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[Ash, Susan, Campbell, Katrina, MacLaughlin, Helen](#), McCoy, Ellen, Chan, Maria, Anderson, Kathryn, Corke, Karen, Dumont, Ruth, Lloyd, Lyn, Meade, Anthony, Montgomery-Johnson, Robyn, Tasker, Tracey, Thrift, Paulett, & Trotter, Bernadeen

(2006)

Evidence Based Practice Guidelines for the Nutritional Management of Chronic Kidney Disease.

Nutrition and Dietetics, 63(Supp 2), pp. 35-45.

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<https://doi.org/10.1111/j.1747-0080.2006.00100.x>

Title Page: as per Journal supplement

Supplement

**Evidence based practice guidelines for nutritional management of cancer cachexia
and evidence based guidelines for the nutritional management of chronic kidney
disease**

**Editor
Linda Tapsell etc**

Evidence Based Practice Guidelines for the Nutritional Management of Cancer Cachexia

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**EVIDENCE BASED PRACTICE GUIDELINES FOR NUTRITIONAL MANAGEMENT OF
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**EVIDENCE BASED PRACTICE GUIDELINES FOR THE NUTRITIONAL
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Introduction

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From the Editor

In recent years, leading health organisations have developed evidence-based guidelines to underpin management of health issues. The Dietitians Association of Australia (DAA) is committed to the promotion and enhancement of best practice in Dietetics in Australia and the publication of this supplement is a landmark effort in this regard. It will act as a useful resource for the continuing of competency standards as well as the credentialing process for the Accredited Practising Dietitians (APDs), Advanced APDs and Fellows professional development program.

The National Health and Medical Research Council (NHMRC) states that evidence based guidelines are needed “to improve the quality of health care, to reduce the use of unnecessary, ineffective or harmful interventions, and to facilitate the treatment of patients with maximum chance of benefit, with minimum risk of harm, and at an acceptable cost”¹ (p1). On a practical level, dietetic evidence-based practice guidelines will assist APDs to access, and more consistently utilise, the best available evidence and specialised treatment recommendations in an information-rich environment.

Through the work of the Practice Advisory committee (PAC), DAA has given its endorsement to the guidelines published here, there are others waiting in the wings reflecting years of invested time and effort by volunteer members. PAC developed guidelines for the endorsement process, provided mentors and education to development groups, and appraised guidelines in order to recommend endorsement by the DAA Board. The rigorous, transparent guideline development process reflects processes recommended by leading research bodies such as the NHMRC. Consultation processes involves a large number of people, ideally patients or support groups, peer group Dietitians, and other health professionals from relevant fields. In 2005 a format for guidelines publication was developed by the DAA National Office so that each set of guidelines published in the journal have a standard format that enables dietitians to readily access the same information quickly and easily.

The Cancer Cachexia were developed by an expert groups of Australian dietitians experienced in the area (Cancer Cachexia Steering Committee). The Chronic Kidney Disease guidelines represent the collaborative efforts of Australian and New Zealand dietitians (Australian New Zealand Renal Guidelines Taksforce) who summarized the nutrition elements of five sets of existing guidelines from leading international agencies.

The publication of these guidelines represent another milestone in the development of the Dietetics profession in Australia and New Zealand and we look forward to this as an ongoing exercise extending across the reach of practice, subject to continual update and review.

Linda C Tapsell PhD FDAA
Editor.

1. National Health and Medical Research Council. A guide to the development, implementation and evaluation of clinical practice guidelines. Canberra: Commonwealth of Australia; 1999.

EVIDENCE BASED PRACTICE GUIDELINES FOR NUTRITIONAL MANAGEMENT OF CANCER CACHEXIA

INTRODUCTION

Scope and Purpose

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 clinical questions were as follows:

- How should patients be identified for referral to the dietitian in order to maximise nutritional intervention opportunities?
- How should nutritional status be assessed?
- 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?
- Does nutrition intervention improve outcomes in patients with cancer cachexia?

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. The guidelines recommend intensive nutrition therapy. This has potential resource implications that may include additional staff, change to staff roles and increased use of high/protein energy supplements if they are considered. Therefore, in applying the guidelines these potential organisational and cost barriers need to be considered. 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.

Methods

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. Initial members of the guideline development team convened in December 2003 were Dr Judy Bauer (Chairperson - The Wesley Hospital, Brisbane), A/Prof Susan Ash (Queensland University of Technology, Brisbane) and Ms Wendy Davidson (Princess Alexandra Hospital, Brisbane). This group developed the initial draft and workshop presentation. Additional members of the team from August 2004 were Ms Jan Hill (Royal Brisbane & Women's Hospital, Brisbane), Ms Teresa Stock (Royal Brisbane & Women's Hospital, Brisbane), Dr Elisabeth Isenring (Flinders University, Adelaide) and Dr Marina Reeves (Queensland Cancer Fund, Brisbane).

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).¹⁸ Participant feedback from the workshop was incorporated into a second draft. The second draft of the guidelines was presented at a workshop for dietitians 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. At both workshops case studies were presented to demonstrate the use of the guidelines. A statistician was consulted to clarify issues related to levels of evidence and incorporation of evidence from post-hoc analyses of randomised trials.

The relevant articles were identified by electronic database searches (up to and including April 2005). The reference lists of relevant articles were also hand searched for any additional studies. In

areas where cachexia-specific data was lacking, results from studies of other groups of patients with cancer have been included, and identified as such.

The following search strategies were used for the electronic databases listed below. Details of the search results were retained by the guideline development team.

Search terms

Term 1	Cancer or neoplasm or carcinoma or tumour Cancer* or neoplasm* or carcinoma or tumo?r
Term 2	Cachexia or cachectic or weight loss or malnourished or wasting Cachex* or cachect* or (weight los*) or malnourished or wast*
Term 3	Nutrition or diet Nutrition* or diet*
Search	= Terms 1 and 2 and 3 Limited to adult humans Search updated with databases available April 2005
Electronic databases	The Cochrane Database of Systematic Reviews The Cochrane Central Register of Controlled Trials (CENTRAL) Medline Advanced 1950 – 2005/01 PubMed (to include early 2005 publications) - Cancerlit CINAHL (1982-current) Web of Science EMBASE Health Source: Nursing/Academic Edition Cancernet Cancer Spectrum Australasian Medical Index (AMI)

The strength of the evidence was assessed using the level of evidence rating system recommended by the National Health and Medical Research Council (NHMRC) publication *A Guide to the Development, Implementation and Evaluation of Clinical Practice Guidelines*.¹⁹ 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 is 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. ¹⁹

For intervention studies, Level I is recommended as the gold standard. It was felt that 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.

The guideline development team also used the *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines - Pilot Program*.²⁰ 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. The grades of recommendation are:

Level A	Body of evidence can be trusted to guide practice
Level B	Body of evidence can be trusted to guide practice in most situations
Level C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
Level D	Body of evidence is weak and recommendation must be applied with caution. ²⁰

The five components that are considered in judging the body of evidence are the volume of evidence, consistency of the results, potential clinical impact of the proposed recommendation, the generalisability of the body of evidence to the target population of the guideline and the applicability of the body of evidence to the Australian healthcare context. A recommendation cannot be graded as A or B unless the volume and consistency of the evidence components are both graded A or B.

Consultation process

The third draft underwent additional peer, expert and consumer review. It was 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. Participant feedback was incorporated into a final draft, which was endorsed by the DAA Practice Advisory Committee (September 2005) and the DAA Board (November 2005).

Review Process

The guidelines should be reviewed every three years to ensure they remain current. Responsibility for review lies with the guideline development team. Next Review Date: 2008.

Applicability

A number of workshops were held during the development stage to identify the applicability of the guidelines for dietitians in the practice area of cancer. These workshops included: the 22nd National Conference of the Dietitians Association of Australia in May 2004; and in Perth in November 2004. Once the guidelines had been endorsed a further workshop was held in Queensland in March 2006, sponsored by Queensland Health, for dietitians to apply the guidelines to particular case studies. Evaluation from all three workshops indicated that the guidelines were applicable for dietetic practice.

Editorial Independence

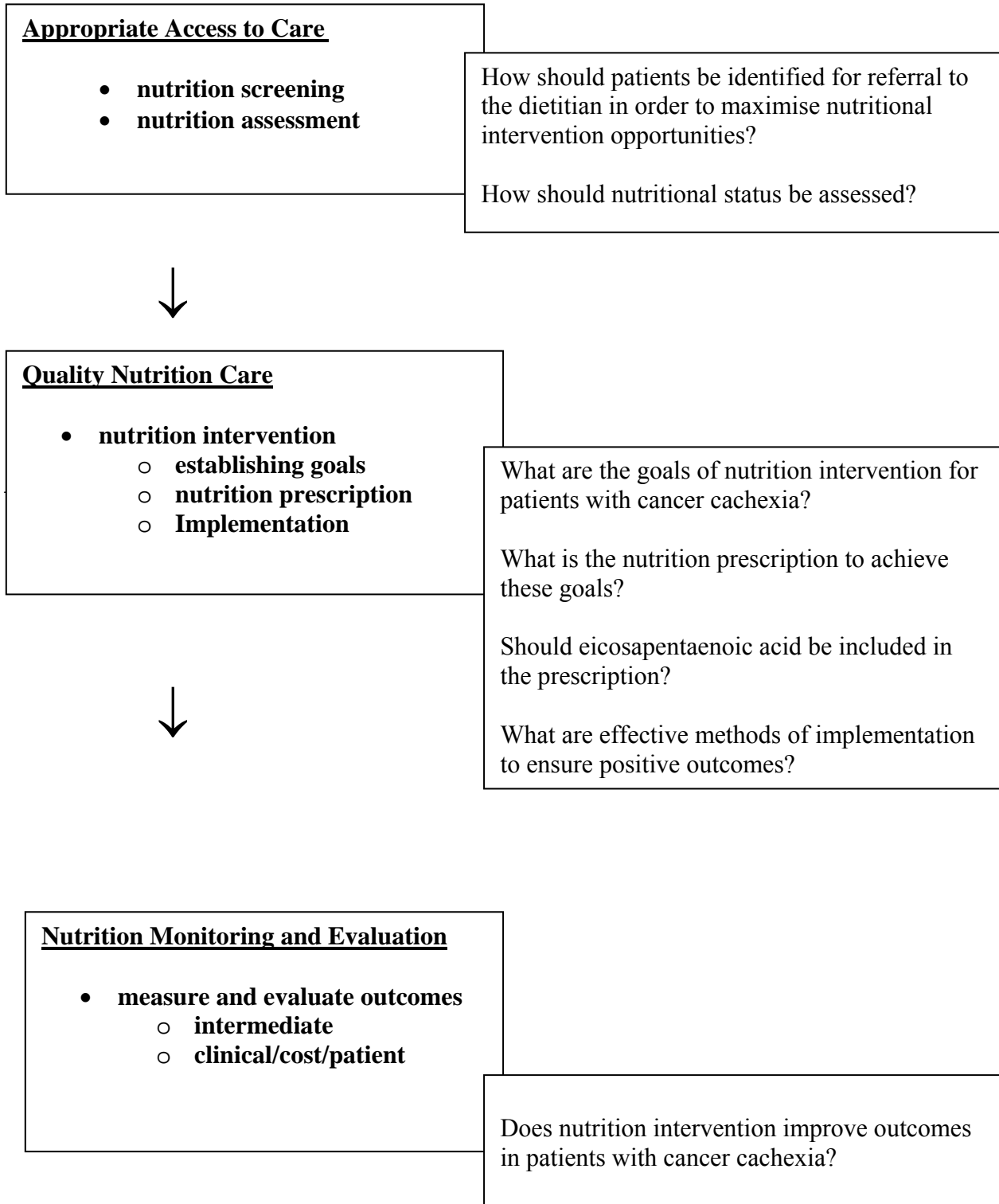
The guidelines were developed without the assistance of external funding. Where guideline development team members were authors of a published article, other members of the guideline development team evaluated the article for levels of evidence. Guideline development team conflict of interest declarations are: off label research support (Abbott: J, Bauer, S. Ash, W. Davidson) and support for conference attendance (Abbott: J, Bauer, S. Ash, W. Davidson; Novartis: J. Bauer, E. Isenring). 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.

EVIDENCE BASED PRACTICE GUIDELINE FRAMEWORK

Figure 1. Framework for evidence based practice guidelines development for the nutritional management of cancer cachexia

Nutrition Care Process

Clinical Questions Related to Stage of Care Process



(Adapted from Hakel-Smith & Lewis, ¹ and Splett, ²)

EVIDENCE BASED STATEMENTS

The evidence based statements are listed under headings based on the nutrition care process.

1. Access to Appropriate Care

Nutrition Screening

Clinical question

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

Evidence Statement	Level of Evidence
The Malnutrition Screening Tool (MST) is an effective screening tool for identifying nutritional risk in cancer patients	Level III-3 ³

Nutrition Assessment

Clinical question

How should nutritional status be assessed?

Evidence Statement	Level of Evidence
Subjective Global Assessment (SGA) is a valid method of assessing nutritional status in patients with cancer cachexia	IV ⁴
The scored Patient-Generated Subjective Global Assessment (PG-SGA) is a valid method of assessing nutritional status in patients with cancer cachexia	III-3 ^{4,5}
Bioelectrical impedance analysis is not suitable for body composition measurement in individual patients with cancer cachexia	III-3 ^{6,7}

2. Quality Nutrition Care

Nutrition Intervention

Establishing goals

Clinical question

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

Evidence Statement	Level of Evidence
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 ⁸

Nutrition Prescription

Clinical question

What is the nutrition prescription to achieve these goals?

Evidence Statement	Level of Evidence
---------------------------	--------------------------

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 ⁸
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 chemotherapy	IV ⁴
Weight stable patients have higher energy intake than weight losing patients in patients with cancer cachexia receiving supportive care	III-2 ⁸
Well-nourished patients with advanced cancer have higher energy and protein intakes compared to malnourished patients with advanced cancer	IV ⁹

Clinical question

Should EPA be included in the prescription in patients with cancer cachexia?

Evidence Statement	Level of Evidence
The prescription of EPA improves outcomes in patients with cancer cachexia	Level C ^{4,8,10-16}
	Body of evidence provides some support for recommendation but care should be taken in its application

Implementation

Clinical question

What are effective methods of implementation to ensure positive outcomes?

Evidence Statement	Level of Evidence
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 ¹⁷
Consumption of a high protein energy supplement enriched with EPA does not reduce total food intake in patients with cancer cachexia receiving chemotherapy	IV ⁴
Frequent clinician contact (minimum fortnightly) improves clinical outcomes in patients with cancer cachexia.	III-3 ^{4,15}

3. Nutrition Monitoring and Evaluation

Measure and Evaluate Outcomes

Clinical question

Does nutrition intervention improve outcomes in patients with cancer cachexia?

Evidence Statement	Level of Evidence
Nutrition intervention improves outcomes in patients with cancer cachexia	Level C ^{4,8,10-16}
	Body of evidence provides some support for recommendation but

Table 1. Summary of recommendations for the nutritional management of cancer cachexia

Point of referral	Anorexia, weight loss $\geq 5\%$ in 6 months and MST ≥ 2
Time for consultation	45-60 mins initially, 15-30 mins follow-up
Bio-chemistry and Clinical	Albumin, blood glucose (for persons with diabetes), Hb, CRP, medications including supplements
Nutrition assessment	Weight, PG-SGA, Protein/Energy intake assessment
Nutrition Intervention	Prescription Promote high protein ($>1.4\text{g/kg/d}$) and energy ($>120\text{g/kg/d}$) intake \pm EPA ($1.4\text{-}2.0\text{g/d}$) Implementation Counselling \pm supplements, symptom management, meal planning and modification, self monitoring,
Support	Liaise with medical and palliative care team, carers and family
Monitoring	Weight, PG-SGA, protein/energy intake minimum fortnightly. Frequency of monitoring will vary as treatment goals change towards endstage.

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APPENDIX 1: BACKGROUND TO EVIDENCE STATEMENTS AND TIPS

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.²⁴ The incidence of malnutrition amongst patients with cancer has been estimated at between 40 – 80%.^{25,26} The prevalence of malnutrition depends on the tumour type, location, stage and treatment.²⁷ 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.²⁸⁻³⁰ 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.³¹

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.³² 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.³³

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.³⁴⁻

³⁶Evaluation of pharmacotherapies is beyond the scope of these guidelines.

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.²¹ 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.²² Patients with cancer cachexia experience anorexia, early satiety, weakness, muscle wasting, 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.²³

There are no definitive methods for diagnosis of cancer cachexia. Clinical signs of anorexia, muscle wasting 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.

The patient target group encompasses any adult patient with cancer fulfilling the diagnostic criteria for cachexia.

Appropriate Access to Care

Nutrition Screening

In Australia, hospital inpatients are generally seen by dietitians as a result of referrals by medical or nursing staff³⁷. 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.^{38,39} 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)).⁴⁰ 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 ADA⁴⁰, 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.^{37,41} A number of reliable and valid nutrition screening tools have been recently published:

- Malnutrition Screening Tool^{3,42}
- Malnutrition Universal Screening Tool⁴³
- Mini Nutrition Assessment-Short Form⁴⁴
- Nutrition Risk Screening⁴⁵

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 (Appendix 2)^{3,42} No studies have been identified that report nutrition screening in patients with cancer cachexia.

Clinical Question

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

Evidence Statement

The Malnutrition Screening Tool (MST) is an effective screening tool for identifying nutritional risk in patients with cancer

Level of Evidence

Level III-3³

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.⁴⁰ Nutrition assessment parameters may be affected by non-nutritional factors resulting in poor sensitivity and specificity.⁴⁶ No single parameter is sufficiently sensitive and specific to determine nutritional status and a combination of parameters should be used.⁴⁷ 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).⁴⁸

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 (Appendix 3).⁴⁹ 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.^{5,29,50-53} A change in score of approximately nine points is required to move one global rating category.⁵³ The PG-SGA score may be more sensitive than the global rating to demonstrate improvement or deterioration in nutritional status.⁵² The scored 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.⁵⁴ In patients with cancer cachexia, two studies report nutritional status based on the global categorisation and the PG-SGA score.^{4,5}

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.⁵⁵ Patients with raised serum C-reactive protein levels have lower energy intake than those with normal levels⁵⁶ and there is some evidence that resting energy expenditure may be increased in these patients.⁵⁷

Anthropometric Assessment

A variety of techniques are available to measure body composition such as Dual Energy X-ray Absorptiometry (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.⁵⁸ Studies examining the validation of BIA in cancer patients are limited^{6,7,59-62} 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.⁷

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-C30⁶³, Functional Assessment of Cancer Therapy (FACT)⁶⁴ and the Short Form Health Survey (SF 36).⁶⁵ 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.⁵³

Clinical Question

How should nutritional status be assessed?

Evidence Statement	Level of Evidence
Subjective Global Assessment (SGA) is a valid method of assessing nutritional status in patients with cancer cachexia	IV ⁴
The scored Patient-Generated Subjective Global Assessment (PG-SGA) is a valid method of assessing nutritional status in patients with cancer cachexia	III-3 ^{4,5}
Bioelectrical impedance analysis is not suitable for body composition measurement in individual patients with cancer cachexia	III-3 ^{6,7}

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:

Table 2. Recommended nutrition assessment parameters for patients with cancer cachexia

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

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 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.⁶⁶

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.¹

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 paediatric patients from the American Society of Parenteral and Enteral Nutrition.⁶⁷

Traditionally, treatment has focussed on weight gain as the goal of nutrition intervention. Some studies have failed to show a positive effect of nutrition intervention when weight gain was the outcome.^{13,14,55} 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.^{8,68,69} Weight stabilisation is an appropriate goal for weight losing cancer patients provided that life expectancy is at least two months.⁸

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.⁷⁰

Clinical Question

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

Evidence Statement	Level of Evidence
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 ⁸

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 (Table 3).

Table 3. Goals of nutrition intervention for patients with cancer cachexia

Measure	Goal
PG-SGA	Reduce or maintain PG-SGA score
Anthropometry:	Stabilise weight and lean body mass
<ul style="list-style-type: none"> • Weight • skin folds, CAMA (if accredited in measuring skin folds) • DEXA, deuterium (if available) 	
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	Improve or maintain functional status score
PG-SGA as surrogate measure of quality of life	Improve or maintain quality of life
Biochemistry	Use to interpret current clinical condition
<ul style="list-style-type: none"> • Serum albumin • C reactive protein • Haemoglobin • Blood glucose 	
Medications	Ensure symptoms are being medically managed
Other	
<ul style="list-style-type: none"> • 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.⁷¹⁻⁷³ 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 patients with cancer.^{4,8,25} 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.^{4,8}

- **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.⁷⁴ 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.^{11,75-77} Table 4 summarises studies in relation to EPA supplementation (EPA capsules and oral nutrition supplements) in patients with cancer.

Table 4. Summary of studies of role of eicosapentaenoic acid in patients with cancer cachexia

Author Year Country	Level of Evidence & Study Design	Patient cancer type and number	Method	Results	Comment
Wigmore et al ¹¹ 1996 UK	Level IV Observational study 12 weeks	18 weight losing pancreatic cancer patients	Dose escalation study to 16g fish oil/day max (Max-EPA)	<u>Energy intake</u> - NA <u>Protein intake</u> - NA <u>Weight</u> - ↓ 2.9kg/mth prestudy, ↑ 0.3kg/month 3 mths <u>LBM</u> - NA <u>Functional capacity</u> - NA <u>Quality of Life</u> - NA <u>Survival</u> - NA <u>Other</u> Patients tolerated median of 12 Max-EPA daily (2.2g EPA + 1.4g DHA). No serious toxicity – 25% steatorrhea, some taste aberrations or transient diarrhoea Changes in weight accompanied by a temporary sig ↓ APPR and stabilisation REE	Demonstrated attenuation of weight loss in cancer cachexia
Gogos et al ¹⁶ 1998 Greece	Level II RCT	64 patients with mixed solid tumour types	18g fish oil (Max- EPA - 3.06g EPA+2.07g DHA) or placebo daily	<u>Energy intake</u> - NA <u>Protein intake</u> - NA <u>Weight</u> - ns improvement <u>LBM</u> - NA <u>Functional capacity</u> - ↑ KPS after 40 days in malnourished patients receiving fish oil only <u>Quality of Life</u> - NA <u>Survival</u> -doubled in patients receiving fish oil only <u>Other</u> No effect of fish oil on albumin or transferrin. No toxicity of fish oil except for mild abdominal discomfort and transient diarrhoea	Demonstrated high doses of omega 3 PUFA given with antioxidant supplementation -prolonged survival in patients with cancer - ↑ KPS in malnourished cancer patients
Burns et al ⁷⁸ 1999 USA	Level IV Observational study	22 weight losing cancer patients	Dose escalation study of fish oil	<u>Energy intake</u> - NA <u>Protein intake</u> - NA <u>Weight</u> - NA <u>LBM</u> - NA <u>Functional capacity</u> - NA <u>Quality of Life</u> - NA <u>Survival</u> - NA <u>Other</u> Maximum tolerated dose 0.3g/kg/day fish oil = 21 x 1g capsules/day containing 7.9g EPA + 5.2g DHA for a 70kg male. Dose limiting toxicity was gastrointestinal – diarrhoea.	Demonstrated maximum tolerated dose EPA
Barber et al ⁷⁹ 1999 UK	Level IV Observational study 7 weeks	20 weight losing pancreatic cancer patients	High protein, energy supplement with 2.18g EPA	<u>Energy intake</u> - ↑ 372 kcals <u>Protein intake</u> - NA <u>Weight</u> - ↓ 3.2kg/month prestudy; ↑ 1 kg 3 wks, ↑ 2.5 kg 7 wks <u>LBM</u> - ↑ LBM 1kg 3wks; ↑ 1.9kg 7 wks <u>Functional capacity</u> - KPS ↑ 10 3 wks; ↑ 10 7 wks <u>Quality of Life</u> - NA <u>Survival</u> - NA <u>Other</u> Median consumption supplement 1.9 cans/day.	First study to demonstrate positive outcomes (weight gain, LBM, KPS, energy) with a combination of EPA and protein/energy
Wigmore et al ⁸⁰ 2000 UK	Level IV Observational study 12 weeks	26 weight losing pancreatic cancer	Dose escalation study of fish oil to 6g/day EPA (95% pure)	<u>Energy intake</u> - NA <u>Protein intake</u> - NA <u>Weight</u> - ↓ 2kg/month prestudy; ↑ 0.5 kg/mth 4 wks; 16 patients weight stable or gained weight 12 wks <u>LBM</u> - NA <u>Functional capacity</u> - NA <u>Quality of Life</u> - NA <u>Survival</u> - NA <u>Other</u> No change in total body water, MAMC, TSF APPR stable. EPA supplement well tolerated –some patients had nausea and/ steatorrhea	Confirmed previous studies that doses of EPA to 6g well tolerated Confirmed EPA was the active ingredient in fish oil capsules.
Fearon et al ¹⁰ 2003	Level II RCT	200 weight losing untreated pancreatic	Randomised to high protein and energy supplement ± EPA	<u>Energy intake</u> - ↑224 kcal E v 68 kcal C, ns; Sig ↑ E baseline to 8 wks only <u>Protein intake</u> - ↑15gE v 6g C, ns; Sig ↑ E baseline to 8 wks only <u>Weight</u> - -0.37kg E v -0.25 kg C, ns; Sig change baseline to 8 wks E & C; Wt ↑	Both E and C supplements attenuated weight loss. ↑ LBM in E only

Multinational	8 weeks	cancer patients		<p>correlated with intake cans E only <u>LBM</u> - \uparrow 0.27 E v 0.12 C, ns; \uparrow LBM correlated intake cans E only <u>Functional capacity</u> - <u>Quality of Life</u> - Global E v C, ns; Post hoc analysis \uparrow QoL and \uparrow wt E only <u>Survival</u> - 142 days E v 128 days C, ns <u>Other</u></p>	<p>Non compliance with protocol in both groups High dropout rate due to death</p>
Bruera et al ⁹ 2003 USA	Level II RCT 2 weeks	60 cachectic cancer patients	Randomised to fish oil capsules or placebo (mean dose EPA 1.8 g)	<p><u>Energy intake</u> - \uparrow 51 kcals E v \downarrow 57 C kcals ns <u>Protein intake</u> - NA <u>Weight</u> - \uparrow 0.03 kg E v \downarrow 0.89 kg C ns <u>LBM</u> - NA <u>Functional capacity</u> - KPS \uparrow 10.0 E v \downarrow 6.9 C ns <u>Quality of Life</u> - NA <u>Survival</u> - NA <u>Other</u> Appetite, tiredness, nausea, well being ns</p>	<p>No effect of fish oil on outcomes but only 2 weeks of treatment Non compliance with protocol in both groups 10% controls high EPA levels High dropout rate due to intolerance of fish oil Outcome of 10% weight gain in cancer patients unrealistic</p>
Jatoi et al ¹³ 2004 USA	Level II RCT 3 months	421 weight losing cancer patients	Randomised to EPA sup v meg ace+control v meg ace+EPA sup	<p><u>Energy intake</u> - NA <u>Protein intake</u> - NA <u>Weight</u> - \uparrow 10%: EPA 6% v Meg+ c 18% v Meg+EPA 11% Ns EPA + Meg+c P=0.004 Any \uparrow: EPA 37% Meg 39 Meg+EPA 45 Ns <u>LBM</u> - NA <u>Functional capacity</u> - <u>Quality of Life</u> - ns <u>Survival</u> - ns <u>Other</u> Appetite \uparrow EPA 63 Meg 69 Meg+epa 66</p>	<p>First study to demonstrate improvement in functional outcomes with a combination of EPA and protein/energy</p>
Moses et al ¹⁵ 2004 UK	Level II RCT 8 weeks	24 weight losing pancreatic cancer patients	Randomised to high protein and energy supplement \pm EPA for 8 weeks Doubly labelled water to assess PAL	<p><u>Energy intake</u> - E 474 kcals v C 166 ns; Baseline change E p<0.05 only <u>Protein intake</u> - Sig \uparrow E 27 v C 4 <u>Weight</u> - E 0.0 v C \downarrow 0.2 ns <u>LBM</u> - E 0.3 v C 0.6 ns <u>Functional capacity</u> - TEE and PAL ns; \uparrow PAL baseline - 8 wks E only <u>Quality of Life</u> - NA <u>Survival</u> - NA <u>Other</u></p>	<p>Demonstrated that weight maintenance suitable goal for patents with cancer cachexia and is associated with \uparrow survival and QoL</p>
Davidson et al ⁸ 2004 Australia	Level III-2 Post hoc analysis RCT 8 weeks	107 pts wt losing (>1kg) or wt stable untreated pancreatic cancer patients	High protein and energy supplement \pm EPA	<p><u>Energy intake</u> - WL 107kJ/kg/day v WS125 P<0.001 <u>Protein intake</u> - <u>Weight</u> - NA <u>LBM</u> - NA <u>Functional capacity</u> - <u>Quality of Life</u> - WS 55 v WL 47.1 P=0.037 <u>Survival</u> - WS 259 days v WL 164 P=0.019 <u>Other</u></p>	<p>Demonstrated improvement in outcomes (dietary intake, QoL, KPS) in cachectic patients receiving chemotherapy and combination of EPA/protein/energy Small number patients</p>
Bauer & Capra ⁴ 2005 Australia	Level IV Observational study 8 weeks	8 weight losing pancreatic and non small cell lung cancer pts receiving chemotherapy	High protein and energy supplement \pm EPA)	<p><u>Energy intake</u> - \uparrow 36 kJ/kg/d <u>Protein intake</u> - \uparrow 0.3 g/kg/d <u>Weight</u> - 2.3 kg - clinically sig <u>LBM</u> - 4.4 kg clinically sig <u>Functional capacity</u> - KPS \uparrow 10 <u>Quality of Life</u> - \uparrow 16.7 <u>Survival</u> - NA <u>Other</u>: \uparrow nutritional status PG-SGA score 9 No change in meal protein or energy intake over 8 wks</p>	<p>Weight stabilisation</p>
Persson et al ¹² 2005 Sweden	Level II RCT 8 weeks	24 weight losing untreated advanced gastrointestinal cancer pts	Randomised to fish oil (4.9 g EPA) or Melatonin (18 mg/day) 4 weeks, both treatments additional 4 weeks	<p><u>Energy intake</u> - \downarrow 65kcal 4 wks, \downarrow 196 8 wks FO; MLT \uparrow 187 kcal 4 wks, \uparrow 19 kcal 8 wks (no stats provided) <u>Protein intake</u> - NA <u>Weight</u> - 38% stable or gain FO; 27% MLT; 63% FO & MLT <u>LBM</u> - NA <u>Functional capacity</u> - KPS stable FO & MLT; ns between groups <u>Quality of Life</u> - stable FO & MLT, ns between groups</p>	<p>Weight stabilisation</p>

Bauer et al ¹⁷ 2005 Australia	Level III-2 Post hoc analysis RCT	200 untreated pancreatic cancer patients	Compliance (C) with 1.5 cans/day high protein and energy supplement ± EPA compared to non- compliant (NC)	<u>Survival</u> - ns	Compliance with prescription 1.5 cans/day supplement no effect on meal intake
	8 weeks			<u>Other</u> : No biochemical/cytokine changes; ↑ plasma EPA levels	
				<u>Energy intake</u> – 30.3 C v 23.0 NC kcal/kg/day	
				<u>Protein intake</u> – 1.26 C v 0.90 NC g/kg/day	
				<u>Weight</u> – 1.7 kg difference (p=0.052)	
				<u>LBM</u> – 44.1 v 43.6 ns	
				<u>Functional capacity</u> - NA	
				<u>Quality of Life</u> – 56.8 v 52.4 ns	
				<u>Survival</u> – NA	
				<u>Other</u> : No change in meal protein or energy intake over 8 wks	

NA – Not assessed; E – experimental product; C – control product; LBM – lean body mass; KPS – Karnofsky Performance Status; QoL – quality of life; PAL – physical activity level ; ns- not significant

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 prescription¹⁰, duration of intervention¹⁴, appropriate endpoints¹³ 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 was scheduled for release in 2005. The guideline development team produced evidence based statements regarding EPA and outcomes and assessed the body of evidence using *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines - Pilot Program 2005* (Table 5).²⁰

Table 5. Assessment of eicosapentaenoic acid (EPA) and outcomes from nutrition intervention in patients with cancer cachexia

What outcomes from nutrition intervention can you expect in patients with cancer cachexia?

The prescription of EPA improves outcomes in patients (Level C: Body of evidence provides some support for recommendation but care should be taken in its application with cancer cachexia)

Evidence Statement	Level of Evidence
Intermediate Outcomes	
Consumption of a high protein energy supplement enriched with EPA for 8 weeks increases protein and energy intake (meals + supplements). Consumption of a standard high protein energy supplement for 8 weeks increases protein and trends towards increasing energy intake in patients with cancer cachexia compared with baseline	II ¹⁰
Consumption of a high protein energy supplement ± EPA for 8 weeks attenuates loss of weight and lean body mass in patients with cancer cachexia receiving supportive care	II ¹⁰
Supplementation with EPA capsules or fish oil for at least 4 weeks attenuates weight loss in patients with cancer cachexia receiving supportive care	III-3 ^{4,11,12}
Consumption of a high protein energy supplement enriched with EPA for 8 weeks increases protein and energy intake and attenuates loss of weight and lean body mass in patients with cancer cachexia receiving chemotherapy	IV ⁴
A higher intake of a high protein energy supplement enriched with EPA is associated with increases in body weight and LBM in patients with cancer cachexia receiving supportive care	III-2 ¹⁰
Consumption of a high protein energy supplement enriched with EPA ± megestrol acetate (median 12 weeks) does not improve weight (≥10% baseline) or appetite better than megestrol acetate alone in patients with cancer cachexia receiving supportive care/chemotherapy/radiotherapy.	II ¹³
Supplementation with fish oil for 2 weeks does not improve appetite, energy intake, weight, or fat-free mass compared with placebo in patients with cancer cachexia receiving supportive care/chemotherapy.	II ¹⁴
Clinical/Cost/Patient Outcomes	
Consumption of a high protein energy supplement enriched with EPA improves total energy expenditure and physical activity level in patients with cancer cachexia receiving supportive care	II ¹⁵
Supplementation with fish oil for at least 4 weeks improves performance status in malnourished patients with cancer cachexia receiving supportive care	III-2 ¹⁶
Supplementation with fish oil for at least 4 weeks improves survival in patients with cancer cachexia receiving supportive care	II ¹⁶
Supplementation with fish oil for 2 weeks does not improve physical function compared with placebo in patients with cancer cachexia receiving supportive care/chemotherapy	II ¹⁴
Consumption of a high protein energy supplement enriched with EPA used alone or in combination with megestrol acetate (median 12 weeks) does not improve quality of life or survival in patients with cancer cachexia receiving supportive care/chemotherapy/radiotherapy	II ¹³
Consumption of a high protein energy supplement ± EPA for 8 weeks does not improve quality of life or survival in patients with cancer cachexia receiving supportive care	II ¹⁰
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 ⁸

Potential Risks EPA

The draft Nutrient Reference Values for Australia and New Zealand recommend acceptable macronutrient distribution ranges to reduce chronic disease whilst still ensuring adequate micronutrient status.⁸¹ 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.⁸¹ 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.⁸² Cancer patients consuming 6 g EPA/d have reported no adverse effects on platelet counts.⁸⁰ 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.^{11,16} Cod liver and halibut liver oil are not suitable sources of EPA as the doses required could provide excess levels of Vitamin A. Dioxin and dioxin like polychlorinated biphenyls are environmental contaminants that accumulate in lipid. Fish oils are potentially a significant source, so fish oil supplements are purified to meet European commission maximum standards for dioxin.⁸³ The main concerns with these toxins relate to long term accumulation, as well as the effect on the foetus or breastfed infant. High short-term intakes in adults are unlikely to significantly increase total body burden.⁸³ Fish oil products and supplements are not a major source of dietary mercury and no recommendation has been made to restrict consumption because of mercury.^{83,84}

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 2000.⁸⁵⁻⁸⁷ 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.⁸⁸

Clinical Questions

**What is the nutrition prescription to achieve these goals?
Should eicosapentaenoic acid be included in the prescription?**

Evidence Statement	Level of Evidence
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 ⁸
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 chemotherapy	IV ⁴
Weight stable patients have higher energy intake than weight losing patients in patients with cancer cachexia receiving supportive care	III-2 ⁸
Well-nourished patients with advanced cancer have higher energy and protein intakes compared to malnourished patients with advanced cancer	IV ⁹
The prescription of EPA improves outcomes in patients with	Level C

cancer cachexia	Body of evidence provides some support for recommendation but care should be taken in its application
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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.
4. 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.

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.^{25,32,89-92} 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.^{4,17,90} 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.⁹³ Recent studies in patients with cancer have demonstrated effective clinical outcomes with weekly to fortnightly dietetic intervention.⁴

^{10,15,32,91,92} 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 such as telephone counselling is required.

Clinical Question

What are effective methods of implementation to ensure positive outcomes?

Evidence Statement	Level of Evidence
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 ¹⁷
Consumption of a high protein energy supplement enriched with EPA does not reduce total food intake in patients with cancer cachexia receiving chemotherapy	IV ⁴
Frequent clinician contact (minimum fortnightly) improves clinical outcomes in patients with cancer cachexia.	III-3 ^{4,15}

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.

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.⁹⁴ 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.⁸ **The evidence based statements in relation to outcomes of nutrition intervention are below.** 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*.²⁰

Clinical Question

Does nutrition intervention improve outcomes in patients with cancer cachexia?

Evidence Statement	Level of Evidence
Nutrition intervention improves outcomes in patients with cancer cachexia	Level C Body of evidence provides some support for recommendation but care should be taken in its application

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.

APPENDIX 2: THE MALNUTRITION SCREENING TOOL[®]

Have you lost weight recently without trying

If no	0
If unsure	2

If yes, how much weight (kg) have you lost?

0.5 – 5.0	1
>5.0 – 10.0	2
>10.0 – 15.0	3
> 15.0	4
Unsure	2

Have you been eating poorly because of a decreased appetite?

No	0
Yes	1

If score 0 or 1 - not at risk of malnutrition

score \geq 2 - at risk of malnutrition

Ferguson M, Bauer J, Banks M, Capra S. Development of a valid and reliable malnutrition screening tool for adult acute hospital patients. *Nutrition* 1999;15:458-464.

APPENDIX 3: THE PATIENT GENERATED SUBJECTIVE GLOBAL ASSESSMENT (PG-SGA)

Name:

Date:

Medical History		A	B	C
WEIGHT	Usual weight.....			
	Current weight.....			
Wt change past 6 months	Amount weight loss.....			
	% weight loss.....			
0-<5% loss		*		
5-10% loss			*	
>10% loss				*
Weight change past 2 weeks				
	Amount.....			
No change; normal weight		*		
Increase to within 5%		*		
Increase (1 level above)		*	*	
No change, but below usual wt			*	
Increase to within 5-10%			*	
Decrease				*
DIETARY INTAKE				
No change; adequate		*		
No change; inadequate			*	
Change	Duration of change.....			
Suboptimal diet			*	
Full liquid			*	
Hypocaloric liquid				*
Starvation				*
Intake borderline; increasing		*		
Intake borderline; decreasing			*	
Intake poor; no change			*	*
Intake poor; increasing			*	
Intake poor decreasing				*
GASTROINTESTINAL SYMPTOMS				
	Frequency (never, daily, no. of			
	Duration (<2wk,			

	times/week)	>2wk)			
Nausea			
Vomiting			
Diarrhoea			
Anorexia			
None; intermittent			*		
Some (daily >2 week)				*	
All (daily >2 week)					*
FUNCTIONAL CAPACITY					
No dysfunction		Duration of change	*		
Difficulty with ambulation/normal activities				*	
Bed/chair-ridden					*
Change past 2 week					
Improved			*		
No change				*	
Regressed					*

Physical examination	A	B	C
SUBCUTANEOUS FAT			
Under the eyes	Slightly bulging area		Hollowed look, depression, dark circles
Triceps	Large space between fingers		Very little space between fingers, or fingers touch
Biceps	Large space between fingers		Very little space between fingers, or fingers touch
MUSCLE WASTING			
Temple	Well-defined muscle/flat	Slight depression	Hollowing, depression
Clavicle	Not visible in Males; may be visible but not prominent in females	Some protrusion; may not be all the way along	Protruding/prominent bone
Shoulder	Rounded	No square look; acromion process	Square look; bones prominent

		may protrude slightly	
Scapula/ribs	Bones not prominent; no significant depressions	Mild depressions or bone may show slightly; not all areas	Bones prominent; significant depressions
Quadriceps	Well rounded; no depressions	Mild depression	Depression; thin
Calf	Well developed		Thin; no muscle definition
Knee	Bones not prominent		Bones prominent
Interosseous muscle between thumb and forefinger	Muscle protrudes; could be flat in females		Flat or depressed area
OEDEMA (related to malnutrition)	No sign	Mild to moderate	Severe
ASCITES (related to malnutrition)	No sign	Mild to moderate	Severe
OVERALL SGA RATING	A	B	C

(Ferguson, Bauer, Banks, Capra, 1996)©

EVIDENCE BASED GUIDELINES FOR THE NUTRITIONAL MANAGEMENT OF CHRONIC KIDNEY DISEASE

INTRODUCTION

Scope and purpose

The purpose of these guidelines is to provide dietitians in Australia and New Zealand with a summary of evidence based clinical guidelines related to the dietetic management of adult patients with chronic kidney disease. The patient target group is any adult patient fulfilling the definition and diagnostic criteria of Chronic Kidney Disease (CKD), excluding those with nephrotic syndrome. These guidelines by definition also exclude acute renal failure and transplantation.

The clinical questions were as follows:

- At what level of GFR should patients be referred to the dietitian in order to maximise nutritional intervention opportunities?
- Which specific measures best reflect nutritional status or change in nutritional status in Chronic Kidney Disease?
- What are the goals of nutrition intervention for CKD?
- What is (are) the appropriate nutritional intervention(s) to optimise nutritional status in Chronic Kidney Disease and prevent malnutrition?
- What is the optimal method of implementation and follow up to ensure nutritional status is maintained or improved?

These guidelines are meant to serve as a general framework for handling patients with particular health problems. It may not always be appropriate to use these guidelines to manage clients because individual circumstances may vary. The independent skill and judgement of the health care provider must always dictate treatment decisions. 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 other¹.

Methods

The Royal Brisbane and Women's Hospital (RBWH) Nutrition and Dietetics Department supported a project dietitian, Helen McLaughlin to undertake the search strategy of existing guidelines. An initial team led by Dr Susan Ash, from Princess Alexandra Hospital with Helen McLaughlin, Suzie Chesterfield and Helen McCoy from RBWH developed the framework and the initial draft, which was circulated to Queensland dietitians working in Nephrology Services. This draft was used for consultation and evaluation at a workshop of dietitians at the 21st National Dietitians Association Australia conference in May 2003. A national panel of experts was defined at the conference, the Australia and New Zealand Renal Guidelines Taskforce (ANZRGT), who have continued to refine the guidelines as discussed elsewhere (see "Consultation Process").

Relevant guidelines and articles were identified by Medline database and Internet key word searches between April 2002 and October 2003. The evidence based practice

guidelines for the dietetic management of chronic kidney disease were developed by summarising the nutrition components of the following published guidelines:

- Caring for Australians with Renal Impairment (CARI) Guidelines²
- Kidney Disease Outcomes Quality Initiative (K/DOQI) Clinical Practice Guidelines³⁻⁸
- American Dietetic Association (ADA) Medical Nutrition Therapy Evidence-Based Guides for Practice: Chronic Kidney Disease (non-dialysis) Medical Nutrition Therapy Protocol⁹
- ADA Guidelines for Nutritional Care of Renal Patients (3rd ed)¹⁰
- European Dialysis and Transplant Nurses Association and European Renal Care Association (EDTNA/ERCA) Guidelines for the Nutritional Care of Adult Renal Patients¹¹.

Where conflicting guidelines answering the same clinical question existed, the guideline with the strongest level of evidence was included. When conflicting supporting evidence was equal in quality and depth, CARI guidelines were selected preferentially as more relevant to the local environment. If similar information was proposed from more than one set of guidelines, all sources were acknowledged. Aspects of nutritional management not included in any of the guidelines were omitted, however some aspects deemed important have been included as practice tips. Due to the difficulties associated with research into nutritional management of kidney disease, an evidence-based approach could not be adopted for all aspects. For published guidelines based on opinion or agreed best practice without supporting research, recommendations have still been included to complete the document but are acknowledged as being open for wider variance in practice. In particular, adherence to process type guidelines may be strictly resource dependant.

The selected guidelines were reformatted into the following components: definition of disease, diagnostic criteria, clinical questions to be addressed, referral criteria, nutrition assessment, nutrition prescription and outcome measures, in line with established nutritional management process. Dietetic management of acute renal failure, transplantation, nephrotic syndrome or kidney disease in paediatrics is not included.

These guidelines include information taken from existing sets of guidelines based on scientific evidence, and where no evidence exists, published guidelines stating consensus opinion from experienced practitioners including dietitians have been included. These guidelines do not address many issues concerning the implementation of dietetic practice, such as using groups or individual consultations, educational strategies or counselling techniques. This is beyond the scope of these guidelines and neither the evidence nor consensus opinion currently exists to promote one form of practice over another.

The Appendices show the definitions and calculations required for the management of Chronic Kidney Disease.

Levels of evidence or opinion have been cited from the above documents and referenced in each guideline. Descriptions of the levels of evidence are listed in Table 1.

Table 1: Levels of evidence from original sources

Reference	Levels of Evidence					
NHMRC¹²	I Systematic Review of all relevant clinical trials	II At least 1 properly designed Randomised Clinical Trial (RCT)	III-1 Well-designed Pseudo-RCT	III-2 Comparative studies with concurrent controls & allocation not randomised (Cohort studies), case control studies, or interrupted time-series with a control group	III-3 Comparative studies with historical control, 2 or more single-arm studies, or interrupted time-series without a parallel control group	IV Case series, either post-test or pre-test and post-test
ADA/Splett, 2000¹		1 Evidence obtained from 1 or more well-designed RCT's	II-1 Evidence obtained from well designed control trials without randomisation	II-2 Evidence obtained from well designed cohort or case-controlled analytic studies, preferably from more than 1 centre or research group	II-3 Evidence obtained from multiple time-series studies with or without intervention, or well designed studies with concurrent comparison groups, studies with dramatic results from uncontrolled experiments	III Descriptive observational studies (no control or comparison group), case series reports and reports from expert committees, opinions of respected authorities and documented clinical experience
ADA, 2002⁹		Grade 1 Studies of strong design for answering the questions		Grade II Studies of strong design but uncertainty attached to the conclusion	Grade III Limited studies of weak design. Evidence from studies of strong	Grade IV The support of the conclusion consists solely of the statement of

addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of serious doubts about generalisability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to adequate statistical power

because of inconsistencies among the results for different studies or because of doubts about generalisability, bias, research design flaws or adequacy of sample size. OR the evidence is solely of studies from weaker designs but results have been confirmed in separate studies and are consistent.

design is either unavailable because no studies have been done or because the studies that have been done are inconclusive due to lack of generalisability, bias, design flaws or inadequate sample size

informed medical commentators based on their clinical experience, unsubstantiated by the results of any research studies

CARI, 2003²	Level A Randomised controlled trials and meta analyses		Level B Descriptive studies	Level C Consensus or opinion
K/DOQI, 2000³		Evidence Mainly convincing scientific evidence limited added opinion	Evidence & Opinion Descriptive studies	Opinion Consensus or opinion
K/DOQI, 2002⁴	S Analysis of individual patient data from a single large, generalisable		C Compilation of original articles into evidence tables	R Review of reviews & selected original articles
				O Opinion

study of high
methodological
quality (for
example
NHANES III)

Guidelines for Nutritional Care of Renal Patients (3rd ed)¹⁰	No levels of evidence or opinion provided
European Guidelines for the Nutritional Care of Adult Renal Patients¹¹	‘Examination of the scientific literature shows a paucity of evidence on dietary advice in renal failure. Therefore the guidelines are based on scientific evidence, where available, and on consensus of what constitutes ‘best practice’ where not’

Consultation process

These practice guidelines have undergone several stages of peer and expert review using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument (The AGREE Collaboration)¹². The rigour of scientific process varies between guidelines. The K/DOQI and CARI guidelines have documented systematic search and review processes in place, which meet the NH&MRC and AGREE criteria for quality. The ADA and EDTNA/ERCA guidelines are less rigorous, but the information extracted from these documents is based on expert opinion and is unable to be assessed using an evidence based practice tool.

The first draft of these guidelines was presented at the Dietitians Association of Australia (DAA) 21st National Conference in Cairns in May 2003 and achieved support in principle. A national panel of experts was defined at the conference, the Australia and New Zealand Renal Guidelines Taskforce (ANZRG) to oversee further development and formulation of the final document. Consultation with nephrologists and renal nurses was undertaken when the guidelines were presented at the 31st Annual Renal Society of Australasia Conference in Brisbane, also in May 2003. The second draft was reviewed by the ANZRG in August 2003 with comments incorporated into the final document. ANZRG launched the guidelines in Queensland on October 30, 2003 with the assistance of the Queensland Health Allied Health Core Practice Group. Following the launch of the 2003 Guidelines, a workshop was conducted at the DAA 22nd National Conference in Melbourne in May 2004, on implementing the guidelines, and the taskforce gathered feedback from the 6 month pilot period since launching the guidelines. Currently, the guidelines are published on the Queensland Health Electronic Publishing Service (QHEPS) Internet site and have been endorsed by DAA.

As part of the DAA endorsement process, consumer input was sourced from Kidney Health Australia's regional Advocacy Committees, which are comprised of CKD patients. A standardised feedback form was developed based on recommendations from the Queensland Health Charter of Patient Rights (<http://www.health.qld.gov.au/qhppc/default.asp>). Feedback from consultation in two states has indicated that overall consumers felt the guidelines provided a standardised approach to care, however were concerned that in their current format were too technical to be understood by consumers. Consumers would have liked to have been involved from the outset and were particularly interested that minority groups such as Indigenous people and those from non English speaking backgrounds be considered in any educational material and that those in rural and remote areas receive the same access to dietetic care as people in metropolitan areas. Discussion at both the National DAA workshops in 2003 and 2004 recognised the importance of involving consumers particularly from Indigenous backgrounds in the development of education materials.

Review process

These guidelines are based on other published guidelines and should be reviewed annually to ensure they remain current. Responsibility for review lies with Royal Brisbane and Women's Hospital in conjunction with the Australia and New Zealand Renal Guidelines Taskforce.

Next Review Date: October 2007.

Applicability

The applicability was tested by dietitians at two National workshops and one state workshop. The cost of implementing the guidelines was a human resource issue and participants in the workshops felt having the guidelines would assist in lobbying for more staff for patient management.

Editorial independence

These guidelines have been developed as a quality activity without external funding, therefore there is no external influence on the content of the guidelines. No member of the guideline taskforce has any conflict of interest to declare relating to the development of these guidelines.

EVIDENCE BASED PRACTICE GUIDELINE FRAMEWORK

The framework for evidence based practice in CKD is presented in Figure 1.

Insert Figure 1 here. **SUMMARY OF EVIDENCE-BASED STATEMENTS**

The evidence based statements are listed under the headings described in the Nutrition Care Process in Figure 1.

Criteria for referral to dietitian

Clinical Question

At what level of Glomerular Filtration Rate (GFR) should patients be referred to the dietitian in order to maximise nutritional intervention opportunities?

Evidence Statement	Level of Evidence
CKD Stages 3 and 4	
CKD Stage 3 (GFR 30-59mL/min)	Level IV ²
CKD Stage 4 (GFR 15-20 mL/min)	Level III ⁴
Protein energy malnutrition increases with deteriorating kidney function and is associated with adverse outcomes	Level III-2 ⁴
Low protein and calorie intake is an important cause of poor nutritional status.	Level III-3 ⁴
CKD Stage 5	
CKD Stage 5 (GFR<15mls/min)	
For patients undergoing haemodialysis and peritoneal dialysis, nutritional status should be routinely assessed at commencement of dialysis and at regular intervals thereafter.	Level I ² , Level III ³

Nutrition Assessment

Clinical Question

Which specific measures best reflect nutrition status or change in nutritional status in CKD?

Evidence Statement	Level of Evidence
CKD Stages 3 and 4	
Maintained percent (%) oedema-free (dry) actual body weight reflects optimal nutritional status.	Level II ²
Body Mass Index (BMI) =18.5-25, reflects optimal nutritional status.	Level IV ³
Subjective global assessment (SGA) and % ideal body weight (BMI) reflect change in nutritional status.	Level IV ³
Total body nitrogen, dual X-ray absorptiometry (DEXA) or bioelectrical impedance (BIA) reflect long term nutritional adequacy.	Level IV ²
CKD Stage 5	

Maintained percent (%) oedema-free (dry) actual body weight reflect optimal nutritional status.	Level II ²
Body Mass Index (BMI) =23-26, reflects optimal nutritional status.	Level II ²
SGA maintained or improved reflects nutritional status.	Level III-3 ²
Nutritional status of patients on peritoneal dialysis should be monitored by methods appropriate to assess total body stores and detect early signs of malnutrition, such as normalised protein nitrogen appearance (nPNA) >0.9, total body nitrogen (TBN) and DEXA within the normal range.	Level IV ^{2,3}

Nutrition Prescription/Intervention

Clinical Question

What are the goals of nutrition intervention for CKD?

Evidence Statement	Level of Evidence
Achieve and maintain desirable weight and adequate nutritional status.	Level III-2 ¹¹
Optimise status of co-morbidities, blood glucose control in diabetes and fluid and sodium control in hypertension, phosphate control in hyperparathyroidism, lipid control and weight management.	Level III-2 ⁴
Normalise or stabilise biochemical markers, such as a normalised protein appearance (n PNA) ≥0.8 g/day in haemodialysis.	Level III-2 ⁴
Normalise or stabilise biochemical markers, such as a nPNA >0.9 g/day in peritoneal dialysis.	Opinion ⁴
Maintain skeletal muscle stores and strength, using subjective global assessment (SGA), TBN and DEXA.	Opinion ⁴

Clinical Question

What are the prescriptions for appropriate nutritional intervention(s) to optimise nutritional status in CKD and prevent malnutrition?

Evidence Statement	Level of Evidence
CKD Stage 3	
Energy. Ideal kilojoule/calorie energy intake determined for age, gender and BMI and level of physical activity needs to be determined. A nutritionally balanced diet with adequate energy intake to maintain a healthy weight needs to be prescribed.	Opinion ²
Protein. A level of protein of 0.75-1.0 g/ideal body weight (IBW)/day is recommended.	Level I ²
CKD Stage 4	
Energy intake of at least 146kJ/kg IBW/day 35 kcal/kg IBW/day) with a moderate protein restriction to prevent protein energy malnutrition.	Level II ²
For patients >60 years, an energy intake of 125 kJ/kg IBW/day is recommended.	Level III-2 ³

Protein intake for patients with GFR<25 mL/min, should not be less than 0.75g/kgIBW/day. At least 50% should be of high biological value.	Level II ²
Phosphate intake restricted to 800-1000mg/day and/or use of phosphate binders is serum phosphate >1.49mmol/L and /or serum parathyroid hormone >7.7 pmol/L on more than 2 consecutive occasions.	Opinion ⁸ Level II ²
Supplementation. Patients on a restricted protein diet (<0.75g/kg IBW/day) should receive thiamine (>1mg/day), riboflavin (1-2mg/day) and vitaminB6 (1.5-2mg/day).	Level IV ²
CKD Stages 3 and 4	
Fat/Carbohydrate. Priority should be given to a diet aimed at preventing protein-energy malnutrition and reducing fat to <30% of daily energy intake with saturated fat limited to <10% energy. Carbohydrate should be utilised to make up the balance of required energy intake.	Opinion ²
Sodium intake of <100mmol/day is recommended if the patient is hypertensive and CKD is progressive.	Opinion ²
Potassium intake should be reduced if serum K > 6mmol/L	Opinion ²
Phosphate intake restricted to 800-1000mg/day and/or use of phosphate binders is serum phosphate >1.49mmol/L and /or serum parathyroid hormone >12.1 pmol/L on more than 2 consecutive occasions.	Opinion ⁸ Level III-2/3 ³
Fluid intake needs to be adjusted to the degree of CKD and prevention of renal disease, oedema management and hypertension management. Once fluid intake requires diuretics a liberal intake should be curbed. Management of hypertension includes limiting fluid intake.	Opinion ²
Vitamin D supplementation is required for patients with GFR<50mL/min and PTH level 3-6 times the normal range or histological evidence of osteodystrophy.	Level II ²
CKD Stage 5	
Energy levels of 125-146kJ(30-35 kcal)/kgIBW/day are recommended to prevent malnutrition.	Level IV ²
Energy levels of at least 146 kJ (35kcal)/kgIBW/day is recommended for those acutely ill < 60years and 125-146 kJ (30-35 kcal)/kgIBW/day for those acutely ill >60years.	Level IV ³
Protein intake is recommended at 1.2-1.4g/kg IBW/day, >50% high biological value protein.	Level IV ²
In haemodialysis, protein intake at least 1.2g/kg IBW/day when acutely ill.	Opinion ⁴
In peritoneal dialysis, protein intake at least 1.3g/kg IBW when acutely ill	Opinion ⁴
In peritoneal dialysis, protein intake at least 1.5g/kgIBW/day with peritonitis.	Opinion ⁴
Fat and Carbohydrate <7% energy from saturated fat, polyunsaturated fat, monounsaturated fat <20%energy, carbohydrate 50-60% energy.	Level III-2 ⁷

Sodium. Individualised treatment is recommended based on oedema and hypertension. 80-110mmol/day if restricted.	Level IV ¹¹
Phosphate. Restrict intake to 800-1000mg/day if serum phosphate >1.8mmol/L, and/or PTH>33.3pmol/L	Opinion ⁴
Fluid. For haemodialysis, restrict fluid to 500mL + previous day's output.	Level III-2 ⁸
For peritoneal dialysis, individualised treatment recommended based on oedema and hypertension. If fluid overloaded, 800 mL+ previous day's output recommended.	Level III-2 ¹¹
	Opinion ¹¹

Implementation and Management

Clinical Question

What are effective methods of implementation to achieve positive outcomes in CKD?

Evidence Statement	Level of Evidence
EDUCATION	
CKD Stage 3	
Patients with decreased dietary intake or malnutrition need dietary modification, counselling and specialised nutrition therapy.	Level IV ⁴
For patients with poorly controlled co-morbidities, refer to medical specialist.	Opinion ANZRG
CKD Stage 4	
Pre end stage kidney disease education forms an important part of management strategy to slow the progression of renal disease and may have a beneficial effect.	Level II ²
Nutrition counselling should encompass appropriate protein and energy intake.	Level III-2 ⁴
Nutrition counselling should include fluid, sodium and potassium intake	Level IV ²
and weight management	Opinion ⁴
CKD Stage 5	
Every patient should receive intensive nutrition counselling based on an individualised care plan.	Opinion ⁴
The care plan should focus on adequate protein and energy intake.	Level IV ²
MONITORING AND EVALUATION	
Recommended times for initial consultation are 45-60mins and review 20-30mins, for all patients.	Opinion ⁹
CKD Stage 5	
Nutrition reviews for dialysis patients need to occur every 6 months.	Opinion ⁹
Timing for outcomes to be monitored include:	
• Monthly	
○ oedema free body weight and BMI	Level II ²
○ serum albumin	Opinion ²

- 3-6 monthly, dialysis adequacy (Kt/V) Level IV²
 - nPNA Level IV²
 - Dietary interview Opinion²
 - SGA Level IV^{2,4}
 - 6-12 monthly, assessment of body stores using TBN /DEXA Opinion⁴
-

Summary of Recommendations for Management of Chronic Kidney Disease

CKD	Stage 3 (GFR 30-59)⁴	Stage 4 (GFR 15-29)⁴	Stage 5⁴ Haemodialysis	Stage 5⁴ Peritoneal Dialysis
Point of referral	GFR<60ml/min ^{2,4}	GFR<30ml/min ³	Upon commencement	Upon commencement
Time for consultation	45-60 mins ⁹	45-60 mins ⁹	45-60 mins ¹⁰	45-60 mins ¹⁰
Bio-chemistry and Clinical	Alb ⁴ , K ⁹ , PO ₄ ⁹ , cr ⁹ , bld glucose & HbA _{1c} (for persons with diabetes) ⁹ , PTH ⁸ , BP ⁹ , lipids ² , GFR ⁹ , Hb ⁹ , medications inc supplements ⁹	Alb ³ , K ⁹ , PO ₄ ⁹ , cr ⁹ , bld glucose & HbA _{1c} (for persons with diabetes) ⁹ , PTH ⁸ , BP ¹³⁹ , lipids ² , GFR ⁹ , Hb ⁹ , medications inc supplements ⁹ ,	Pre dial: Alb ^{2,3} , urea ² , K ¹⁰ , PO ₄ ² , CaxPO ₄ ² , lipids ⁷ , PTH ⁸ , Post dial: urea ¹⁰ HbA _{1c} (if diab) ¹⁰ , HD freq & fluid gains ^{10,4} , BP ¹⁰ , medications ¹⁰ , Kt/V ³	Alb ^{2,3} , K ¹⁰ , PO ₄ ¹⁰ , lipids ⁷ , PTH ⁸ , CaxPO ₄ ² , urea &/or cr ² , HbA _{1c} (if diab) ¹⁰ , PD prescription & fluid gains ¹⁰ , BP ¹⁰ , medications ¹⁰ , Kt/V ³
Nutrition assessment	dry wt ^{2,4} , BMI ² , %IBW/SGA ⁴ , diet assessment/nPNA ^{2,4} , activity level and limitations ⁹	dry wt ^{2,3} , BMI ² , %IBW/SGA ³ , diet assessment/nPNA ^{2,3} , activity level and limitations ⁹	Dry wt ² , BMI ² , %IBW ³ , SGA ^{2,3} , diet assessment ^{2,3} or nPNA ^{2,3}	Dry wt ² , BMI ² , %IBW ³ , SGA ^{2,3} , diet assessment ^{2,3} or nPNA ^{2,3}
Nutrition intervention	Ideal for age, gender, BMI and phys activity level ²	At least 146kJ/kg IBW (BMI 18.5-25) ² , 125-146kJ/kg IBW >60 yr ³	125-146kJ/kg IBW (BMI 22-25) ² acute illness: >146kJ/kg IBW if <60yr ³ , >125kJ/kg IBW if > 60yr ³	146kJ (35kcal)/kg IBW (BMI 22-25) ² inc glucose from dialysate ⁹ acute illness: >146 kJ/kg IBW /day ³
- Protein	0.75-1.0g/kg IBW/day ²	0.75-1.0g/kg IBW ² with adequate kJ intake ² >50% HBV ²	1.2-1.4g/kg IBW ² >50% HBV ³ acute illness: > 1.2 g /kg IBW ³	min 1.2g/kg IBW ² ; >50% HBV ³ acute illness: >1.3g /kgIBW ³ ; peritonitis: 1.5g/kg IBW ¹¹
- Sodium	<100mmol if hypertensive and CKD is progressive ²	<100mmol if hypertensive and CKD is progressive ²	80 –110 mmol/day ¹¹	Indiv treatment recommended, if restricted

				80-110 mmol/day ¹¹
- Potassium	Not usually restricted, If K ⁺ > 6.0 limit intake ⁶ to 1mmol/kg IBW/ day	If K ⁺ >6.0 limit intake ² to 1mmol/ kg IBW/day	1mmol/kg IBW/day ¹⁰	Indiv treatment recommended, if restricted 1mmol/ kg IBW/day ¹⁰
- Phosphate	if >1.49 mmol/L, (or >target PTH) restrict to 800-1000mg/day (adj for protein) &/or binders ⁸	if >1.49 mmol/L, (or >target PTH) restrict to 800-1000mg/day (adj for protein) &/or binders ⁸	if >1.78 mmol/L, (or >target PTH) restrict to 800-1000mg/day (adj for protein) &/or binders ⁸	if >1.78 mmol/L, (or >target PTH) restrict to 800-1000mg/day (adj for protein) &/or binders ⁸
- Fluid	Individualised based on CKD, oedema and hypertension ²	Individualised based on CKD, oedema and hypertension ²	500ml + PDUO ¹¹	Indiv treatment recommended, if fluid overloaded or hypertensive: 800ml + PDUO ¹¹
Nutrition counselling	adequate protein and energy ^{2,4} , bld glucose control in DM ⁴ , fluid and Na control in HT ⁴ , lipid ² & weight ⁴ control, meal plan ⁹ , self monitoring ⁹ , physical activity ¹⁵	protein and energy intake ^{2,3} , Na, K & fluid intake ² , wt control ^{2,9} , meal plan ⁹ , recipe modification, self monitoring ⁹ , physical activity ⁹	individual care plan ³ , adequate protein and energy intake ² , fluid & electrolyte management ¹⁰ , self monitoring ¹⁰ , meal plan ¹⁰ , physical activity ¹⁰	individual care plan ³ , adequate protein intake ² , appropriate energy intake ² , self monitoring ¹⁰ , meal plan ¹⁰ , physical activity ¹⁰
Review & frequency of follow up	Dry wt & BMI monthly ² , 20-30 min ⁹ r/v every 6-12 months if no evidence of malnutrition, more frequently if malnourished ⁴	Dry wt & BMI monthly ² , 20-30 min ⁹ r/v every 1-3 months ² , more frequently if inadequate intake, concomitant illness, GFR < 15 or malnourished ³ ; SGA every 6-12 months ²	Dry wt, BMI & alb monthly ² , 45-60 min ¹⁰ r/v every 3-6 months inc nPNA, Kt/V, diet assessment & SGA ² , more frequently if clinically indicated ²	Dry wt, BMI & alb monthly ² , 45-60 min ¹⁰ r/v every 6 months inc nPNA, Kt/V, diet assessment & SGA ² , more frequently if clinically indicated ²

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APPENDIX 1: BACKGROUND TO EVIDENCE STATEMENTS

Diagnosis and Referral

Chronic Kidney Disease (CKD) is defined as the presence of kidney damage for 3 months or more, as defined by structural or functional abnormalities, with or without decreased glomerular filtration rate (GFR), OR, GFR less than 60ml/min for more than 3 months with or without kidney damage². Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies⁴.

Table 2: Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min/1.73m ²)
1	Kidney damage with normal or ↑ GFR	≥ 90
2	Kidney damage with mild ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney failure	< 15 (or dialysis)

CALCULATIONS

Estimated Glomerular Filtration Rate (eGFR)

Modification of Diet in Renal Disease (MDRD) formula¹⁶

$$\text{eGFR} = 186 \times ([\text{SCR}/88.4]^{-1.154}) \times (\text{age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African-American})$$

NB the African-American factor is not used in Australia

where eGFR = estimated glomerular filtration rate (mL/min/1.73m²), SCR = serum creatinine concentration (µmol/L), and age is expressed in years.

An automated calculator for MDRD-based eGFR can be found at <http://www.kidney.org.au>.

As the MDRD formula has not been validated in children, its use should be restricted to people over 18 years of age.

eGFR values over 60 mL/min/1.73m² should be reported as “> 60mL/min/1.73m²”, rather than as a precise figure.

Specific clinical settings in which eGFR is not appropriate for use and GFR should be measured directly include:

- populations in which the MDRD equation is not validated (eg, Asian people) or in which validation studies have not been performed (eg, Aboriginal and Torres Strait Islander populations);
- severe malnutrition or obesity;
- extremes of body size and age;
- exceptional dietary intake (eg, vegetarian diet or creatine supplements);
- disease of skeletal muscle, paraplegia, etc; and
- rapidly changing kidney function.

Normalised protein nitrogen appearance (nPNA)²

1. Chronic renal failure

nPNA may be approximated by the Randerson formula

$$\text{nPNA (g/kg/day)} = \frac{[\text{urea excretion (mmol/day)} \times 0.209] + 15.71}{\text{weight (kg)}}$$

1. Haemodialysis

The most widely used method calculates the urea generation rate from the end of the first dialysis to the beginning of the second dialysis and relies predominantly on the difference between the post and pre dialysis urea values .

Several methods are used to calculate the urea generation rate from which the PNA are calculated.

$$\text{PNA} = \frac{\text{UGR}}{0.154} (\text{g}/24 \text{ hrs}) + 1.7 + \text{Urinary protein losses}$$

$$\text{UGR} (\text{g}/24 \text{ hrs}) = \text{Urea} (\text{mmol}/24 \text{ hrs}) \times 0.028$$

Note: In all cases urinary urea and protein losses need to be measured and included in the calculations used to estimate protein intake.

1. Peritoneal dialysis

Given that daily changes in body nitrogen are usually negligible in stable patients on peritoneal dialysis, the urinary nitrogen appearance (UNA) is usually represented as the sum of dialysate and urinary losses. The protein equivalent of total nitrogen appearance (PNA) expresses the nitrogen appearance in terms of protein.

$$\text{PNA} (\text{grams of protein}/24\text{hrs}) = \text{TNA} (\text{grams of nitrogen}/24 \text{ hrs}) \times 6.25.$$

Because of the constant relationship between the measured UNA and the total nitrogen appearance, the protein equivalent of total nitrogen appearance (PNA) is determined from the UNA, or from the urea appearance (UA) by the following formulae¹⁷.

$$\text{PNA} (\text{g}/\text{day}) = 20.1 + 7.5 \times \text{UNA} (\text{g}/24 \text{ hrs})$$

or

$$\text{PNA} (\text{g}/\text{day}) = 20.1 + 0.209 \times \text{UA} (\text{mmol}/24 \text{ hrs})$$

1. *Calculation of Ideal Body Weight (IBW)*

Aim for weight to be within BMI of 20-25 if GFR 15-59 and a BMI of 23-26 on a dialysis modality. A patient's ideal body weight can be adjusted (as per the equation below), particularly if a patient is obese BMI>30.

Adjusted Body Weight = [(Actual Weight – Ideal Weight) x 0.25] + Ideal Body Weight (IBW).

When to use actual or adjusted body weight:

Use actual body weight (dry weight for dialysis patients) when:

- Weight is within reasonable range of ideal or standard body weight (recommended BMI range).
- Recent weight change has not occurred.
- The patient is not malnourished.
- The patient has been slightly overweight or underweight almost all of their lives.

Use adjusted body weight when patients are overweight/obese, using clinical judgement.