



Complete Summary

GUIDELINE TITLE

Oncology evidence-based nutrition practice guideline.

BIBLIOGRAPHIC SOURCE(S)

American Dietetic Association (ADA). Oncology evidence-based nutrition practice guideline. Chicago (IL): American Dietetic Association (ADA); 2007 Oct. Various p. [46 references]

GUIDELINE STATUS

This is the current release of the guideline.

The guideline will undergo a complete revision every three to five years.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Cancer, including:

- Breast cancer
- Colorectal cancer
- Head and neck cancer
- Esophageal cancer
- Hematological malignancies
- Lung cancer
- Pancreatic cancer

GUIDELINE CATEGORY

Counseling
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Nutrition
Oncology

INTENDED USERS

Dietitians

GUIDELINE OBJECTIVE(S)

Overall Objective

- To help dietetic practitioners, patients and consumers make shared decisions about health care choices in specific clinical circumstances
- To provide medical nutrition therapy (MNT) guidelines aimed at managing symptoms, preventing weight loss and maintaining optimal nutritional status during cancer treatment

Specific Objectives

- To define evidence-based recommendations for registered dietitians (RDs) that are carried out in collaboration with other healthcare providers
- To guide practice decisions that integrate medical, nutritional and behavioral elements
- To reduce variations in practice among RDs
- To promote self-management strategies that empower the patient to take responsibility for day-to-day management
- To enhance the quality of life for the patient, utilizing customized strategies based on the individual's preferences, lifestyle and goals
- To develop guidelines for interventions that have measurable clinical outcomes
- To define the highest quality of care within cost constraints of the current healthcare environment

TARGET POPULATION

Adults 19 years and older who are receiving oncology treatment or care

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Referral to a registered dietitian
2. Nutritional assessment of patients with breast, colorectal, esophageal, hematological, lung or pancreatic cancer being treated with chemotherapy and/or radiation therapy:
 - Medical history and relevant laboratory tests
 - Nutrition-focused assessment including:
 - Height, weight, and body mass index
 - Comprehensive diet history, including current dietary intake and willingness to undertake behavior change
 - Physical activity pattern
 - Psychosocial and economic issues impacting nutrition therapy
 - Consideration of co-morbid conditions and need for additional modifications in nutrition care plan

Management/Treatment

1. Individualized prescription for medical nutrition therapy for patients with breast, colorectal, esophageal, hematological, lung or pancreatic cancer being treated with chemotherapy and/or radiation therapy based on:
 - Dietary interventions
 - Enteral (EN) and parenteral nutrition (PN)
 - Resting energy expenditure
 - Protein needs
 - Use of honey during radiation
 - Medical food supplements (MFS)
 - Physical activity interventions
 - Behavioral interventions
 - Pharmacology or surgery, when indicated

2. Monitoring and evaluation

Note: The following interventions were considered but not recommended: oral arginine supplement, routine use of PN for breast cancer patients, PN to prevent weight loss or improve effectiveness of treatment, vitamin E oral supplements for head/neck cancer, postoperative use of arginine-enhanced MFS or EN, antioxidants (vitamin C, vitamin E, beta-carotene, selenium), and Omega-3 fatty acids.

Note: The following interventions were considered, but it was determined that inadequate evidence exists to show a benefit: eicosapentaenoic acid-enhanced MFS, honey to prevent mouth sores and, vitamin E (alphatocopherol, 670 to 1000 mg) oral supplement to promote tolerance in breast cancer patients.

MAJOR OUTCOMES CONSIDERED

- Weight loss/nutritional status
- Length of hospital stay
- Unplanned hospital admissions
- Quality of life
- Toxicity symptoms (e.g., incidence or severity of mucositis)
- Tolerance of treatment
- Treatment interruptions
- Survival/mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Searches of PubMed and hand searches of other relevant literature were performed on the following topics:

- Use of medical nutrition therapy and dietitian intervention
- Determination of resting metabolic rate (RMR) in cancer patients
- Use of enteral and parenteral nutrition in cancer patients
- Use of oral vitamin and antioxidant supplements
- Use of omega-3 fatty acid-enhanced medical food supplement and oral supplements and eicosapentaenoic acid-enhanced medical food supplement and fish oil supplements

General Exclusion Criteria

As a general rule, studies are excluded if the:

- Study sample size is less than 10 in each treatment group
- Drop-out rate was >20%

Inclusion Criteria

- Study design preferences: randomised controlled trials, clinical controlled studies, large nonrandomized observational studies, cohort and case-control studies
- Limited to articles in English

The American Dietetic Association (ADA) has determined that for narrowly focused questions dealing with therapy or treatment, six well designed randomized controlled trials that demonstrate similar results is sufficient to draw a conclusion.

No one study design was preferred for all questions. The preferred study design depended on the type of question. The ADA uses the following principles in the table below for identifying preferred study design.

Type of Question	Preferred Study Designs (in order of preference)
Diagnosis questions	Sensitivity & specificity of diagnostic test Cross-sectional study
Etiology, causation, or harm questions	Prospective cohort

Type of Question	Preferred Study Designs (in order of preference)
	Case control study Cross-sectional study
Therapy and prevention questions	Randomized controlled trial Nonrandomized trial
Natural history and prognosis questions	Cohort study

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Grading the Strength of the Evidence for a Conclusion Statement or Recommendation Conclusion Grading Table

Strength of Evidence Elements	Grade I Good/Strong	Grade II Fair	Grade III Limited/Weak	Grade IV Expert Opinion Only	Grade V Grade I Assigned
Quality <ul style="list-style-type: none"> Scientific rigor/validity Considers design and execution 	Studies of strong design for question Free from design flaws, bias and execution problems	Studies of strong design for question with minor methodological concerns OR Only studies of weaker study design for question	Studies of weak design for answering the question OR Inconclusive findings due to design flaws, bias or execution problems	No studies available Conclusion based on usual practice, expert consensus, clinical experience, opinion, or extrapolation from basic research	No evidence that pertains to question being addressed
Consistency Of findings across studies	Findings generally consistent in direction and	Inconsistency among results of studies with strong design	Unexplained inconsistency among results from different	Conclusion supported solely by statements of	NA

Strength of Evidence Elements	Grade I Good/Strong	Grade II Fair	Grade III Limited/Weak	Grade IV Expert Opinion Only	Grade V Expert Opinion Only Grade I Assignment
	size of effect or degree of association, and statistical significance with minor exceptions at most	OR Consistency with minor exceptions across studies of weaker designs	studies OR Single study unconfirmed by other studies	informed nutrition or medical commentators	
Quantity <ul style="list-style-type: none"> • Number of studies • Number of subjects in studies 	One to several good quality studies Large number of subjects studies Studies with negative results having sufficiently large sample size for adequate statistical power	Several studies by independent investigators Doubts about adequacy of sample size to avoid Type I and Type II error	Limited number of studies Low number of subjects studies and/or inadequate sample size within studies	Unsubstantiated by published studies	Relevant studies have not been done
Clinical Impact <ul style="list-style-type: none"> • Importance of studies outcomes • Magnitude of effect 	Studied outcome relates directly to the question Size of effect is clinically meaningful Significant (statistical) difference is large	Some doubt about the statistical or clinical significance of effect	Studies outcome is an intermediate outcome or surrogate for the true outcome of interest OR Size of effect is small or lacks statistical and/or clinical significance	Objective data unavailable	Indicate area for future research
Generalizability	Studied population,	Minor doubts about	Serious doubts about	Generalizability limited to scope	NA

Strength of Evidence Elements	Grade I Good/Strong	Grade II Fair	Grade III Limited/Weak	Grade IV Expert Opinion Only	Grade V Grade I Assignment
To population of interest	intervention and outcomes are free from serious doubts about generalizability	generalizability	generalizability due to narrow or different study population, intervention or outcomes studied	of experience	

This grading system was based on the grading system from: Greer N, Mosser G, Logan G, Wagstrom Halaas G. *A practical approach to evidence grading. Jt Comm. J Qual Improv.* 2000; 26:700-712. In September 2004, The ADA Research Committee modified the grading system to this current version.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Step 1: Formulate the question

Specify a question in a defined area of practice; or state a tentative conclusion or recommendation that is being considered. Include the patient type and special needs of the target population involved, the alternatives under consideration, and the outcomes of interest.

Step 2: Gather and classify evidence reports

Conduct a systematic search of the literature to find evidence related to the question, gather studies and reports, and classify them by type of evidence. Classes differentiate primary reports of new data according to study design, and distinguish them from reports that are a systematic review and synthesis of primary reports.

Step 3: Critically appraise each report

Review each report for relevance to the question and critique for scientific validity. Abstract key information from the report and assign a code to indicate the quality of the study by completing quality criteria checklist.

Step 4: Summarize evidence in a narrative and an overview table

Combine findings from all reports in a table that pulls out the important information from the article worksheets. Write a brief narrative that summarizes

and synthesizes the information abstracted from the articles that is related to the question asked.

Step 5: Develop a conclusion statement and grade the strength of evidence supporting the conclusion

Develop a concise conclusion statement (the answer to the question), taking into account the synthesis of all relevant studies and reports, their class and their quality ratings. Assign a grade to indicate the overall strength or weakness of evidence informing the conclusion statement.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The recommendations are based on the work performed by the American Dietetic Association Oncology evidence analysis working group.

The expert work group, which includes practitioners and researchers with a depth of experience in the specific field of interest, develops the guideline. The guideline development involves the following steps:

Review Evidence Based Conclusions

The work group meets to review the materials resulting from the evidence analysis, which may include conclusion statements, evidence summaries, and evidence worksheets.

Formulate Recommendations for the Guideline Integrating Conclusions from Evidence Analysis

The work group uses an expert consensus method to formulate recommendations, taking into account the following:

- Recommendations for what the dietitian should do and why
- Rating of recommendations based on strength of supporting evidence
- Label of Conditional (clearly define a specific situation) or Imperative (broadly applicable to the target population without restraints on the pertinence)
- Risks and Harms of Implementing the Recommendations, including potential risks, harms, or adverse consequences
- Conditions of Application, including organizational barriers or conditions that may limit application
- Potential Costs Associated with Application
- Recommendation Narrative
- Recommendation Strength Rationale, evidence strength and methodological issues
- Minority Opinions, when the expert working group cannot reach consensus on a recommendation

- Supporting Evidence

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Criteria for Recommendation Rating

Statement Rating	Definition	Implication for Practice
Strong	A Strong recommendation means that the workgroup believes that the benefits of the recommended approach clearly exceed the harms (or that the harms clearly exceed the benefits in the case of a strong negative recommendation), and that the quality of the supporting evidence is excellent/good (grade I or II)*. In some clearly identified circumstances, strong recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms.	Practitioners should follow a Strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Fair	A Fair recommendation means that the workgroup believes that the benefits exceed the harms (or that the harms clearly exceed the benefits in the case of a negative recommendation), but the quality of evidence is not as strong (grade II or III)*. In some clearly identified circumstances, recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits outweigh the harms.	Practitioners should generally follow a Fair recommendation but remain alert to new information and be sensitive to patient preferences.
Weak	A Weak recommendation means that the quality of evidence that exists is suspect or that well-done studies (grade I, II, or III)* show little clear advantage to one approach versus another.	Practitioners should be cautious in deciding whether to follow a recommendation classified as Weak , and should exercise judgment and be alert to emerging publications that report evidence. Patient preference should have a substantial influencing role.
Consensus	A Consensus recommendation	Practitioners should be flexible in

Statement Rating	Definition	Implication for Practice
	means that Expert opinion (grade IV)* supports the guideline recommendation even though the available scientific evidence did not present consistent results, or controlled trials were lacking.	deciding whether to follow a recommendation classified Consensus , although they may set boundaries on alternatives. Patient preference should have a substantial influencing role.
Insufficient Evidence	An Insufficient Evidence recommendation means that there is both a lack of pertinent evidence (grade V)* and/or an unclear balance between benefits and harms.	Practitioners should feel little constraint in deciding whether to follow a recommendation labeled as Insufficient Evidence and should exercise judgment and be alert to emerging publications that report evidence that clarifies the balance of benefit versus harm. Patient preference should have a substantial influencing role.

*Conclusion statements are assigned a grade based on the strength of the evidence. Grade I is good; grade II, fair; grade III, limited; grade IV signifies expert opinion only and grade V indicates that a grade is not assignable because there is no evidence to support or refute the conclusion. The evidence and these grades are considered when assigning a rating (Strong, Fair, Weak, Consensus, Insufficient Evidence - see chart above) to a recommendation.

Adapted by the American Dietetic Association from the American Academy of Pediatrics, Classifying Recommendations for Clinical Practice Guideline, Pediatrics. 2004;114;874-877.

COST ANALYSIS

An analysis was performed of potential costs associated with application of the recommendations in the guideline.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Each guideline is reviewed internally and externally using the AGREE (Appraisal of Guidelines for Research and Evaluation) instrument as the evaluation tool. The external reviewers consist of a multidisciplinary group of individuals (may include dietitians, doctors, psychologists, pharmacists, nurses, etc.). The review is done electronically. The guideline is adjusted by consensus of the expert panel and approved by American Dietetic Association's Evidence-Based Practice Committee prior to publication on the Evidence Analysis Library (EAL).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Ratings for the strength of the recommendations (Strong, Fair, Weak, Consensus, Insufficient Evidence), conclusion grades (I-V), and statement labels (Conditional versus Imperative) are defined at the end of "Major Recommendations"

Oncology (Onc) Breast Cancer: Chemotherapy Determination of Resting Energy Expenditure

Onc-Breast Cancer: Determination of Resting Energy Expenditure (REE) and Chemotherapy

Use of indirect calorimetry to measure REE is more accurate than estimation in early stage and advanced metastatic breast cancer patients. If measurement of REE is not possible or not thought to be imperative, use the Harris-Benedict Equation (HBE) to estimate calorie requirements. Limited evidence indicates that the mean estimated REE was comparable to measured REE in these populations. No research was available to compare HBE using individual error or to compare HBE with other predictive equations in these populations.

Weak, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Breast Cancer: Chemotherapy and Use of Arginine Oral Supplement

Onc-Breast Cancer: Arginine and Chemotherapy

Use of an oral arginine supplement to improve long-term clinical response for patients with breast cancer prior to the start of neoadjuvant chemotherapy is not currently recommended. Evidence is not available to evaluate the safety of arginine or its effect on cancer symptoms for patients with breast cancer receiving chemotherapy. One randomized controlled trial (RCT) demonstrated a statistically significant histopathological response in tumor sizes less than 6 cm, however there was no improvement in short-term clinical response.

Weak, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Breast Cancer: Auto-Hematopoietic Stem Cell Transplant (Auto-HCT) and Use of Parenteral Nutrition (PN)

Onc-Breast Cancer: Auto-HCT and PN

Parenteral nutrition should not be routinely recommended for breast cancer patients undergoing auto-HCT who are well-nourished prior to treatment. While PN may preserve nutritional status and lean body mass in these patients, it does not appear to affect length of hospital stay (LOS) or survival, and may increase risk of infectious complications.

Weak, Imperative

Recommendation Strength Rationale

Conclusion statement is a Grade III

Oncology (Onc) Breast Cancer: Radiation and the Use of Antioxidant Vitamin E Oral Supplement

Onc-Breast Cancer: Vitamin E and Radiation

If vitamin E (alpha tocopherol, 670 to 1000 mg) oral supplement is proposed to promote tolerance or reduce late-effects of radiation, advise that no research is available on the impact of vitamin E supplementation to promote tolerance of radiation. Evidence is inconclusive on the benefit of vitamin E for treatment of chronic radiation-induced fibrosis. Vitamin E supplementation may have adverse effects such as nutrient-nutrient interactions, drug-nutrient interactions (e.g., anti-coagulant and anti-hypertensive medications/herbal supplements) and disease-related complications.

Weak, Conditional

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Colorectal Cancer: Radiation and Medical Nutrition Therapy (MNT)

Onc-Colorectal Cancer: Radiation and MNT

Dietitians should provide weekly medical nutrition therapy that includes an individualized nutrition prescription and counseling for patients with colorectal cancer undergoing pelvic radiation. Individualized counseling with a focus on the consumption of regular foods may improve calorie and protein intake, nutrition status, quality of life (QOL) and reduce symptoms of anorexia, nausea, vomiting and diarrhea.

Fair, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Esophageal Cancer: Chemoradiation and Medical Nutrition Therapy (MNT)

Onc-Esophageal Cancer: Chemoradiation and MNT

The dietitian should provide MNT consisting of a pre-treatment evaluation and weekly visits for six weeks during chemoradiation treatment for esophageal cancer to improve outcomes. MNT may reduce the amount of weight loss, unplanned hospitalizations, LOS, as well as improves tolerance to treatment and the likelihood of receiving prescribed radiation dose.

Weak, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Esophageal Cancer: Chemoradiation and Use of Enteral Nutrition

Onc-Esophageal Cancer: Chemoradiation and Use of Enteral Nutrition (EN)

Enteral nutrition (EN) may be used to increase calorie and protein intake in esophageal cancer patients undergoing chemoradiation therapy. EN has been shown to maintain weight, however EN has not been shown to improve tolerance to therapy or survival.

Weak, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Esophageal Cancer: Chemoradiation and Use of Parenteral Nutrition

Onc-Esophageal Cancer: Use of Parenteral Nutrition and Chemoradiation

Use of parenteral nutrition (PN) to prevent weight loss or improve effectiveness of treatment for patients with esophageal cancer receiving chemoradiation therapy (CRT) is not recommended. PN has not been shown to prevent weight loss or improve effectiveness of treatment, even though patients were able to tolerate a higher dose of CRT. PN may have adverse effects such as complications related to refeeding syndrome, inadequate glycemic control and increased risk of infections.

Weak, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Head and Neck Cancer: Chemoradiation and Determination of Resting Energy Expenditure (REE)

Onc-Head and Neck Cancer: Chemoradiation and Determination of REE

Use of indirect calorimetry to measure resting energy expenditure (REE) is more accurate than estimation in patients with advanced head and neck cancer undergoing chemoradiation therapy. If measurement of REE is not possible or not thought to be imperative, use the Harris Benedict Equation (HBE) to estimate calorie needs. However, limited evidence indicates that HBE underestimates REE in this population.

Weak, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Head and Neck Cancer: Radiation Determination of Protein Needs

Onc-Head and Neck Cancer: Determination of Protein Needs and Radiation

The protein needs for patients with head and neck cancer undergoing radiation therapy may be higher than the recommended daily allowance (RDA). Limited evidence indicates patients consuming the RDA for protein experienced a significant decrease in weight and lean body mass (LBM) during treatment. More defined protein intervention studies are needed.

Weak, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Head and Neck Cancer: Radiation and Use of Medical Food Supplement

Onc-Head and Neck Cancer: Medical Food Supplements and Radiation

Dietitians should consider use of MFS to improve protein and calorie intake for patients with head and neck cancer undergoing radiation therapy. Use of MFS may be associated with fewer treatment interruptions, a reduction of mucosal damage, and may minimize weight loss.

Fair, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade II**

Oncology (Onc) Head and Neck Cancer: Radiation and Medical Nutrition Therapy (MNT)

Onc-Head and Neck Cancer: MNT and Radiation Therapy

Medical nutrition therapy that consists of nutrition assessment, intensive intervention, and ongoing monitoring and evaluation by a registered dietitian (RD) should be provided for patients with head/neck cancer being considered for radiation therapy. MNT has been shown to improve calorie and protein intake, maintain anthropometric measurements and improve quality of life (QOL).

Onc-Head and Neck Cancer: MNT and Pre-Treatment Evaluation

The dietitian should provide MNT consisting of a pre-treatment evaluation and weekly visits during radiation treatment for head and neck cancer to improve outcomes.

Strong, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade II**

Oncology (Onc) Head and Neck Cancer: Radiation and Use of Enteral Nutrition (EN)

Onc-Head and Neck Cancer: Radiation and Use of EN

Use enteral nutrition to increase calorie and protein intake for outpatients with stage III or IV head and neck cancer undergoing intensive radiation treatment. Maintenance of nutritional status by EN during radiation therapy may improve tolerance of therapy to promote better outcomes.

Strong, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade II**

Oncology (Onc) Head and Neck Cancer: Radiation and Use of Honey

Onc-Head and Neck Cancer: Use of Honey and Radiation

If the topical use of honey is proposed to prevent mouth sores caused by radiation treatment for patients with head and neck cancer, advise that its use may or may not be beneficial. Limited evidence shows that topical use of honey has been associated with decreased incidence of severe mucositis, weight gain and reduced treatment interruptions; however, the risks of interference with effectiveness of radiation treatment and infectious complications were not evaluated.

Weak, Conditional

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Head and Neck Cancer: Radiation

Onc-Use of Antioxidant Vitamin E Oral Supplement

Use of vitamin E oral supplements to enhance efficacy, improve tolerance and reduce late-effects of radiation therapy for patients with head/neck cancer is not recommended. While limited evidence supports the use of vitamin E oral supplements to reduce late effects (osteoradionecrosis), there is strong research reporting an increased risk for second primary cancers and decreased survival rate with use of vitamin E in doses greater than or equal to 400 International Units (IU) (268 mg).

Weak, Imperative

Recommendation Strength Rationale

- **Conclusion statements are Grades II and III**

Oncology (Onc) Head and Neck Cancer: Surgery and Use of Arginine-Enhanced Medical Food Supplement or EN

Onc-Head and Neck Cancer: Post-Operative Use of Arginine

Post-operative use of arginine-enhanced MFS or EN to improve outcomes for patients with head and neck cancer is not recommended. Arginine-enhanced versus non-arginine-enhanced MFS and EN did not produce significant changes in weight and body composition in either well-nourished or malnourished subjects. Most evidence shows there is no impact of arginine-enhanced MFS or EN on immune function. Limited research reported that arginine-enhanced EN can improve post-operative complications and LOS in malnourished patients.

Fair, Imperative

Onc-Head and Neck Cancer: Pre-Operative Use of Arginine

Pre-operative use of arginine-enhanced EN to improve outcomes for patients with head and neck cancer is not recommended. No significant improvement in clinical outcomes, nutritional status, or surgery-induced immune suppression was

observed among malnourished compared to patients receiving a non-enhanced EN, or those who did not receive EN.

Fair, Imperative

Recommendation Strength Rationale

- **Conclusion statement are Grades II and III**

Oncology (Onc) Head and Neck Cancer: Surgery and Use of Eicosapentaenoic Acid (EPA)-Enhanced Medical Food Supplement (MFS)

Onc-Head and Neck Cancer: Surgery and EPA-Enhanced MFS

If the use of an EPA-enhanced MFS is proposed to decrease post-surgical complications (e.g., infections and weight loss) for oral and laryngeal cancer patients, advise inadequate evidence exists to show a benefit. While one study comparing EPA- versus arginine-enhanced MFS found that an EPA supplement led to an increase in weight, there were no differences in fat-free mass or infectious complications.

Weak, Conditional

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Hematological Malignancies (HCT): Chemotherapy and Medical Nutrition Therapy (MNT)

Onc-HCT: Chemotherapy and MNT

Medical Nutrition Therapy that consists of nutrition assessment, intensive intervention, and ongoing monitoring and evaluation by a registered dietitian may be of benefit to patients with acute leukemias undergoing chemotherapy. Daily monitoring of intake and incorporating patient preferences have been shown to increase nutrition intake which positively affects body weight and tumor-therapy side effects (e.g., fatigue and anorexia).

Weak, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Hematological Malignancies (HCT): Determination of Calorie Needs

Onc-HCT: Determination of Calorie Needs

Use indirect calorimetry to measure REE for adult patients with hematologic malignancies undergoing allogeneic HCT. When indirect calorimetry is not available, limited evidence indicates that the estimated energy requirements are 30-35 kcal per kg per day during the first month post-transplant, and may be higher during acute graft-versus-host disease (GVHD) and/or for patients receiving >75% of their total daily energy intake via PN.

Fair, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade II**

Oncology (Onc) Hematological Malignancies (HCT): Determination of Protein Needs

Onc HCT: Determination of Protein Needs

The protein needs for patients with hematologic malignancies undergoing allogeneic HCT are higher than the RDA. Limited evidence suggests that more than 2.2g protein per kg may be needed to maintain nitrogen balance. Further research is needed to define protein requirements in this population.

Fair, Conditional

Recommendation Strength Rationale

- **Conclusion statement is a Grade II**

Oncology (Onc) Hematological Malignancies (HCT): Use of Oral Glutamine

Onc-HCT: Use of Oral Glutamine

Use of oral glutamine to decrease incidence or severity of mucositis or to support recovery following hematopoietic cell transplantation for hematologic malignancies is not currently recommended. Glutamine supplementation did not show an effect on the incidence or severity of oral mucositis, diarrhea, oral intake or PN requirements among patients with hematologic malignancies receiving autologous or allogeneic HCT.

Fair, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Hematological Malignancies (HCT): Use of Parenteral Nutrition

Onc-HCT: Use of Parenteral Nutrition (PN)

Parenteral nutrition should only be used in selected HCT patients due to increased risk of treatment complications, increased cost, and a lack of significant improvement in treatment outcomes. Dietitians should regularly screen and monitor HCT patients for signs of malnutrition and prolonged periods of poor oral intake to identify patients who might benefit from PN. Patients most likely to benefit from PN include patients receiving allogeneic transplants from mismatched donors.

Fair, Imperative

Onc-HCT: Use of Lipid-Based PN Formulations

Patients receiving PN while undergoing HCT should receive 25 to 30% of energy as lipids. Provision of lipids is necessary to prevent fatty acid deficiency, and may improve blood glucose control.

Fair, Conditional

Onc-HCT: Use of Glutamine-Enhanced PN Formulations

Use of parenteral glutamine to decrease incidence or severity of mucositis or diarrhea following hematopoietic cell transplantation for hematologic malignancies is not currently recommended. No clear evidence indicates that use of parenteral glutamine alters incidence or duration of mucositis or diarrhea. In addition, parenteral glutamine has not been shown to decrease LOS, time to engraftment or the number of infectious complications.

Fair, Imperative

Recommendation Strength Rationale

- **Conclusion statements are Grades II and III**

Oncology (Onc) Non-Small Cell Lung Cancer: Chemotherapy and Determination of Resting Energy Expenditure

Onc-Lung Cancer: Chemotherapy and Determination of REE

Use of indirect calorimetry to measure REE is more accurate than estimation in patients with non-small cell lung cancer (NSLC) undergoing chemotherapy. If measurement of REE is not possible or not thought to be imperative, use HBE to estimate calorie needs. However, limited evidence indicates that the HBE may underestimate energy needs by an average of 12-13%.

Weak, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Lung Cancer: Chemotherapy and Use of Antioxidant Vitamins C, E and Beta-Carotene Oral Supplements

Onc-Lung Cancer: Chemotherapy and Use of Antioxidant Supplements

The use of antioxidants (vitamin C, vitamin E, beta-carotene, selenium) above the tolerable upper intake level to improve treatment outcomes in patients with advanced non-small cell lung cancer undergoing chemotherapy is not recommended. In this population, use of high-dose multiple oral antioxidants did not significantly influence response to treatment, survival, survival time, and toxicity. More studies are needed.

Weak, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Lung Cancer: Chemotherapy and Medical Nutrition Therapy

Onc-Lung Cancer: MNT and Chemotherapy

Medical Nutrition Therapy that consists of nutrition assessment, intensive intervention, and ongoing monitoring and evaluation by an RD may be of benefit to patients with small cell lung cancer undergoing chemotherapy. Providing MNT may improve protein and calorie intake, which has been shown to improve weight status and QOL.

Weak, Imperative

Recommendation Strength Rationale

- **Conclusion statement is a Grade III**

Oncology (Onc) Pancreatic Cancer: Use of Omega-3 Fatty Acid-Enhanced MFS or Oral Supplements

Once-Pancreatic Cancer: Use of Omega-3 Supplements for Weight Loss

Use of omega-3 fatty acids to alter the prolonged acute-phase response is not recommended for pancreatic cancer patients. Consumption of an omega-3 fatty acid-enhanced medical food supplement (mean dose 2.2 g daily) or an oral supplement (2 g EPA daily) for pancreatic cancer patients experiencing weight loss has not been shown to reduce serum C-reactive protein (CRP) concentrations after 12 weeks of EPA supplementation and there are potential drug-nutrient interactions (e.g., anti-coagulant and anti-hypertensive medications/herbal supplements).

Fair, Imperative

Onc-Pancreatic Cancer: Use of Omega-3 Supplements for Anticachectic Effects

Use of supplemental omega-3 fatty acids for anticachectic effects leading to changes in body composition (e.g., increase in LBM, weight gain or weight stabilization) is not recommended for patients with pancreatic cancer. EPA as a capsule or in a medical food supplement was not associated with an increase in LBM. Evidence that fish oil supplements stabilize weight or produce weight gain is inconclusive. There are potential drug-nutrient interactions (e.g., anti-coagulant and anti-hypertensive medications/herbal supplements).

Strong, Imperative

Recommendation Strength Rationale

- **Conclusion statement are Grades I and III**

Definitions:

Conditional versus Imperative Recommendations

Recommendations can be worded as **conditional** or **imperative** statements. Conditional statements clearly define a specific situation, while imperative statements are broadly applicable to the target population without restraints on their pertinence. More specifically, a conditional recommendation can be stated in if/then terminology (e.g., If an individual does not eat food sources of omega-3 fatty acids, then 1g of EPA and DHA omega-3 fatty acid supplements *may* be recommended for secondary prevention).

In contrast, imperative recommendations "require," or "must," or "should achieve certain goals," but do not contain conditional text that would limit their applicability to specified circumstances. (e.g., Portion control should be included as part of a comprehensive weight management program. Portion control at meals and snacks results in reduced energy intake and weight loss).

Grading the Strength of the Evidence for a Conclusion Statement or Recommendation Conclusion Grading Table

Strength of Evidence Elements	Grade I Good/Strong	Grade II Fair	Grade III Limited/Weak	Grade IV Expert Opinion Only	Grade V Grade I Assignment
Quality <ul style="list-style-type: none"> • Scientific rigor/validity • Considers design and 	Studies of strong design for question Free from design flaws, bias and	Studies of strong design for question with minor methodological concerns	Studies of weak design for answering the question OR	No studies available Conclusion based on usual practice, expert consensus,	No evidence that pertains to question being addressed

Strength of Evidence Elements	Grade I Good/Strong	Grade II Fair	Grade III Limited/Weak	Grade IV Expert Opinion Only	Grade V Expert Opinion Only Grade I Assignment
execution	execution problems	OR Only studies of weaker study design for question	Inconclusive findings due to design flaws, bias or execution problems	clinical experience, opinion, or extrapolation from basic research	
Consistency Of findings across studies	Findings generally consistent in direction and size of effect or degree of association, and statistical significance with minor exceptions at most	Inconsistency among results of studies with strong design OR Consistency with minor exceptions across studies of weaker designs	Unexplained inconsistency among results from different studies OR Single study unconfirmed by other studies	Conclusion supported solely by statements of informed nutrition or medical commentators	NA
Quantity <ul style="list-style-type: none"> • Number of studies • Number of subjects in studies 	One to several good quality studies Large number of subjects studies Studies with negative results having sufficiently large sample size for adequate statistical power	Several studies by independent investigators Doubts about adequacy of sample size to avoid Type I and Type II error	Limited number of studies Low number of subjects studies and/or inadequate sample size within studies	Unsubstantiated by published studies	Relevant studies have not been done
Clinical Impact <ul style="list-style-type: none"> • Importance of studies outcomes • Magnitude of effect 	Studied outcome relates directly to the question Size of effect is clinically	Some doubt about the statistical or clinical significance of effect	Studies outcome is an intermediate outcome or surrogate for the true outcome of interest	Objective data unavailable	Indicate area for future research

Strength of Evidence Elements	Grade I Good/Strong	Grade II Fair	Grade III Limited/Weak	Grade IV Expert Opinion Only	Grade V Grade I Assignment
	meaningful Significant (statistical) difference is large		OR Size of effect is small or lacks statistical and/or clinical significance		
Generalizability To population of interest	Studied population, intervention and outcomes are free from serious doubts about generalizability	Minor doubts about generalizability	Serious doubts about generalizability due to narrow or different study population, intervention or outcomes studied	Generalizability limited to scope of experience	NA

This grading system was based on the grading system from: Greer N, Mosser G, Logan G, Wagstrom Halaas G. A practical approach to evidence grading. *Jt Comm. J Qual Improv.* 2000; 26:700-712. In September 2004, The ADA Research Committee modified the grading system to this current version.

Criteria for Recommendation Rating

Criteria for Recommendation Rating

Statement Rating	Definition	Implication for Practice
Strong	A Strong recommendation means that the workgroup believes that the benefits of the recommended approach clearly exceed the harms (or that the harms clearly exceed the benefits in the case of a strong negative recommendation), and that the quality of the supporting evidence is excellent/good (grade I or II)*. In some clearly identified circumstances, strong recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated	Practitioners should follow a Strong recommendation unless a clear and compelling rationale for an alternative approach is present.

Statement Rating	Definition	Implication for Practice
	benefits strongly outweigh the harms.	
Fair	A Fair recommendation means that the workgroup believes that the benefits exceed the harms (or that the harms clearly exceed the benefits in the case of a negative recommendation), but the quality of evidence is not as strong (grade II or III)*. In some clearly identified circumstances, recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits outweigh the harms.	Practitioners should generally follow a Fair recommendation but remain alert to new information and be sensitive to patient preferences.
Weak	A Weak recommendation means that the quality of evidence that exists is suspect or that well-done studies (grade I, II, or III)* show little clear advantage to one approach versus another.	Practitioners should be cautious in deciding whether to follow a recommendation classified as Weak , and should exercise judgment and be alert to emerging publications that report evidence. Patient preference should have a substantial influencing role.
Consensus	A Consensus recommendation means that Expert opinion (grade IV)* supports the guideline recommendation even though the available scientific evidence did not present consistent results, or controlled trials were lacking.	Practitioners should be flexible in deciding whether to follow a recommendation classified Consensus , although they may set boundaries on alternatives. Patient preference should have a substantial influencing role.
Insufficient Evidence	An Insufficient Evidence recommendation means that there is both a lack of pertinent evidence (grade V)* and/or an unclear balance between benefits and harms.	Practitioners should feel little constraint in deciding whether to follow a recommendation labeled as Insufficient Evidence and should exercise judgment and be alert to emerging publications that report evidence that clarifies the balance of benefit versus harm. Patient preference should have a substantial influencing role.

*Conclusion statements are assigned a grade based on the strength of the evidence. Grade I is good; grade II, fair; grade III, limited; grade IV signifies expert opinion only and grade V indicates that a grade is not assignable because there is no evidence to support or refute the conclusion. The evidence

and these grades are considered when assigning a rating (Strong, Fair, Weak, Consensus, Insufficient Evidence - see chart above) to a recommendation.

CLINICAL ALGORITHM(S)

The following algorithms are provided in the original guideline document:

- Oncology guideline
- Oncology nutrition assessment
- Oncology nutrition diagnosis
- Oncology nutrition intervention recommendations
 - Breast cancer
 - Lung cancers
 - Head and neck cancers
 - Pancreatic cancer
 - Hematological malignancies
 - Esophageal cancer
- Oncology nutrition monitoring and evaluation

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

The guideline contains conclusion statements that are supported by evidence summaries and evidence worksheets. These resources summarize the important studies (randomized controlled studies [RCTs], clinical studies, observational studies, cohort and case-control studies) pertaining to the conclusion statement and provide the study details.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Improved percentage of individuals who are able to meet their nutritional needs, reduced incidence of treatment interruptions, and positive impact on the patient's treatment.

POTENTIAL HARMS

Risk/Harm Considerations

Use clinical judgment when evaluating patients with co-morbid conditions or those receiving palliative care.

Determination of Resting Energy Expenditure (REE)

- Anxiety may be caused by indirect calorimetry procedures employing a face mask or canopy.
- In some individuals, estimation of REE with predictive equations will lead to under- or overfeeding.

Chemoradiation and Use of Enteral Nutrition

- Insertion of a percutaneous endoscopic gastrostomy (PEG) tube using the pull technique has been associated with an increased risk for tumor implantation in the gastrostomy site.

Use of Lipid-Based Parenteral Nutrition (PN) Formulations

- Triglyceride (TG) levels should be monitored regularly while the patient is receiving PN solutions containing lipids. Lipid administration should be slowed, the total dosage decreased, or discontinued if the patient develops hyperlipidemia.
- Some individuals have allergies to components of intravenous (IV) lipid solutions. Discontinue lipids immediately if the patient shows signs of allergic response (dyspnea, cyanosis, flushing, sweating, dizziness, headache, back or chest pain, nausea, or vomiting).

Use of Honey and Radiation

- Care should be taken to use pasteurized honey in the immunocompromised patient population to reduce risk of infection and food borne illness.
- Care should be taken by patients with diabetes or impaired glucose metabolism to account for any carbohydrate provided by the honey consumed.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Use of high protein diets may be contraindicated in patients with hepatic disease and renal disease.
- Clinical judgment is critical. Careful consideration should be given to the application of these guidelines for patients receiving hospice, palliative care, or those with significant medical co-morbidities.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These nutrition practice guidelines are meant to serve as a general framework for handling clients with particular health problems. It may not always be appropriate to use these nutrition practice guidelines to manage clients because individual circumstances may vary. For example, different treatments may be appropriate for clients who are severely ill or who have co-morbid, socioeconomic, or other complicating conditions. The independent skill and

judgment of the health care provider must always dictate treatment decisions. These nutrition practice guidelines are provided with the express understanding that they do not establish or specify particular standards of care, whether legal, medical, or other.

- While the guideline represents a statement of best practice based on the latest available evidence at the time of publishing, they are not intended to overrule professional judgment. Rather, they may be viewed as a relative constraint on individual clinician discretion in a particular clinical circumstance.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The publication of this guideline is an integral part of the plans for getting the American Dietetic Association Medical Nutrition Therapy (ADA MNT) evidence-based recommendations on oncology to all dietetics practitioners engaged in, teaching about, or researching oncology as quickly as possible. National implementation workshops at various sites around the country and during the ADA Food Nutrition Conference Expo (FNCE) are planned. Additionally, there are recommended dissemination and adoption strategies for local use of the *ADA Oncology Evidence-Based Nutrition Practice Guideline*.

The guideline development team recommended multi-faceted strategies to disseminate the guideline and encourage its implementation. Management support and learning through social influence are likely to be effective in implementing guidelines in dietetic practice. However, additional interventions may be needed to achieve real change in practice routines.

Implementation of the Oncology guideline will be achieved by announcement at professional events, presentations and training. Some strategies include:

- **National and Local Events** – State dietetic association meetings and media coverage will help launch the guideline
- **Local Feedback Adaptation** – Presentation by members of the work group at peer review meetings and opportunities for continuing education unites (CEUs) for courses completed
- **Education Initiatives** – The guideline and supplementary resources are freely available for use in the education and training of dietetic interns and students in approved Commission on Accreditation of Dietetics Education (CADE) programs
- **Champions** – Local champions will be identified and expert members of the guideline team will prepare articles for publications. Resources are provided that include PowerPoint presentations, full guidelines, and pre-prepared case studies.
- **Practical Tools** – Some of the tools that will be developed to help implement the guideline include specially designed resources such as clinical algorithms, a pocket guide, slide presentation, training and tool kits

Specific distribution strategies include:

Publication in Full – The guideline will be available electronically at the ADA Evidence Analysis Library website (www.adaevidencelibrary.com) and will be announced to all the dietetic practice groups. The ADA Evidence Analysis Library will also provide downloadable supporting information and links to relevant position papers.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American Dietetic Association (ADA). Oncology evidence-based nutrition practice guideline. Chicago (IL): American Dietetic Association (ADA); 2007 Oct. Various p. [46 references]

ADAPTATION

The levels of evidence was based on the grading system from: Greer N, Mosser G, Logan G, Wagstrom Halaas G. *A practical approach to evidence grading. Jt Comm. J Qual Improv.* 2000; 26:700-712. In September 2004, The American Dietetic Association (ADA) Research Committee modified the grading system to this current version.

The grades of recommendation were adapted by the American Dietetic Association (ADA) from the American Academy of Pediatrics, *Classifying Recommendations for Clinical Practice Guideline, Pediatrics.* 2004;114;874-877.

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2007 Oct

GUIDELINE DEVELOPER(S)

American Dietetic Association - Professional Association

SOURCE(S) OF FUNDING

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GUIDELINE COMMITTEE

Oncology Evidence-Based Guideline Workgroup

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

In the interest of full disclosure, American Dietetic Association (ADA) has adopted the policy of revealing relationships workgroup members have with companies that sell products or services that are relevant to this topic. Workgroup members are required to disclose potential conflicts of interest by completing the ADA Conflict of Interest Form. It should not be assumed that these financial interests will have an adverse impact on the content, but they are noted here to fully inform readers.

None of the work group members listed above disclosed potential conflicts of interest.

GUIDELINE STATUS

This is the current release of the guideline.

The guideline will undergo a complete revision every three to five years.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [American Dietetic Association Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Executive summary of recommendations. Chicago (IL): American Dietetic Association; April 2008. Available from the [American Dietetic Association Web site](#).

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on November 7, 2008. The information was verified by the guideline developer on December 9, 2008.

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