating Equivalent: Fair)
- Effectiveness Unlikely (EAL Rating Equivalent: Weak).
- Minority Opinions

None.

• Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations' rated consensus will not have supporting evidence linked).

References

References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

August DA, Huhmann MB; American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors. A.S.P.E.N. clinical guidelines: nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation. *JPEN J Parenter Enteral Nutr.* 2009 Sep-Oct; 33 (5): 472-500. doi: 10.1177/0148607109341804. No abstract available. PMID: 19713551.

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<u>Oncology</u>
<u>Oncology</u> (ONC) Guideline (2013)

Recommendations Summary

ONC: Nutrition Monitoring and Evaluation of Adult Oncology Patients 2013

<u>Click here</u> to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the <u>Supporting Evidence Section</u> below.

Recommendation(s)

ONC: Monitoring and Evaluation of Adult Oncology Patients

Following the nutrition intervention, to check progress, the registered dietitian (RDN) should monitor and evaluate the following components of <u>adult</u> oncology patients at each visit and compare to desired individual outcomes relevant to the nutrition diagnosis and intervention. This may include, but is not limited to:

Anthropometric measurements:

- Weight change
- <u>BMI</u>

Food/Nutrition-related history:

- Energy and <u>protein</u> intake
 Changes in food and fluid/beverage intake
 Adequacy and appropriateness of nutrient intake/nutrient administration
 Actual daily intake from <u>enteral nutrition</u> (EN) and <u>parenteral nutrition</u> (PN) and other nutrient sources
 Changes in type, texture, or temperature of food and liquids
 Use of <u>medical food supplements</u> (MFS)
 Food avoidance and intolerances
 Meal/snack pattern changes
- Meal/snack pattern changes
- Prescription medications, over-the-counter medications, herbal preparations and complementary alternative medicine productsFactors affecting access to foodFeeding method or need for placement (e.g., oral, enteral or parenteral)

Biochemical data, medical tests and procedures:

- Biochemical indices
- Implications of diagnostic tests and therapeutic procedures

Nutrition-focused physical findings:

- Vital signs
- Loss of muscle mass
- Loss of <u>subcutaneous fat</u>
- <u>Nutrition impact symptoms</u> including but not limited to: Nausea, vomiting, diarrhea, constipation, stomatitis, mucositis, alterations in taste and smell, and anxiety
- Presence of pressure ulcers or wounds
- Functional indicators (i.e., <u>Karnofsky score</u>, grip strength)
 <u>Localized or generalized fluid accumulation</u>

Client history:

- Patient/Family/Client Medical/Health History:
 - Nutrition impact symptoms including but not limited to: Dysphagia, depression and pain fatigue
 - Medical treatment/therapy
 - Other diseases, conditions and illnesses including cancer cachexia

Social history:

Psychological/socioeconomic issues (e.g., social support)

Monitoring and evaluation of the above factors is needed to correctly/effectively diagnose nutrition problems that should be the focus of further nutrition interventions. Inability to achieve optimal nutrient intake may contribute to poor outcomes.

Rating: Consensus

Imperative

ONC: Monitoring and Evaluating Adult Oncology Patients with Cancer Cachexia

As part of monitoring and evaluation, in patients with lung, pancreatic or head and neck and gastrointestinal (GI) cancers, or those who are at high risk for weight loss or have experienced <u>unintended weight loss</u>, the registered dietitian nutritionist (RDN) should monitor and evaluate <u>nutrition impact symptoms</u>, <u>markers of inflammation</u> [e.g., elevated <u>C-reactive protein</u> (CRP)] and other signs of wasting, which may indicate <u>pre-cachexia</u> or <u>cancer cachexia</u>.

Rating: Consensus

Conditional

• Risks/Harms of Implementing This Recommendation

There are no potential risks or harms associated with the application of this recommendation.

- Conditions of Application

 - <u>RDN</u>s should be appropriately trained to conduct a nutrition-focused physical exam
 If necessary data are not available, the RDN should use professional judgment to request or obtain additional data.
- Potential Costs Associated with Application

Accessibility and costs of additional laboratory testing should be considered.

Recommendation Narrative

Frequent monitoring and evaluation should be performed to document the presence of (or expected potential for) altered nutrition status, <u>nutrition impact symptoms</u> or measurable adverse effects on body composition, function, <u>OoL</u> or clinical outcomes. Appropriate <u>MNT</u> interventions can lead to improvement in clinical outcomes.

Monitoring should include the six indicators of malnutrition (energy intake, interpretation of weight loss, body fat, muscle mass, fluid accumulation, reduced grip strength), laboratory values, nutrition impact symptoms, and planned oncology treatments.

• Recommendation Strength Rationale

Consensus.

<u>Minority Opinions</u>

None.

• <u>Supporting Evidence</u>

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

<u>References</u>
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