Evidence Based Practice Guidelines for Nutritional Management of Cancer Cachexia

September 2005

Table of Contents

Introduction

Objective and search strategy
The purpose of these guidelines is to provide dietitians in Australia with a user-friendly summary of the evidence to support the nutritional management of adult patients with cancer cachexia. This best available evidence is presented and used as a basis for providing recommendations about clinical practice.

The relevant articles were identified by electronic database searches (up to and including April 2005). The search strategy is described in Appendix 1. The reference lists of relevant articles were also hand searched for any additional studies. In areas where cachexia-specific data is lacking, results from studies of other groups of patients with cancer have been included, and identified as such.

The strength of the evidence was assessed using the level of evidence rating system recommended by the NHMRC publications *A Guide to the Development, Implementation and Evaluation of Clinical Practice Guidelines* (1999). A table was developed to collate the evidence for screening, assessment, intervention and monitoring and evaluation against key outcome indicators. Levels of evidence, quality of study design, the strength of the effect and relevance to practice were considered in ranking the evidence.

The evidence rating system used in the guidelines are as follows:

Level I Evidence obtained from a systematic review of all relevant randomised controlled trials

Level II Evidence obtained from at least one properly designed randomised controlled trial

Level III-1 Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method)

Level III-2 Evidence obtained from comparative studies with concurrent control and allocation not randomised (cohort studies), case-control studies, or interrupted time series with a control group

Level III-3 Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel group

Level IV Evidence obtained from case studies, either post-test or pre- and post-test.

For intervention studies, Level I is recommended as the gold standard. Clinical nutrition studies are difficult to complete in a blinded fashion and often the group most likely to benefit from the intervention is excluded for ethical reasons. For these reasons, recommendations based on lower levels of evidence but with strong quality of design, strength of effect and relevance has been included.

Guideline Development and Consultation Process
A Steering Committee of dietitians with research expertise in nutritional management of cancer cachexia and evidence based guideline development produced the first draft of the clinical practice guidelines. The draft was modelled on other guidelines developed for the nutritional management of disease. A workshop of dietitians was convened at the 22nd National Conference of the Dietitians Association of Australia in May 2004 to consider the draft guidelines and provide peer review. Participants evaluated the guidelines using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument (The AGREE Collaboration). Participant feedback from the workshop was incorporated into a second draft. The second draft of the guidelines was presented at a workshop in Perth in November 2004, where again evaluation was completed using the AGREE tool. Participant feedback from the workshop was incorporated into the third draft. A statistician was consulted to clarify issues related to levels of evidence and incorporation of evidence from post –hoc analyses of randomised trials. The third draft has undergone additional peer, expert and consumer review. It has been distributed to previous workshop participants, DAA oncology experts, DAA oncology interest groups, international dietitians who had expressed an interest in participation, oncologists, nurses, other professionals working in the area of cancer and consumers for additional comment. A list of contributing organisations and individuals is found in appendix 7. Participant feedback was incorporated into a final draft which has been submitted to the DAA Practice Advisory Committee for endorsement.

Use of Guidelines
This document is a general guide to appropriate practice to be followed only subject to the dietitian's judgement in each individual case. The guidelines are designed to provide information to assist decision-making and are based on the best information available at the date of compilation. These guidelines for practice are provided with the express understanding that they do not establish or specify particular standards of care, whether legal, medical or other.

Editorial Independence

The guidelines have been developed without the assistance of external funding. Articles were evaluated for levels of evidence by members of the steering committee other than the article author. Steering committee conflict of interest declarations are provided in Appendix 8. The workshops conducted in 2004 at the DAA Conference in Melbourne and Perth were externally sponsored. The views or interests of the workshop sponsors have not influenced the final recommendations.

Review Process

The guidelines should be reviewed every three years to ensure they remain current. Responsibility for review lies with the Cancer Cachexia Steering Committee. Next Review Date: 2008.

Cancer Cachexia Steering Committee

NAME & POSITION	PHONE	EMAIL	MEMBER FROM
Adjunct A/Prof Judy Bauer Nutrition Services Manager The Wesley Hospital Medical Research Fellow Wesley Research Institute, QLD	(07) 3232 7918	judithba@wesley.com.au	Dec, 2003
A/Prof Susan Ash School of Public Health Queensland University of Technology, QLD	(07) 3864 3524	s.ash@qut.edu.au	Dec, 2003
Ms Wendy Davidson Dietitian Nutritionist Princess Alexandra Hospital, QLD	(07) 3240 2486	wendy_davidson@health.qld.gov.au	Dec, 2003
Ms Jan Hill Dietitian Nutritionist Royal Brisbane & Women's Hospital, QLD	(07) 3636 7997	Jan_Hill@health.qld.gov.au	Aug, 2004
Dr Elisabeth Isenring NHMRC Post Doctoral Research Fellow Flinders University, SA	(08) 8204 6303	Elisabeth.Isenring@flinders.edu.au	Aug, 2004
Dr Marina Reeves Senior Research Officer Queensland Cancer Fund, QLD	(07) 3258 2322	Mreeves@qldcancer.com.au	Aug, 2004
Ms Teresa Stock Dietitian Nutritionist Royal Brisbane & Women's Hospital, QLD	(07) 3636 7997	Teresa_Stock@health.qld.gov.au	Aug, 2004

2. Evidence Based Practice Guideline Framework

The guidelines have used a combination of the nutrition care process for dietetic professionals (Hakel-Smith & Lewis, 2004) and an outcomes model of care (Splett, 1996) as an organising framework. The stages the nutrition care process are:

- Appropriate access to nutrition care (Nutrition Screening; Nutrition Assessment; Collection of evidence)
- Quality Nutrition Care - Nutrition intervention (Establishing goals; Prescription and implementation)
- Nutrition monitoring and evaluation - Outcomes (Measure and evaluate outcomes)

Key clinical questions have been developed for each stage of the process. Although the nutrition care process is common to the nutritional management of many clinical conditions, the questions developed and the outcomes measured are specific to the nutritional management of cancer cachexia.

Nutrition Care Process	**Clinical Questions Related to Stage of Care Process**
Appropriate Access to Care • **Nutrition Screening** • **Nutrition Assessment**	How should patients be identified for referral to the dietitian in order to maximise nutritional intervention opportunities? How should nutritional status be assessed?
↓	
Quality Nutrition Care • **Nutrition intervention** o **Establishing goals** o **Nutrition prescription** o **Implementation**	What are the goals of nutrition intervention for patients with cancer cachexia? What is the nutrition prescription to achieve these goals? Should eicosapentaenoic acid be included in the prescription? What are effective methods of implementation to ensure positive outcomes?
↓	
Nutrition Monitoring and Evaluation • **Measure and Evaluate Outcomes** o **Intermediate** o **Clinical/Cost/Patient**	Does nutrition intervention improve outcomes in patients with cancer cachexia?

3. Summary of Evidence Based Statements

The evidence based statements are listed under headings described in the nutrition care process

	Level of Evidence	Study
1.Access to Appropriate Care		
Nutrition Screening		
How should patients be identified for referral to the dietitian in order to maximise nutritional intervention opportunities?		
The Malnutrition Screening Tool (MST) is an effective screening tool for identifying nutritional risk in cancer patients.	III-3	Ferguson et al, 1999b
Nutrition Assessment		
How should nutritional status be assessed?		
Subjective Global Assessment (SGA) is a valid method of assessing nutritional status in patients with cancer cachexia	IV	Bauer & Capra, 2005
The scored Patient Generated Subjective Global Assessment (PG-SGA) is a valid method of assessing nutritional status in patients with cancer cachexia	III-3	Bauer & Capra, 2005 Read et al, 2005
Bioelectrical impedance analysis is not suitable for body composition measurement in individual patients with cancer cachexia	III-3	Simons et al, 1995 Bauer & Capra, 2005
2. Quality Nutrition Care		
Nutrition Intervention		
Establishing goals		
What are the goals of nutrition intervention for patients with cancer cachexia?		
Weight stabilisation is an appropriate goal for patients with cancer cachexia	III-2	Davidson et al, 2004
Nutrition Prescription		
What is the nutrition prescription to achieve these goals?		
Energy and protein requirements for weight stabilisation are approximately 120 kJ/kg/d and 1.4 g protein/kg/d in patients with cancer cachexia receiving supportive care	III-2	Davidson et al, 2004
Energy and protein requirements for weight stablisation are approximately 120 kJ/kg/d and 1.4 g protein/kg/d in patients with cancer cachexia receiving chemotherapy	IV	Bauer & Capra, 2005
Weight stable patients have a higher energy intake than weight losing patients in patients with cancer cachexia receiving supportive care	III-2	Davidson et al, 2004
Well-nourished patients with advanced cancer have higher energy and protein intakes compared to malnourished patients with advanced cancer	IV	Bruera et al, 1984
Should EPA be included in the prescription in patients with cancer cachexia?		
The prescription of EPA improves outcomes in patients with cancer cachexia	NHMRC Grade of Recommendation C – Body of evidence provides some support for recommendation but care should be taken in its application	
Implementation		
What are effective methods of implementation to ensure positive outcomes?		
Compliance with a nutrition prescription of 1.5 cans/d of a high protein energy supplement ± EPA does not reduce total food intake in patients with cancer cachexia receiving supportive care	III-2	Bauer et al, 2005
Consumption of high protein energy supplement enriched with EPA does not reduce total food intake in patients with cancer cachexia receiving chemotherapy	IV	Bauer & Capra, 2005
Frequent clinician contact (minimum fortnightly) improves clinical outcomes in patients with cancer cachexia.	III-3	Moses et al, 2004 Bauer & Capra, 2005
3. Nutrition Monitoring and Evaluation		
Measure and Evaluate Outcomes		
Does nutrition intervention improve outcomes in patients with cancer cachexia?		
Nutrition intervention improves outcomes in patients	NHMRC Grade of Recommendation C –	

with cancer cachexia	Body of evidence provides some support for recommendation but care should be taken in its application

4. Cancer Cachexia Background

Cancer Cachexia Definition

The term cancer cachexia is derived from the Greek words kakos and hexis meaning poor condition. Cachexia has been defined as a syndrome characterised by the progressive loss of lean tissue and body fat, and losses are often in excess to that explained by the associated anorexia. There are often additional metabolic derangements, including anaemia, acute phase protein response and alterations in plasma lipid profile (Moldawer et al, 1997). The development of cachexia is common in people with solid tumours such as pancreatic, lung, gastric and colorectal cancer.

Weight loss in cancer cachexia is different from the weight loss of starvation or anorexia. This is due to accelerated loss of skeletal muscle in relation to adipose tissue, presence of pro-inflammatory cytokines and prolonged acute phase protein response (APPR) that contributes to increased resting energy expenditure and weight loss (Tisdale, 1996). Patients with cancer cachexia experience anorexia, early satiety, weakness, sarcopenia, fatigue, anaemia and severe weight loss. In starvation more than three-quarters of the weight lost is from body fat and only a small amount from muscle. In cancer cachexia, weight loss arises equally from loss of muscle and fat (Cohn et al, 1981).

Diagnostic Criteria

There are no definitive methods for diagnosis of cancer cachexia. Clinical signs of anorexia and weight loss of $\geq$ 5% over 6 months in patients diagnosed with cancer would be expected but clinical judgement is required. Weight loss due to mechanical obstruction, treatment or side effects, which would be expected to resolve once the obstruction is bypassed/removed or treatment ceased should not be classified as cachexia. These patients still require nutrition intervention but the focus of these guidelines is on cancer cachexia.

Patient Target Group

Any adult patient with cancer fulfilling the diagnostic criteria for cachexia.

Overview

The majority of cancer patients experience weight loss as their disease progresses and in general, weight loss is a major prognostic indicator of poor survival and impaired response to cancer treatment (DeWys et al, 1980). The incidence of malnutrition amongst patients with cancer has been estimated at between 40 – 80% (Ollenschlager et al, 1991; Kern et al, 1988). The prevalence of malnutrition depends on the tumour type, location, stage and treatment (Shike, 1996). The consequences of malnutrition may include an increased risk of complications, decreased response and tolerance to treatment, a lower quality of life, reduced survival and higher health-care costs (Grant et al, 1994; Ottery, 1996; Nitenberg et al, 2000). Cancer cachexia has been implicated in the deaths of 30 to 50% of all cancer patients, as many die from the wasting associated with the condition (Palomares et al, 1996).

The causes of weight loss in patients with cancer are multifactorial and may be due to symptoms reducing intake, treatment related or mechanical obstruction, or cachexia. Symptoms such as anorexia, depression, anxiety, fatigue, early satiety and pain can result in a decreased appetite and food intake. Cancer treatment may result in weight loss, for example surgery (malabsorption), radiotherapy (nausea, pain, diarrhoea, mucositis), and chemotherapy (nausea, vomiting, diarrhoea, mucositis). Weight loss may be due to mechanical obstruction caused by the cancer itself, such as obstruction of the oesophagus causing swallowing problems and reduced intake. Appropriate nutrition support provided during radiotherapy can help to overcome some of the nutrition impact symptoms and help patients to maintain weight compared with standard practice where patients continued to lose weight during radiotherapy treatment (Isenring et al, 2004b). However if the weight loss is due to cachexia, it may not be reversible because host intermediary metabolism (carbohydrate, protein and lipid metabolism) is abnormal, limiting the success of nutrition intervention (De Blaauw et al, 1997).

Numerous drug therapies (eg. megestrol, steroids) have been trialled in patients with cancer cachexia to stimulate appetite or attenuate metabolic changes. Several trials with synthetic progesterone agents have demonstrated a beneficial influence on weight, however this is largely due to an increase in fat mass (Chen et al, 1997; Simons et al, 1998; McQuellon et al, 2002). Evaluation of pharmacotherapies is beyond the scope of these guidelines.

5. Evidence Based Statements, Clinical Questions, Practice Recommendations and Tips

5.1 Appropriate Access to Care - Nutrition Screening and Assessment

Nutrition Screening

In Australia, hospital inpatients are generally seen by dietitians as a result of referrals by medical or nursing staff (Ferguson et al, 1998). Studies have found the prevalence of malnutrition to be similar between those patients who were referred to a dietitian by medical staff and those who were not referred (Banks, 1995, Christensen et al, 1985). It is recommended that in addition to referrals by medical staff, nutrition screening be performed on admission to hospital or in the outpatient setting during the planning stages of commencing anti-cancer therapies.

Nutrition screening is the process of identifying patients with characteristics commonly associated with nutrition problems that may require comprehensive nutrition assessment (American Dietetic Association (ADA), 1994). The purpose of nutrition screening is to quickly identify clients who are malnourished or at risk of becoming malnourished who would benefit from nutrition support and prioritise resources to those clients who most need nutrition support. According to the ADA (1994), an effective nutrition screening tool should be:

- Simple, quick, reliable, valid and inexpensive
- Easily administered with minimal nutritional expertise
- Applicable to most patients and designed to incorporate only routine data and tests available on admission

Many nutrition screening tools have been developed to identify clients at risk of malnutrition in the acute care setting and the community. Problems identified with numerous published nutrition screening tools include requiring specialised nutrition knowledge, biochemical parameters that may not be immediately available, requiring complex calculations or not being evaluated in terms of reliability or validity (Ferguson, 1998; Jones 2002). A number of reliable and valid nutrition screening tools have been recently published:

- Malnutrition Screening Tool – Ferguson et al, 1999a, 1999b (Appendix 3)
- Malnutrition Universal Screening Tool – British Association of Parenteral and Enteral Nutrition - Stratton et al, 2004
- Mini Nutrition Assessment-Short Form – Rubenstein et al, 2001
- Nutrition Risk Screening – Kondrup et al, 2003.

When selecting an appropriate nutrition screening tool, it is imperative that the tool has been validated in the client population in which it is to be applied. The Malnutrition Screening Tool (MST) is a valid screening tool for identifying nutrition risk in patients with cancer (Ferguson et al, 1999b). No studies have been identified that report nutrition screening in patients with cancer cachexia.

Evidence Based Statements

The Malnutrition Screening Tool (MST) is an effective screening tool for identifying nutritional risk in patients with cancer.	Level III-3	Ferguson et al, 1999a,b

How should patients be identified for referral to the dietitian in order to maximise nutritional intervention opportunities?

Practice Recommendation

Identify "at risk" patients in oncology wards and outpatient clinics using a nutrition screening tool such as the Malnutrition Screening Tool that has been validated for oncology patients.

PRACTICE TIPS:

1. Nutrition assistants, administration or nursing staff may implement the MST.
2. The MST can be incorporated into admission forms or patient information sheets.
3. Repeat nutrition screening during treatment at least fortnightly for patients initially screened at low risk.
4. If a patient has been referred to the dietitian by other methods eg direct referral from medical oncologist, nutrition screening is unnecessary – proceed to nutrition assessment.

Nutrition Assessment

Nutrition assessment is a comprehensive approach to defining nutritional status using medical, nutrition and medication histories, physical examination, anthropometric measurements and laboratory data (ADA, 1994). Nutrition assessment parameters may be affected by non-nutritional factors resulting in poor sensitivity and specificity (Jeejeebhoy, 2000). No single parameter is sufficiently sensitive and specific to determine nutritional status and a combination of parameters should be used (Gibson, 1990). Several nutrition assessment tools have been published which use a combination of parameters.

Subjective global assessment
Subjective global assessment (SGA) determines nutritional status on the basis of a medical history (weight change, dietary intake change, presence of gastrointestinal symptoms that have persisted for greater than two weeks, functional capacity) and physical assessment (evidence of loss of subcutaneous fat, muscle wasting, oedema or ascites). The features are combined subjectively into an overall or global assessment where patients are rated as being well nourished (SGA A), moderately or suspected of being malnourished (SGA B) or severely malnourished (SGA C) (Detsky et al, 1987).

Scored Patient-Generated Subjective Global Assessment
The scored Patient-Generated Subjective Global Assessment (PG-SGA) is an adaptation of SGA specifically developed for use in the cancer population (Ottery, 2000). It contains additional questions regarding short term weight loss, a more extensive range of nutrition impact symptoms and for each component of the PG-SGA, points (0-4) are awarded depending on the impact on nutritional status. Typical scores range from 0-47 with a higher score reflecting a greater risk of malnutrition. The PG-SGA score has been correlated with a number of objective parameters (% weight loss, body mass index (BMI)), measures of morbidity (survival, length of stay, quality of life), has a high degree of inter-rater reproducibility and high sensitivity and specificity when compared with other validated nutritional assessment tools (Ottery, 1996; Persson *et al*, 1999; Ottery *et al*, 2002; Bauer et al, 2002; Isenring et al, 2003; Read et al, 2005). A change in score of approximately nine points is required to move one global rating category (Isenring et al, 2003). The PG-SGA score may be more sensitive than the global rating to demonstrate improvement or deterioration in nutritional status (Bauer, 2002). The PG-SGA has been recommended as the nutrition assessment tool for patients with cancer by the Oncology Nutrition Dietetic practice group of the American Dietetic Association (McMallum & Polisena, 2000). In patients with cancer cachexia, two studies report nutritional status based on the global categorisation and the PG-SGA score (Bauer & Capra, 2005; Read et al, 2005).

Biochemistry Assessment
Biochemistry may be influenced by disease and treatment and therefore it is important to use clinical judgement when interpreting values. For example, serum albumin may be low due to the acute phase protein response. However, serum albumin has been shown to be an independent prognostic variable for survival in patients with cancer (Evans et al, 1987). Patients with raised serum C-reactive protein levels have lower energy intake than those with normal levels (Wigmore et al, 1997) and there is some evidence that resting energy expenditure may be increased in these patients (Falconer et al, 1994).

Anthropometric Assessment
A variety of techniques are available to measure body composition such as Dual Energy X-ray Absortiometry (DEXA), anthropometric measurements (eg triceps skinfold thickness (TSF); corrected arm muscle area (CAMA)), deuterium and bioelectrical impedance analysis (BIA). DEXA and deuterium are expensive methods that are impractical in the clinical setting but may be of use in research studies. Serial anthropometric measurements may be useful to monitor change however accredited training in anthropometry is recommended. BIA measures tissue conductivity and can be used to assess total body water (TBW) from which fat free mass (FFM) can be calculated. It is important that a BIA prediction equation is used that has been validated in the population under study (Heymsfield et al, 1996). Studies examining the validation of BIA in cancer patients are limited (Simons et al, 1995, 1999; McMillan et al, 2000; Isenring et al, 2004; Bauer et al, 2005) and no equation has been developed or validated in patients with cancer cachexia. At a group level, these equations are suitable to predict TBW in patients with cancer cachexia but for an individual, they are unsuitable for use (Bauer et al, 2005).

Functional Assessment
Tools used to assess functional status include Karnofsky Performance Status and Eastern Cooperative Oncology Group (ECOG). A variety of tools have been developed and validated to measure quality of life such as the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 (Aaronsen et al 1993), Functional Assessment of Cancer Therapy (FACT) (Cella et al1993) and the Short Form Health Survey (SF 36)(Ware et al 1992). In patients with cancer, the PG-SGA score has been shown to be associated with quality of life (EORTC-QLQC30), and therefore can be used to predict the direction and magnitude of change in quality of life (Isenring et al, 2003).

Evidence Based Statements

Subjective Global Assessment (SGA) is a valid method of assessing nutritional status in patients with cancer cachexia	IV	Bauer & Capra, 2005

The scored Patient-Generated Subjective Global Assessment (PG-SGA) is a valid method of assessing nutritional status in patients with cancer cachexia	III-3	Bauer & Capra, 2005 Read et al, 2005
Bioelectrical impedance analysis is not suitable for body composition measurement in individual patients with cancer cachexia	III-3	Simons et al, 1995 Bauer & Capra, 2005

How should nutritional status be assessed?

Practice Recommendation

1. Use the scored Patient Generated - Subjective Global Assessment (PG-SGA) as the nutrition assessment tool in patients with cancer cachexia.

PRACTICE TIPS:

Suggested Parameters to be used in assessment	
Nutrition Assessment Tool	PG-SGA: Record both the global rating (SGA-A well nourished, SGA-B moderately malnourished, SGA-C severely malnourished) and the PG-SGA score (1-47), which need to be determined independently. The diagnosis of malnutrition is based on the global rating. Nutrition impact symptoms are a major component of the PG-SGA score. Some clients with cancer may have a high score due to presence of multiple nutrition impact symptoms yet still be well nourished. The score is more sensitive than the global rating to demonstrate improvement or deterioration in nutritional status and hence can be used when the global rating has not changed. The lower the PG-SGA score, the better the client's nutritional status.
Anthropometry	Record height, body weight, body mass index (BMI) Due to the prevalence of overweight and obesity, clients with cachexia may have a BMI>25 kg/m^2 yet still be moderately or severely malnourished due to weight loss, reduced intake, functional capacity, presence of nutrition impact symptoms, etc. Determine lean body mass if technology available -deuterium, DEXA, bioelectrical impedance (BIA) – group level only Record anthropometric measurements - TSF , CAMA
Dietary intake	Assess dietary intake, especially energy and protein, quantitatively Determine use of vitamin/mineral supplements and complementary medicines Assess dietary restrictions and beliefs, texture of diet and other barriers to food intake, hydration
Symptoms/side effects	GI symptoms (nausea, vomiting, constipation, diarrhoea, steatorrhea, early satiety) Appetite and taste changes Presence of pain Mood change
Functional status and quality of life	Determine functional status and level of fatigue, using PG-SGA, Karnofsky Performance Scale or Eastern Co-operative Oncology Group. PG-SGA score can be used as surrogate measure of quality of life
Biochemistry	Determine serum albumin C reactive protein Haemoglobin Blood glucose
Medications	Review medications and note if patients is taking analgesics, enzymes, laxatives, antiemetics, alternative therapies

5.2 Quality Nutrition Care – Nutrition Intervention

Nutrition intervention is the second stage of the clinical judgements made in the nutrition care process. The key aspects of nutrition intervention are establishing the goals of treatment, determining the nutrition prescription and the implementation of the nutrition care. The success or otherwise of nutrition intervention depends equally on these components (Capra et al, 2002).

Establishing goals

Having identified the nutrition problem by assessing and interpreting the evidence and data collected about the patient, a judgement about the goals of treatment must be made. Established goals provide the criteria to be measured in the outcome evaluation step, where effectiveness of the nutrition intervention is evaluated (Hakel-Smith, 2004).

When discussing nutrition intervention options with patients and carers, it is important to present realistic potential outcomes. The goals and outcomes of nutrition intervention will be dependent on patient's diagnosis and prognosis. If goal requirements cannot be achieved with oral intake, alternative means of nutrition support should be considered.

Refer to guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients from the American Society of Parenteral and Enteral Nutrition (2002).

Traditionally, treatment has focussed on weight gain as the goal of nutrition intervention. Some studies (Evans et al, 1987; Bruera et al, 2003; Jatoi et al, 2004) have failed to show a positive effect of nutrition intervention when weight gain was the outcome. Other studies using weight stabilisation as an outcome of nutrition intervention have shown positive effects. Weight losing patients with advanced gastrointestinal and non-small cell lung cancer whose weight stabilises have a longer survival and improved quality of life than those who continue to lose weight (Andreyev et al, 1998; Davidson et al, 2004; Ross et al, 2004). Weight stabilisation is an appropriate goal for weight losing cancer patients provided that life expectancy is at least two months (Davidson et al, 2004).

Continue to reassess stage of treatment and disease, and whether any change to palliative care status. Determine level of support from the patients General Practitioner, carer and palliative care team. When a patient is having palliative treatment or palliative supportive care at end stage of disease, intensity of dietary intervention may need to be adapted. Liaise with patient/family/carers and medical team to determine level of intervention required. Unnecessary dietary restrictions can be relaxed (e.g. cholesterol lowering modifications). Discuss treatment with patient for indication of satisfaction with intensity of care.

If end stage, the dietitian may advocate for patient with carer or family to reduce intensity of dietary treatment. The desired outcomes are maximising patient comfort and maintaining quality of life. In many cases this may mean a patient will not meet full nutrition requirements, for example if tube feeding is refused or supplement drinks are not liked. Each case should be assessed individually and with full discussion with the team to determine new goals of care. Patients in the final weeks of life are unlikely to be able to maintain their lean body mass. Any weight gain that does occur at this time is likely to be due to fluid retention. For comfort measures refer to DAA paper: Nutrition priorities in palliative care of oncology patients (Aust J Nutr Diet 1994;51:91-92).

Evidence Based Statements

Weight-losing patients with cancer cachexia who stabilise their weight have greater quality of life and survival duration than those who continue to lose weight.	III-2	Davidson et al, 2004

What are the goals of nutrition intervention for patients with cancer cachexia?

Practice Recommendation

1. Weight stabilisation is an appropriate goal for patients with cancer cachexia

PRACTICE TIPS:

1. Nutrition intervention goals should be individualised taking into consideration prognosis, psychosocial issues and the patient's wishes.

Goals of Nutrition Intervention	
Measure	**Goal**
PG-SGA	Reduce or maintain PG-SGA score
Anthropometry: • Weight • skin folds, CAMA (if accredited in measuring skin folds) • DEXA, deuterium (if available)	Stabilise weight and lean body mass
Dietary intake	Achieve appropriate current energy and protein intake
Symptoms or side effects identified in the PG-SGA	Minimise symptoms which impact on nutritional intake and status
Karnofsky Performance Scale or ECOG PG-SGA as surrogate measure of quality of life	Improve or maintain functional status score Improve or maintain quality of life
Biochemistry • Serum albumin • C reactive protein • Haemoglobin • Blood glucose	Use to interpret current clinical condition
Medications	Ensure symptoms are being medically managed
Other • Assess need for texture modification of diet or alternative nutrition support • Assess social situation and need for education of carers/family/other social support e.g Meals-on-Wheels	Ensure appropriate nutrition support is provided Meet energy and protein requirements

Nutrition Prescription

- **Protein and Energy Requirements**

Measurement of energy expenditure via indirect calorimetry is the most accurate method for determining individuals' energy requirements. Energy expenditure of patients with cancer has been shown to vary greatly (Staal-van den Brekel et al, 1997; Jatoi et al, 2001; Reeves, 2004). Treatment and disease stage may alter metabolic requirements over time. Energy intakes in excess of 120 kJ/kg/day have been needed for weight maintenance in some studies of cancer patients (Davidson et al, 2004; Ollenschlager et al, 1992; Bauer & Capra 2005). Protein intake is often reduced as the result of taste alterations, poor appetite and fatigue. Protein requirements for advanced cancer patients have not been elucidated. However protein intake in excess of 1.4 g/kg/day have been required for weight maintenance in some studies of cancer patients (Davidson et al, 2004; Bauer & Capra, 2005).

- **Eicosapentaenoic acid**

A novel approach to the nutrition intervention in patients with cancer cachexia has been the prescription of pharmacological doses of eicosapentaenoic acid (EPA), an omega-3 polyunsaturated fat. The major dietary sources of EPA in Australia are marine oils, seafood, meat and eggs with the average Australian intake at 0.056 g per day (Meyer, 2002, NHMRC, 1991). Studies in both animals and humans have indicated that EPA supplementation reduces production of pro-inflammatory cytokines such as interleukin-6, interleukin-1 and tumour necrosis factor and in cultured cancer cell lines increases cell death rate (Endres et al., 1989; Wigmore 1996; Tisdale and Beck, 1991; Caughey et al, 1996). Appendix 5 summarises studies in relation to EPA supplementation (EPA capsules and oral nutrition supplements) in patients with cancer. The results of studies of supplementation with EPA either in the form of capsules or high protein energy supplements enriched with EPA, are inconsistent. Although positive changes have been demonstrated in outcomes (improving energy and protein intake, body composition, performance status, quality of life) in patients with cancer cachexia receiving high protein energy supplements enriched with EPA in open trials (Level IV studies), in general these results have not been confirmed in randomised trials (Level II studies). Issues such as compliance with the prescription (Fearon et al, 2003), duration of intervention (Bruera et al, 2003), appropriate endpoints (Jatoi et al, 2004) and the treatment group (supportive care/chemotherapy/mixed therapy) are important to consider when evaluating study outcomes. A common weakness of the four randomised controlled trials investigating EPA is the limited discussion of dietetic involvement. Therefore whether or not patients received dietary counselling, the recommendations and frequency of contact were not documented and could also limit the efficacy of EPA or fish oil. Further studies in different patient groups with cancer are required.

A Cochrane review of the role of EPA in cancer cachexia is being undertaken in the UK and is scheduled for release in 2005. The Steering Committee has evaluated the role of EPA in cancer cachexia using a new grading system of recommendations recently released by NHMRC - *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines - Pilot Program 2005* (**www.nhmrc.gov.au/advice/consult.htm** - accessed 9/5/05). This grading system for recommendations has been developed as an interim measure to assist guideline developers in assessing the entire body of evidence and indicating the strength of each guideline recommendation.

Potential Risks EPA

The draft Nutrient Reference Values for Australia and New Zealand recommend acceptable macronutrient distribution ranges to reduce chronic disease whilst still enuring adequate micronutrient stats. The lower to upper ends of the recommended intake range for omega 3 fats (DHA:EPA:DPA) are 190 mg/day to 610 mg/day for men and 90 mg/day to 430 mg/day for women, where the upper end of the range is based on 90th percentile of current intake. (NHMRC, 2004.) The United States Food and Drug Administration has concluded that fish oil concentrate is Generally Recognised As Safe (GRAS) provided that combined intake of EPA and DHA from all added sources does not exceed 3 g/person/day. (http://www.cfsan.fda.gov/~rdb/opa-g105.html - accessed 16/5/05). Cancer patients consuming 6 g EPA/d have reported no adverse effects on platelet counts (Wigmore et al, 2000). No studies, however, have been conducted specifically on EPA in cancer patients who are using anticoagulants. It is therefore advisable to exercise caution with the use of EPA supplements in cancer patients on anticoagulant therapies such as warfarin. Use in such situations should be with the knowledge and approval of the patient's doctor. Large dose of fish oil can cause gastrointestinal side effects (Wigmore et al, 1996; Gogos et al, 1998). Cod liver and halibut liver oil are not suitable sources of EPA as the doses required could provide excess levels of Vitamin A. Fish oil products and supplements are not a major source of dietary mercury and there is no recommendation to restrict consumption because of mercury (www.foodauthority.nsw.gov.au/pregnancy.htm - accessed 15/5/05).

Complimentary and Alternative Therapy

Australian studies have shown that between 22%-52% of patients with cancer use complimentary or alternative therapy with up to $2.3 billion spent in 2000 (Begbie et al, 1996; Miller et al, 1998; MacLennan et al, 2002). Evaluation of complimentary or alternative therapy is beyond the scope of these guidelines – refer to The Cancer Council Australia's 2005 Position Statement on Complementary & Alternative Therapies.

Evidence based Statements

Energy and protein requirements for weight stabilisation are approximately 120 kJ/kg/d and 1.4 g protein/kg/d in patients with cancer cachexia receiving supportive care	III-2	Davidson et al, 2004
Energy and protein requirements for weight stablisation are approximately 120 kJ/kg/d and 1.4 g protein/kg/d in patients with cancer cachexia receiving chemotherapy	IV	Bauer & Capra, 2005
Weight stable patients have higher energy intake than weight losing patients in patients with cancer cachexia receiving supportive care	III-2	Davidson et al, 2004
Well-nourished patients with advanced cancer have higher energy and protein intakes compared to malnourished patients with advanced cancer	IV	Bruera et al, 1984

The prescription of EPA improves outcomes in patients with cancer cachexia		NHMRC Grade of Recommendation C – Body of evidence provides some support for recommendation but care should be taken in its application

What is the nutrition prescription to achieve these goals?

Practice Recommendations

1. Improving energy and protein intake remains the first step in nutrition intervention for weight losing cancer patients

2. If indirect calorimetry is unavailable, aim for an energy intake of approximately 120 kJ/kg/day.

3. Aim for a protein intake of approximately 1.4 g/kg/day.

Should eicosapentaenoic acid be included in the prescription?

Practice Recommendation

1. EPA can be considered as a component of nutrition intervention in cancer cachexia but patients should first be assessed for suboptimal symptom control or inadequate intake. If using EPA, aim for an intake of 1.4 – 2 g EPA/day which needs to be consumed for at least four weeks to achieve clinical benefit.

PRACTICE TIPS:

1. An individual's energy requirements are best determined by measurement of energy expenditure (e.g. indirect calorimetry), however in practice this is rarely available. Due to high variation in energy expenditure, use clinical judgement with respect to energy requirements taking into consideration age, treatment and treatment goals. Regular monitoring of intake and weight will determine whether energy needs are being met.
2. Prior to commencing nutrition support, assess the patient for risk of refeeding syndrome.
3. EPA: Potential sources include dietary intake, capsules or a high protein energy supplement enriched with EPA. To achieve 1.4 – 2 g EPA/day patients need to consume at least 8-11 capsules of fish oil (180 mg EPA/capsule), 300 - 400 g oily fish, 310-445ml of a high protein energy supplement enriched with EPA (0.45g EPA/100ml) or combination of these.

Nutrition Implementation

The implementation of dietetic care involves counselling of the patient and/or carers to maximise food intake and facilitation of optimal symptom control. Counselling, especially in conjunction with high protein energy supplements, has been shown to increase intake and attenuate weight loss in a range of cancer patients (Arnold et al 1989, Ollenschlager et al, 1992, McCarthy et al 1999, Ovesen et al, 1993, Isenring et al, 2004, Ravasco et al, 2005). A concern expressed by many patients is that consumption of high protein energy supplements may reduce their meal intake. In patients with cancer, high protein energy supplements have been shown to increase intake without negatively impacting on spontaneous food intake (Bauer & Capra, 2005; McCarthy and Weihofen, 1999). Prognosis, economic circumstances and client preferences need to be considered in decisions regarding supplement usage.

Nutrition counselling is effective both during phases of active treatment (chemotherapy and radiotherapy) and supportive care. Recommended time for initial consultation is 45-60 minutes and review consultation 15-30 minutes (Gillbreath et al, 1998). Recent studies in patients with cancer have demonstrated effective clinical outcomes with weekly to fortnightly dietetic intervention (Isenring et al, 2004; Ravasco et al 2005; Fearon et al, 2003; Moses et al, 2004; Ovesen et al, 1993; Bauer & Capra, 2005). Dietetic practice regarding the implementation of medical nutrition therapy in clients with cancer, however, varies considerably, often depending on resources available. Further research regarding innovative methods of nutrition implementation eg telephone counselling is required.

Evidence Based Statements

Compliance with a nutrition prescription of 1.5 cans/d of a high protein energy supplement ± EPA does not reduce total food intake in patients with cancer cachexia receiving supportive care	III-2	Bauer et al, 2005
Consumption of a high protein energy supplement enriched with EPA does not reduce total food intake in patients with cancer cachexia receiving chemotherapy	IV	Bauer & Capra, 2005
Frequent clinician contact (minimum fortnightly) improves clinical outcomes in patients with cancer cachexia.	III-3	Moses et al, 2004 Bauer & Capra, 2005

What are effective methods of implementation to ensure positive outcomes?

Practice Recommendations

1. Nutrition counselling assists cancer patients to optimise their intake.
2. High protein and energy supplements play a valuable role in improving intake and do not simply take the place of usual meals.
3. Regular nutrition intervention improves clinical outcomes.

PRACTICE TIPS:

1. Implementation of high protein, high energy dietary advice:
   - Discuss good sources of protein in the diet – meat, fish and poultry, and encourage with at least one serve a day. If vegan/vegetarian ensure adequate alternative sources of protein.
   - If protein intake is reduced due to taste changes emphasise good oral hygiene, encourage with alternative sources of protein – eggs, dairy, legumes and nuts, suggest marinating meats in juice or wine to disguise a bitter taste
   - For patients with chewing and swallowing difficulties, ensure protein in adequate in texture modified diets e.g. minced meats, pureed meat/chicken/fish, scrambled or poached eggs, mashed beans, peanut paste, lentil/bean soups
   - Encourage patients to consider high protein/energy supplements as an essential component of treatment.
   - Assess need for alternative nutrition support if oral intake inadequate and liaise with medical team regarding options available and discuss with patient.

2. Compliance issues with EPA to consider in implementation:
   - decreased appetite and nutrition impact symptoms → difficult to consume adequate quantities of fish, capsules or supplements;
   - capsules – number required, large size, side effects (burping, fishy aftertaste, tolerance);
   - high protein energy nutrition supplements enriched with EPA– ensure adequate quantity consumed each day, consider taste, consider cost;
   - need to develop gastrointestinal tolerance to fish oil and high protein energy supplements enriched with EPA – gradually increase dose.

3. Use the PG-SGA to identify barriers to food intake and facilitate optimal symptom control:
   - nausea, constipation, vomiting, diarrhoea, mouth sores, pain - liaise with medical and support team and instigate appropriate medical and nutrition treatment
   - taste changes, early satiety, aversion to smells - use strategies to manage these
   - dry mouth and/or swallowing problems - modify texture as required and liaise with other allied health professional support e.g. speech pathology.
   - The Cancer Councils in each state provide valuable patient resources describing the management of nutrition impact symptoms.

4. If patient is using complimentary or alternative therapies, provide appropriate information.

5.3 Nutrition Monitoring and Evaluation

Measure and Evaluate Outcomes – Intermediate and Clinical/Cost/Patient

Nutrition intervention may lead to a variety of outcomes. Intermediate outcomes include changes in dietary intake, symptoms, biochemistry, anthropometric measures or nutrition status. These changes will then impact upon and result in clinical, cost and patient outcomes. This includes morbidity and mortality, length of hospital stay, functional capacity or quality of life (NHMRC, 2000). A variety of outcomes have been demonstrated in nutrition intervention studies in patients with cancer. To date, in cancer cachexia, intervention studies have focused on using fish oil or EPA supplements in management of outcomes. Weight stabilisation may improve length and quality of life in patients with cancer cachexia (Davidson et al, 2004). The evidence based statements in relation to nutrition intervention are in Appendix 6. The body of evidence has been evaluated using the *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines - Pilot Program 2005*.

Evidence Based Statements

Nutrition intervention improves outcomes in patients with cancer cachexia	NHMRC Grade of Recommendation C – Body of evidence provides some support for recommendation but care should be taken in its application

Does nutrition intervention improve outcomes in patients with cancer cachexia?

Practice Recommendation

1. A range of outcomes can be measured in patients with cancer cachexia including protein and energy intake, appetite, weight, lean body mass, functional status, quality of life and survival.

2. Consumption of high protein energy supplement enriched with EPA over a period of at least 8 weeks improves intake, total energy expenditure and physical activity level and attenuates weight loss in patients with cancer cachexia.

3. There is conflicting evidence about whether EPA supplementation can improve quality of life, appetite, lean body mass, and survival. This may be due to studies not being conducted for long enough (at least 4 weeks) or because improvement rather than attenuation was the outcome goal.

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