Better care through better nutrition: Value and effects of Medical Nutrition

A SUMMARY OF THE EVIDENCE BASE

Medical Nutrition International Industry

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A summary of the evidence base

Medical Nutrition International Industry

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Introduction

Health and social care systems face many challenges in the quest to provide patients with the best of care, not least in the face of increasingly tight fiscal times. Interventions that have been shown to improve patient outcome whilst providing economic benefits should be integral to the planning and provision of safe and effective patient care. Nutrition intervention with medical nutrition in the management of disease-related malnutrition has been shown to have significant benefits both for patients and healthcare systems.

Policy makers, payers and care providers need access to information that helps them to make informed, evidence-based decisions about the types of care they recommend and provide. This report aims to synthesise relevant information on the rationale for and value of medical nutrition as a key nutritional intervention strategy in the management of disease-related malnutrition. It is intended to provide all stakeholders with an up-to-date and practical summary of the evidence base on disease-related malnutrition and the benefits of medical nutrition, including oral nutritional supplements (ONS), enteral tube feeding (ETF), and parenteral nutrition (PN).

The term **'malnutrition'** encompasses overweight and obesity as well as under-nutrition, but in line with common practice internationally, the term 'malnutrition' is used in this report to refer to 'under-nutrition'. The term 'disease-related malnutrition' (DRM) is also frequently used since most malnutrition arises due to the consequences of disease.

This document is an updated and expanded version of previous reports prepared in 2009, 2010 and 2012. It draws on the key elements of a comprehensive systematic review of the scientific evidence base for the management of disease-related malnutrition.[i] Using a pragmatic approach to identify relevant additional publications,[ii] this document builds on the systematic review by adding data on the prevalence, causes and consequences of malnutrition and the nutritional, functional, clinical and economic benefits of medical nutrition. In the 2018 update data from key systematic reviews on the benefits of ETF have been added along with information about the increasing use of ETF to manage malnutrition across health-care settings. It includes data from countries outside Europe as well as data specifically examining the paediatric area. The 2018 update also includes a description of the indications for PN and its use in different countries, together with a summary of studies supporting the nutritional, functional, and economic benefits of PN, identified from a pragmatic review of the literature. Furthermore, this document includes a unique collation of relevant guidelines relating to medical nutrition (ONS, ETF and PN), as well as examples of good practice.

There is a growing body of evidence from individual studies and meta-analyses demonstrating the benefits of medical nutrition in improving nutritional status, reducing adverse health outcomes, and reducing the economic burden of malnutrition on society. Evidence-based internationally recognized (e.g. NICE), international and professional guidelines for nutritional intervention with medical nutrition in general and specific patient populations are also widely available. However, the implementation of good nutritional practices remains ad hoc, and poor awareness of the value of nutritional care, and especially ONS, is prevalent. In combination with pressure on finite healthcare budgets which places nutritional care funding under threat, this will lead to poorer health outcomes and higher healthcare costs in the longer term.

This compilation aims to encourage further documentation and sharing of information, experience and practical tools in the fight against malnutrition. Contributions are welcomed to ensure that this remains a "living document" that ultimately aims to enhance patient care.

Mike Wallace, Moreno Perugini and Tomaso Piaggio on behalf of the MNI

[i]Stratton RJ, Green CJ, Elia M. Disease-related malnutrition: an evidence based approach to treatment. Wallingford: CABI Publishing; 2003. [ii] Section 1 mainly based on publications up to May 2012 as per previous version. Sections 2-4 mainly based on publications up to May 2016.

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WRITERS

The MNI would like to thank Fionna Page BSc (Hons), RD for the collation and writing of this report. Fionna is a registered dietitian with many years of experience spanning both clinical practice (in particular nutrition support in hospital and community care settings) and the medical food industry.

Fionna Page BSc (Hons), RD

The MNI would also like to thank Julie Winstone PhD for writing the new chapter on parenteral nutrition. Julie is a medical writer with substantial expertise across a broad range of clinical areas, including nutrition.

Julie Winstone PhD

Medical Nutrition International Industry (MNI)

The Medical Nutrition International Industry (MNI) is the international trade association of companies providing products and services that support patient management and rehabilitation by the appropriate use of specialised nutritional support, including enteral and parenteral nutrition. The members of MNI are leading international companies in the development, manufacture and provision of Medical Nutrition and supporting services, namely Abbott, Baxter, B. Braun, Fresenius Kabi, Nestlé Health Science and Nutricia Advanced Medical Nutrition.

MNI's mission is to support the quality of nutritional interventions and services to best serve the interests of patients, healthcare professionals and healthcare providers, and to work to make specialised nutritional solutions available to more people around the world.

MNI nurtures and supports further research to fully explore the potential of Medical Nutrition in improving the health of patients suffering from acute or chronic disease. Working alongside the European Nutrition for Health Alliance (ENHA), an independent organisation that pursues a multi-stakeholder partnership in the European healthcare arena, the European Society for Clinical Nutrition and Metabolism (ESPEN) and the European Union Geriatric Medicine Society (EUGMS), MNI promotes the transition of clinical nutrition research into standard practice through dissemination, support and implementation of best practices and guidelines related to malnutrition and Medical Nutrition. Through constructive engagement with policy makers, MNI aims to promote a balanced policy environment that enables the Medical Nutrition industry to meet the growing healthcare needs and expectations of its stakeholders. In collaboration with regulatory authorities and scientific bodies, MNI strives to shape a regulatory and reimbursement framework capable of meeting the needs of patients, healthcare professionals, payers and healthcare providers.

MNI is committed to achieving better care through better nutrition, across all ages and healthcare settings. Acutely aware of the pressures faced by healthcare organisations and that nutritional care is not always considered as an integral part of patient care, MNI aims to ensure that the evidence base for medical nutrition is available to decision makers and practitioners, thereby demonstrating the value of medical nutrition in improving patient outcomes and lowering the significant financial costs associated with malnutrition.

MNI also offers an annual grant to reward initiatives related to an optimal nutritional care approach. The grant selection is supported by ESPEN and the grant is awarded at the ESPEN Congress each year. Outlines of the annual submissions and winners as well as general information are available to view on the MNI website http://medicalnutritionindustry.com/grant/mni-grant/ or contact **secretariat@medicalnutritionindustry.com**

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Foreword from ESPEN, EUGMS, ESPGHAN and EFAD

Representatives of the European organisations of the European Society for Clinical Nutrition and Metabolism (ESPEN), the European Union Geriatric Medicine Society (EUGMS), the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Federation of the Associations of Dietitians (EFAD) share the same vision as the MNI in striving to ensure that there is wide awareness of the issue of malnutrition, that its identification and effective management is integrated into everyday patient care across specialities and that an environment is created that nurtures research to fully explore the potential of Medical Nutrition in improving the health of patients. Dissemination of information about malnutrition and its management including nutritional support plays a key role in these efforts.

This document provides an up-to-date, easy to access, practical compilation of the prevalence, causes and consequences of disease-related malnutrition in all age groups across many regions of the world. It presents the evidence base for oral nutritional supplements (ONS) and enteral tube feeding (ETF) and parenteral nutrition (PN), organised with particular emphasis on different age groups and care settings. For the first time the many national, international and professional guidelines that recommend the use of ONS, ETF and PN have been collated and grouped according to age group and clinical condition. This resource illustrates the wealth of organisations that have recognised the value in ensuring that nutritional support is integrated into patient care. Finally, the report showcases examples of initiatives to raise the awareness of the issue of malnutrition but also to ensure appropriate intervention and follow up in practice to benefit patients and healthcare systems.

Access to relevant, evidence-based and thoughtfully constructed information poses a challenge for policy makers, payers and care providers so it is with pleasure that we commend this resource to all involved in delivering the best in nutritional care for patients and healthcare systems. The unique collation of topics on this subject makes this report essential reading for all involved.

EUROPEAN SOCIETY FOR CLINICAL NUTRITION AND METABOLISM (ESPEN)

ESPEN promotes the need for research, education and the use of evidence-based practice and guidance in the field of Medical Nutrition and metabolism and in particular in the identification and management of malnutrition.

Advances in modern medicine have revolutionised patient care. However, the focus of care has often emphasised the system or organ that gives rise to the disease. Therefore managing a patient's needs in a truly holistic way has become more challenging. ESPEN has recognised this challenge. Medical Nutrition provides an opportunity for integration in the way in which it can bring many disciplines of medicine together to tackle a multi-faceted issue such as malnutrition.

Central to this is the need for organisations to work together to identify and share information and good practice. This document, helping the practitioner to use ONS, ETF and PN, is an excellent example of how this can be achieved.

Professor André Van Gossum
Chairman, ESPEN

Professor Stéphane Schneider
Chairman, Educational and Clinical Practice Committee, ESPEN

EUROPEAN UNION GERIATRIC MEDICINE SOCIETY (EUGMS)

In times of demographic change or more so demographic chance, the fast ageing European societies are faced with an immense increase in older adults with chronic diseases, multi-morbidity and the constant danger of functional decline or even disability. Preventive and therapeutic measures to preserve functionality and by that independence are the most important tasks for all professionals within the health system caring for older persons. Besides treating acute and chronic diseases, the triad of nutrition, physical activity and social contacts is necessary to guarantee good functionality. In line with this, adequate nutritional intake and care is a cornerstone to allow 'healthy ageing'.

The EUGMS is working with different organizations in order to foster awareness of nutritional problems in older adults, especially at the interface between sarcopenia and the frailty syndrome. Goals are ubiquitous screening for malnutrition, adapted and adequate assessment, timely implementation of therapeutic strategies and effective monitoring for nutritional problems in all settings where older adults live. Fighting against malnutrition is a key topic for the EUGMS, as prevention and/or treatment of nutritional problems is effective and acts on every organ system, which is especially important in multimorbid older persons.

Professor Cornel Sieber
EUGMS delegate for Optimal Nutritional Care for All campaign (ONCA)

EUROPEAN SOCIETY FOR PAEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION (ESPGHAN)

Malnutrition is not ‘expected’ in our affluent, developed society. This is true in all age groups, but particularly in infants and children where malnutrition is considered by many to be limited to war-torn or famine-stricken developing countries. This document highlights that this is not the case and that malnutrition affects children and young people in many developed countries. The prevalence of disease-related malnutrition has not decreased over the last 30 years. Yet like in adults and older people, the problem is often overlooked or not treated. Efforts continue to look for reliable ways to identify risk of malnutrition with practical screening tools specifically designed for use in children.

Although there are gaps in our knowledge of some topics in paediatric malnutrition such as the specific clinical and economic effects of medical nutrition in children, there is a wealth of data from good quality studies and meta-analyses in adults from which to draw on that demonstrate clear benefits for paediatric patients and healthcare systems.

ESPGHAN seeks to improve standards of care and education and does so in collaboration with other key organisations. We welcome the inclusion of information on malnutrition in children in this document and see its dissemination as an additional opportunity to further our aim of achieving clinical excellence for children and their families.

Dr Jessie Hulst
Chairman, ESPGHAN Working group on Malnutrition

EUROPEAN FEDERATION OF THE ASSOCIATIONS OF DIETITIANS (EFAD)

The proportion of older adults in the EU is expanding and ageing can affect social, mental, emotional and physiological abilities, which may impact on the older adults' ability to optimize nutritional intake. The role of the dietitian is essential in both primary and secondary prevention of malnutrition and working with older adults in a strategic, educational, clinical and administrative role. And dietitians work actively in all care settings for older adults: acute hospital, community, residential care sites, nursing homes, community primary care teams, and rehabilitation teams. To this end this dossier is able to provide much need evidenced based rationales for optimising the nutritional health of older adults and reducing the risk or reversing malnutrition. It is timely and to be welcomed not only by health professionals but also by those they serve.

The prevention and management of nutrition-related disorders requires specialising in a 'person-centred' approach by the whole team, which must always include the patient and caregivers as partners in the care process. This approach requires an understanding of the individual's food habits in a social and medical context. The more we can share and learn together the more we advance our best practice for reducing the impact of malnutrition. EFAD supports the wealth of information in this report and our role to share, with our colleagues, in seeking better nutrition for all who are poorly nourished through research, education and practice.

Professor Anne E de Looy
Honorary President of the European Federation of the Associations of Dietitians (EFAD)

EFAD EUROPEAN FEDERATION OF THE ASSOCIATIONS OF DIETITIANS

Foreword from The European Nutrition for Health Alliance (ENHA)

In recent years, the most attention by far in affluent countries has been paid to the problem of overweight and obesity – both of which are very visible in our communities. What may surprise many to know is that the issue at the other end of the spectrum, under-nutrition, also constitutes a major problem – which is at least as big a problem as obesity – particularly in hospitals, care homes and communities, where diseases and disabilities are common.

The issue of malnutrition has begun to be recognised at European level. Already back in 2003, the Council of Europe Committee of Ministers adopted a resolution on food and nutritional care in hospitals. In 2008, malnutrition was incorporated in two White Papers, where traditionally attention on nutrition was restricted to the problem of obesity. In June 2009, representatives of health ministries from the EU member states and several other stakeholder groups met in Prague and issued a declaration and a set of action points under the banner 'Stop disease-related malnutrition and diseases due to malnutrition!' The 2009 'Prague Declaration' called for the following actions to fight malnutrition:

- public awareness and education;
- guideline development and implementation;
- mandatory screening;
- research on malnutrition;
- training in nutritional care for health and social care professionals;
- national nutritional care plans endorsed and their implementation and funding across all care settings secured;
- consideration of malnutrition as a key topic for forthcoming EU Presidencies.

Later in 2009, the Council of Europe's Belgian delegation of the Committee of Experts on Nutrition, Food and Consumer Health published 'Nutrition in care homes and home care. Report and recommendations: from recommendations to action'. This report contains an analysis of the major barriers to appropriate nutritional care and explores the roles and responsibilities of all care givers in these specific settings. With the purpose to improve awareness, screening and management of malnutrition, recommendations for action on various levels have been compiled by experts from several Council of Europe member states.

In November 2010, at a Nutrition Day Conference in the European Parliament, leading policy makers and nutrition experts called for routine nutritional risk screening for all hospital patients and pointed out the enormous economic burden for the healthcare system related to malnutrition.

In October 2011 in Warsaw, the ENHA joined with representatives from the European Parliament, the Ministry for Health in Poland, the Polish Presidency of the European Union, ESPEN, the Polish Society for Parenteral and Enteral Nutrition (POLSPEN), scientific and professional associations, and industry, patient and health insurance groups to issue a declaration calling for action on the 4 key areas to address disease-related malnutrition:

- screening;
- awareness;
- reimbursement;
- education.

As a result screening for nutritional risk began in all hospitals in Poland in January 2012.

On the 4-5th November 2014 representatives from eight countries in Europe joined the European Nutrition for Health Alliance (ENHA) and its partners to discuss how to ensure 'Optimal Nutrition Care for All' in healthcare systems across Europe. The conference focused on shared learning, developing new ideas and milestones for achievement in developing National Nutritional Care Plans. At the close of the conference, participants were invited to sign the Charter for 'Optimal Nutritional Care for All'; pledging commitment to a world where every patient who is malnourished or at risk of undernutrition is systematically screened and has access to appropriate, equitable, high quality nutritional care. The 'Optimal Nutritional Care for All' initiative (ONCA) is increasingly used by participating countries as an overarching principal on which to build their work. The campaign acts as an umbrella, bringing existing activities together and enabling planned activities; as countries report that being a part of a multi-country effort to address malnutrition has provided leverage on a national level.

All documents mentioned above can be accessed via http://www.european-nutrition.org/. Activities are ongoing at national and European level to drive for routine screening in a range of healthcare settings.

To further strengthen the position of nutritional care, awareness of the added value of evidence-based practical nutritional care (economic as well as clinical benefits) must be explicit, and decision makers must be convinced. The increasing recognition of malnutrition as a public health issue on the political agenda means that the time is right for action by governments, health and social care organisations, and healthcare professionals.

In line with these aims supported by ENHA, the MNI has compiled data on the prevalence, causes and consequences of malnutrition and the evidence base for the clinical and economic benefits of medical nutrition.

Professor Olle Ljungqvist
Chair, ENHA

The European Nutrition for Health Alliance

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How to use this document

NAVIGATION

To aid navigation when using an electronic version of the report, 4 different types of **hyperlinks** have been included:

- links from the Contents to the start of each Section/Appendix;
- links within the document. e.g. to Appendices, where 'BACK' buttons will take the user back to the respective section;
- tabs on the right-hand side of the page link to the Contents and the selected Section/Appendix;
- links to external web pages for more information.

The '**bookmark**' function can be used as an alternative way to navigate between Sections of the document. When you open the document as a PDF you will see a toolbar on the left hand side of the screen. Click on the bookmark icon. This opens a navigation toolbar where you can expand and collapse a comprehensive contents list. Click on the Section or subsection title to move to that part of the document.

STRUCTURE

The report has been structured as follows:

- **SECTION 1:** The Burden of Malnutrition which outlines key information relating to identifying malnutrition, its prevalence, causes and consequences. Data has been presented primarily by **age group** and **healthcare setting**. Symbols help the reader to identify relevant information.
- **SECTION 2:** Medical nutrition which gives an overview of ONS, ETF and PN and their role as part of good nutritional care.
- **SECTION 3:** Benefits of ONS, ETF and PN: The primary focus is on **nutritional, functional, clinical and economic effects** and **outcomes**. Where possible, data is also grouped by healthcare setting and age group.
- **SECTION 4:** Guidelines and Good practice: This unique collation of guidelines and examples of good practice related to the use of ONS, ETF and PN in the management of disease-related malnutrition (DRM) is structured according to **country, healthcare setting** and **patient group**.

REFERENCES

Reference lists are provided at the end of each Section and at the end of each Appendix.

SYMBOLS

Throughout the document the symbols shown below are used to indicate the focus of the information in terms of the **healthcare setting** and **age/patient group**. Most data relates to **adults in general** and therefore the symbols are used to highlight when data relates specifically to **older people, children or patients with cancer**.

Healthcare setting*	Symbol	Age/patient group*	Symbol
Hospital		Older people (in general people aged > 65 years of age)	
Community		Children (in general anyone aged < 18 years of age)	
Across healthcare settings**		Patients with Cancer	

*It is recognised that definitions of healthcare settings and age groups differ across countries, in national and professional guidelines and reports and in studies. Every attempt has been made to include descriptions of age groups and health-care settings in this report (either within the body of the text or in the related tables and Appendices), but in some cases this detail was not available. For more information about healthcare settings, refer to Definition of terms on page 15.
**Used to indicate that the data from studies in hospital or the community was combined, e.g. in meta-analyses, or that the studies included interventions that started during hospital admission and continued after discharge

Definition of terms

Adherence
A term used to describe how well a patient or client is following the advice of his/her healthcare professional or treatment plan. Also known as compliance or concordance.

Cachexia
A number of definitions of cancer cachexia have been proposed[1-3] and a practical, easy-to-use classification of cancer cachexia has been developed, defined as ≥ 10% weight loss associated or not with anorexia, early satiation and fatigue; weight loss of < 10% is defined as pre-cachectic.[4]

Care settings
These terms are not used consistently across different countries. For the purposes of this document:

- **Hospital** The term 'hospital' refers to care in a hospital as an inpatient;
- **Outpatient** The term 'outpatient' refers to a patient who attends a hospital or clinic for diagnosis or treatment but does not occupy a bed;
- **Community** The term 'community' refers to care outside the hospital setting and can include people in institutions, in sheltered housing or in their own homes:
  - ~ sheltered housing – groups of housing units provided for older or disabled people who require occasional assistance from a resident warden but who do not need full residential care;
  - ~ institution – refers to care which does not take place in hospital or at home, i.e. it includes care in nursing homes, residential homes, long-term care institutions and mental health units (all of these are sometimes referred to informally as 'care homes');[ii]
  - ~ nursing home – residents usually require nursing care and are more dependent than residents in residential care;
  - ~ residential home – residents may need assistance with meals or personal care. Qualified nurses are not required to be present.

Cost-effectiveness
The difference in costs is compared with the difference in consequences in an incremental analysis.[5]

Dietary advice /counselling
The provision of information with the aim of increasing the frequency of consumption of food and fluids and increasing the energy and nutrient content of the foods and fluids consumed.

Economic evaluation
The comparative analysis of alternative courses of action in terms of both their costs and consequences.[5]

Enteral Nutrition (EN)
Enteral nutrition (also known as enteral tube feeding) is nutrition therapy given via a tube or stoma into the intestinal tract distal to the oral cavity.[6] [iii] Enteral formulas are defined as FSMP (see below).

Enteral Tube Feeding (ETF)
The term Enteral Tube feeding (ETF) is used synonymously with Enteral Nutrition (see defintion above).

Failure to thrive/Faltering growth
Inadequate growth in early childhood. Although no agreed consensus exists for the definition of faltering growth,[7] in practice, abnormal growth patterns such as a fall across centiles, plateauing or fluctuating weight should trigger further assessment.[8] The term 'failure to thrive' is also used in older people and is defined as 'a syndrome involving poor nutrition, including decreased appetite and weight loss (often with dehydration), inactivity, depression, impaired immunity, and low cholesterol.'[9]

Food fortification
Food fortification aims to increase the energy and nutrient density of foods and fluids without significantly increasing their volume.

Foods for Special Medical Purposes (FSMP)
FSMPs are one of the food categories governed by EU Regulation No 609/2013 for Foods for Specific Groups (FSG).[10] To supplement the FSG Regulation, specific legislation for FSMPs has been introduced and updates the previous EU directive governing FSMPs; this legislation is found in Commission Delegated Regulation (EU) 2016/128 of 25 September 2015 supplementing Regulation (EU) 609/2013 of the European Parliament and of the Council as re-gards specific compositional and information requirements for food for special medical purposes.

A FSMP is defined within the FSG Regulation as 'a food specially processed or formulated and intended for the dietary management of patients, including infants, to be used under medical supervision; it is intended for the exclusive or partial feeding of patients with a limited, impaired or disturbed capacity to take, digest, absorb, metabolise or excrete ordinary food or certain nutrients contained therein, or metabolites, or with other medially-determined nutrient requirements, whose dietary management cannot be achieved by modification of the normal diet alone'.

[ii]Where details of the care setting have been provided in original reports, this information has been included in this report to help to establish the exact setting where studies, care or interventions have taken place. However, in some cases the detail is incomplete as this information was not available. [iii]Definitions of Enteral Nutrition may vary, for example in the US the term EN comprises tube feeding only. Where the definition varies in the text this is highlighted in the text or as a footnote where relevant.

Healthcare system
A healthcare system is the sum total of all of the organisations, institutions and resources whose primary purpose is to improve health.[11] In the UK, for example, healthcare includes hospitals, maternity units and services provided by district nurses.

Home Enteral Nutrition (HEN)
HEN is another term used to describe the process of receiving ETF in a setting outside of hospital. It is often used synonymously with HETF. In some countries or studies the term HEN may also include patients receiving nutritional support in the form of ONS and fortified foods given orally. If this is the case this is identified in the text where relevant.

Home Enteral Tube feeding (HETF)
HETF describes the process of enteral tube feeding in a setting outside of hospital. This is usually the patient's own home, residential care home or nursing home.

Home Parenteral Nutrition (HPN)
Parenteral nutrition administered outside the hospital, either at home or at nursing home.

Malnutrition
Malnutrition can be defined as a 'state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease'.[6] Some definitions of malnutrition include over-nutrition (overweight and obesity) as well as under-nutrition[12] but in the context of this report 'malnutrition' is used to mean under-nutrition.

Furthermore, the term "malnutrition" is used in this report to encompass the additional concept of nutritional risk (see definition below), reflecting common practice whereby these terms are often used interchangeably. Where possible in relation to studies and trials, attempts have been made in this report to describe in detail the definitions and methods used for detecting malnutrition/nutritional risk where feasible.

Medical nutrition
A term used to describe commercially available products for nutritional intervention, including oral nutritional supplements (ONS), enteral tube feeding (ETF) and parenteral nutrition (PN).

Nutritional assessment
A detailed, more specific and in-depth evaluation of a patient's nutritional state, typically by an individual with nutritional expertise (e.g. a dietitian, a clinician with an interest in nutrition or a nutrition nurse specialist) or by a nutritional support team. This will usually be conducted in the case of nutritional problems identified by the screening process or when there is uncertainty about the appropriate course of action. The assessment process allows more specific nutritional care plans to be developed for the individual patient.[13] Further details of what measures should be included as part of nutritional assessment are outlined in ESPEN guidelines.[6]

Nutritional care programme
A range of activities, including nutritional screening, care planning, nutritional interventions (food, ONS, tube and/or parenteral feeding) and follow-up, designed to ensure that patients' nutritional needs are evaluated, met and regularly reviewed.

Nutritional risk
Severe malnutrition (under-nutrition) is clinically obvious. However, there is uncertainty about recognising lesser degrees of malnutrition. In the absence of universally accepted criteria for identifying malnutrition with high sensitivity and specificity, the concept of risk is invoked. Risk is a measure of likelihood that malnutrition is present or likely to develop.[13] It also reflects the risk of a poor outcome as a result of impaired nutritional status.[14] Prior to the diagnosis of malnutrition the criteria for being 'at nutritional risk' according to any validated nutritional risk screening tool must be fulfilled.[6]

Nutritional screening
Risk screening is a rapid process performed to identify subjects at nutritional risk, and should be performed using an appropriate validated tool in all subjects that come in contact with healthcare services.[6]

Nutritional support/Nutritional intervention/ Nutrition Therapy
Nutrition therapy describes how nutrients are provided to manage any nutritional-related condition. Nutrition or nutrients can be provided orally (regular diet, therapeutic diet e.g. fortified food, ONS), as enteral tube feeding or as parenteral nutrition.[6] These terms are often used interchangeably.

Nutritionally complete
A product may be called 'nutritionally complete' if it contains all essential macronutrients and micronutrients in a quantity and balance that allows the product to be used as a sole source of nutrition.

Oral nutritional supplements (ONS)
Multi-nutrient liquid, semi-solid or powder products that provide macronutrients and micronutrients with the aim of increasing oral nutritional intake. ONS are typically used to supplement food intake which is insufficient to meet requirements. However, in many cases, ONS are nutritionally complete and could also be used as a sole source of nutrition.

ONS are distinct from dietary supplements which provide vitamins, minerals and or/trace elements in a pill format (also known as food supplements) and they must comply with the information and compositional requirements of Foods for Special Medical Purposes (FSMP).[15]

Parenteral Nutrition (PN)
Parenteral Nutrition - also known as 'intravenous feeding' - is a method of getting nutrition directly into the blood circulation, bypassing the gastrointestinal tract. PN is delivered via a catheter inserted into a peripheral or central vein. Parenteral nutrition represents an alternative or additional approach for nutritional intervention when other routes are not succeeding (not necessarily having failed completely) or when it is not possible or would be unsafe to use other routes (i.e. oral or tube).[16]

Public health
Public health is concerned with improving the health of the population rather than treating the diseases of individual patients.[17]

Social care system
Social care includes nursing homes, residential homes, care at home and adult placement schemes.

Starvation
The term 'starvation-related malnutrition' has been proposed to describe when there is chronic starvation without inflammation. Examples of this include medical conditions like anorexia nervosa.[18]
The ESPEN diagnoses tree of malnutrition describes malnutrition (undernutrition) without disease as 'socioeconomic or psychologic related malnutrition' arising from poverty, self-neglect etc. and 'hunger-related malnutrition' arising from deprivation of food e.g. in developing countries or as a result of natural disasters.[6]

Stunting (in children)
A deficit in height-for-age that signifies slowing of skeletal growth and reflects chronic malnutrition.[19]

Under-nutrition
Malnutrition includes both over-nutrition (overweight and obesity) and under-nutrition (underweight). For the purposes of this report the term malnutrition will be used to mean under-nutrition (also frequently referred to as disease-related malnutrition, see 'Malnutrition' on page 16).

The ESPEN diagnoses tree of malnutrition describes malnutrition (undernutrition) without disease as 'socioeconomic or psychologic related malnutrition' arising from poverty, self-neglect etc. and 'hunger-related malnutrition' arising from deprivation of food e.g. in developing countries or as a result of natural disasters.[6]

Wasting (in children)
A deficit in weight-for-height resulting from failure to gain weight or from weight loss. It reflects a process occurring in the recent past and it is indicative of acute malnutrition.[19]

Abbreviations

ADL	Activities of daily living
BANS	British artificial nutrition survey
BAPEN	British association for parenteral and enteral nutrition
BCM	Body cell mass
BIA	Bioelectrical impedance analysis
BMI	Body mass index
BSI	Bloodstream infection
CAPD	Continuous ambulatory peritoneal dialysis
CD	Crohn's disease
CI	Confidence interval
CIF	Chronic intestinal failure
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
CR BSI	Catheter-related bloodstream infection
CRE	Chronic radiation enteritis
CVC	Central venous catheter
DHA	Docosahexaenoic acid
DRM	Disease-related malnutrition
ECF	Enterocutaneous fistula
ECM	Extracellular mass
ECMO	Extracorporeal membrane oxygenation
EHNA	European nutrition for health alliance
E/N	Energy/nitrogen (ratio)
EN	Enteral nutrition
EORTC QLQ-C30	European organisation for research and treatment of cancer core quality of life questionnaire
EPA	Eicosapentaenoic acid
ESPEN	European society for clinical nutrition and metabolism (formerly european society of parenteral and enteral nutrition)
ESPGHAN	European society for paediatric gastroenterology, hepatology and nutrition
ETF	Enteral tube feeding
EU	European union
EUGMS	European union geriatric medicine society
FACT-G	Functional assessment of cancer treatment – general questionnaire
FFM	Fat-free mass
FIM	Functional independence measure
FSMP	Food for special medical purpose
GI	Gastrointestinal
GP	General practitioner
HAN	Home artificial nutrition
HD	Haemodialysis
HETF	Home enteral tube feeding
HFA	Height-for-age
HIV	Human immunodeficiency virus
HR	Hazard ratio
HSCT	Haematopoietic stem cell transplantation
IBD	Inflammatory bowel disease
IBW	Ideal body weight
ICER	Incremental cost-effectiveness ratio
ICU	Intensive care unit
IDPN	Intradialytic parenteral nutrition
IF	Intestinal failure
INS	International nutrition survey
IV	Intravenous
LBW	Low birth weight
LBM	Lean body mass
LOS	Length of stay (in hospital)
MAMC	Mid arm muscle circumference
MCB	Multichamber bag
MUAC	Mid upper arm circumference
MNA	Mini nutritional assessment
MNA-SF	Mini nutritional assessment-short form
'MUST'	'Malnutrition universal screening tool'
MNI	Medical nutrition international industry
MOS SF-36	Medical outcomes survey short-form 36
NHS	National health service
NICE	National institute for health and clinical excellence
N/R	Not reported
NRI	Nutritional risk index
NRS-2002	Nutrition risk score 2002
ONS	Oral nutritional supplements
ONCA	Optimal nutritional care for all campaign
OR	Odds ratio
PDPN	Peridialytic parenteral nutrition
PICC	Peripherally inserted central catheter
PICU	Paediatric intensive care unit
PN	Parenteral nutrition
PS	Performance status
QOL	Quality of life
QALY	Quality adjusted life year
RBP	Retinol-binding protein
RDBPCT	Randomised double blind placebo controlled trial
RCT	Randomised controlled trial
RNI	Reference nutrient intake
RR	Relative risk
SBS	Short bowel syndrome
SCCM	Society of critical care medicine
SD	Standard deviation
SGA	Subject global assessment
SGNA	Subjective global nutritional assessment
SPN	Supplemental parenteral nutrition
TPN	Total parenteral nutrition
TSFT	Triceps skin fold thickness
UC	Ulcerative colitis
VLBW	Very low birth weight
WFA	Weight-for-age
WFH	Weight-for-height
WHO	World health organization

Executive summary

IDENTIFYING MALNUTRITION

'Malnutrition' includes both over-nutrition (overweight and obesity) as well as under-nutrition, but in the context of this report 'malnutrition' (and disease-related malnutrition) is used to mean under-nutrition and nutritional risk. Severe malnutrition may be clinically obvious but as uncertainty exists in detecting lesser degrees of malnutrition, screening for nutritional risk should be used to identify those individuals who are at risk of adverse outcome and who might benefit clinically from nutritional support. Despite the availability of screening tools, malnutrition still often goes undetected and thus untreated in hospitals, care homes and in people living in their own homes all across Europe and other parts of the world. Often less than 50% of patients identified as malnourished receive nutritional intervention. The opportunity for early identification and appropriate management of malnutrition or risk of malnutrition is therefore often missed.

PREVALENCE OF MALNUTRITION

Based on work done in the UK (showing > 3 million adults are at risk of malnutrition) and extrapolated to the rest of Europe, an estimated 20 million adults are at risk of malnutrition in the European Union (EU) and 33 million adults are at risk across Europe. Malnutrition is widespread in all healthcare settings; about 1 in 4 adult patients in hospital and more than 1 in 3 patients in care homes are malnourished or at risk of malnutrition. As many as 1 in 3 older people living independently are at risk. Almost 1 in 5 children admitted to Dutch hospitals has acute or chronic malnutrition.

CAUSES OF MALNUTRITION

Malnutrition is primarily caused by insufficient dietary intake with disability and disease at the heart of the problem. Food intake is often reduced because of the effects of disease and its treatment, for example poor appetite, swallowing problems and the side effects of drugs. Patients with cancer may have taste changes or nausea due to treatment and patients with neurological conditions or following a stroke may not be able to swallow or feed themselves. More than 50% of patients in hospital don't eat the full meal they are given and 30% of nursing home residents eat less than half their lunch, meaning that patients often fail to meet their nutritional needs. But there is more to malnutrition than poor food intake. Lack of a clear description of responsibilities for health authorities, institutions, and healthcare workers, and inadequate training and equipment for screening exacerbates the problem of malnutrition. Therefore a multi-disciplinary approach is needed to identify and implement appropriate and effective solutions.

CONSEQUENCES OF MALNUTRITION

Malnutrition leads to far-reaching physical and psycho-social consequences such as impaired immune response, impaired wound healing, reduced muscle strength and fatigue, inactivity, apathy, depression and self-neglect. In children, growth and development is adversely impacted by malnutrition. Malnutrition has a particularly high adverse impact in the older person impairing function, mobility and independence. Malnutrition is also associated with poorer quality of life.

Malnourished hospital patients experience significantly higher complication rates than well-nourished patients and the risk of infection is more than three times greater. Average length of hospital stay may be increased by 30% in malnourished patients. In community patients malnourished patients visit family doctors more often and have more frequent hospital admissions than well-nourished patients.

FINANCIAL COSTS OF MALNUTRITION

As a result of increased morbidity and healthcare resource use, malnutrition is costly to the individual, to society and to the economy. The estimated cost of managing patients at risk of malnutrition in the EU is €120 billion and €170 billion across Europe. This estimate is based on economic evidence from the UK undertaken in 2005 showing costs for managing patients at risk of malnutrition exceed €15 billion. A recent update puts the figure at £19.6 billion for England alone so it is highly likely that the figures above are now a very conservative estimate of the true cost of malnutrition in Europe. The extra cost of treating a patient with malnutrition is 2-3 times greater than for a non-malnourished patient. Failure to address malnutrition risk appropriately puts unnecessary additional pressure on already constrained healthcare systems and leads to sub-optimal quality of care. The application of evidence-based nutritional screening programmes should help to address this.

CLINICAL BENEFITS OF MEDICAL NUTRITION

Good nutritional care is a vital part of overall care and includes screening for malnutrition and nutritional care planning which includes appetising and nutritious food and nutritional support such as oral nutritional supplements (ONS), enteral tube feeding (ETF) and parenteral nutrition (PN). Decisions about which form of nutritional support is most suitable for patients should take account of whether good quality evidence shows it to be effective. There is extensive, good quality clinical evidence that ONS are an effective and non-invasive solution to malnutrition in patients who are able to consume some normal food but not enough to meet nutritional requirements. ONS have proven nutritional, functional, clinical and economic benefits in both the hospital and community setting in a wide variety of patient groups. Meta-analyses show that ONS lead to weight gain, reductions in mortality, reductions in complication rates and reductions in the proportion of patients admitted or readmitted to hospital. Intervention with high-protein ONS has been shown to reduce overall readmissions by 30%. ETF is a life-saving technique without which patients with a functioning gut, who are unable to consume sufficient food and drink via the oral route to meet their nutritional needs, would die due to dehydration and starvation. Systematic reviews have shown a number of benefits of ETF such as improving nutritional intake in patients across healthcare settings; attenuating loss of body weight and lean tissue mass in hospital patients; improving body weight and lean tissue mass in patients in the community and improving growth in children in the community. ETF is associated with reductions in mortality and complications in hospital patients, including patients who are critically ill. PN is a life-sustaining therapy for patients who cannot be fed adequately and/or safely with ONS or ETF, such as those with, but not limited to, chronic intestinal failure (CIF). Home PN (HPN) is the cornerstone of treatment for adults and children with CIF resulting from benign or malignant disease. Because PN is a life-saving treatment for these patients, evaluation of its efficacy versus no nutrition support in randomized controlled trials (RCTs) is not possible. However, a number of RCTs and many prospective and retrospective observational studies have shown nutritional, functional, and clinical benefits with PN in different age groups, conditions, and healthcare settings. Higher protein and energy intake in critically ill patients is associated with significantly reduced in-hospital and 60 day mortality.

FINANCIAL BENEFITS OF MEDICAL NUTRITION

Potential cost savings as a result of reduced healthcare use have been demonstrated in patients supplemented with ONS and can be realised in both the hospital and the community setting. Economic modelling undertaken by NICE (2006 and 2012) showed ONS to be cost-effective as part of a screening programme.

Comprehensive systematic reviews have shown that managing malnutrition with ONS can produce **an average cost saving of around 10%** compared to standard care across a broad range of patient groups. Besides improving the well-being of patients, fighting malnutrition with ONS is an opportunity for healthcare providers to control costs. This is especially relevant in light of the ageing population and the high prevalence of chronic disease that adversely impacts nutritional status, which in turn contributes to increased cost burden. Controlling and managing malnutrition is an effective solution.

There is limited data available in the literature about the potential cost savings and cost-effectiveness of ETF across healthcare settings, from different countries and in particular in children. However, in England an economic evaluation of the use of nutritional support including ONS, ETF and PN ultimately saves rather than costs money (£119,000 – £432,000 per 100,000 depending on the model used) (See Section 3, Figure 3.14). The report highlights that it is necessary to make a commitment to invest money before the financial benefits can be reaped.

Published data about the potential cost savings and cost-effectiveness of PN across healthcare settings and in different countries are limited. However, PN has been shown to compare favourably with other supportive treatments used in the ICU (e.g., dialysis). Furthermore, timely use of PN in the ICU has also been shown to significantly reduce the total cost of acute hospital care. HPN is also likely to be cost-saving compared with hospital-based PN for many healthcare systems as it shortens length of hospital stay for patients who are ready to be discharged but who require intravenous nutrition.

MEDICAL NUTRITION AS AN INTEGRATED PART OF KEY GUIDELINES AND GOOD PRACTICE

Many national, international and professional guidelines exist that include ONS and ETF as an integral part of patient care. However, continued effort is needed to ensure guidelines are updated to reflect the evidence base, to integrate good nutritional care into guidelines for specific diseases (e.g. nutritional support as part of cancer care guidelines), and to ensure that these guidelines are embedded in practice. Consideration should be given to innovative ways to facilitate the sharing of good practice at local, national and international level.

Recommendations

The MNI is committed to supporting efforts to fight malnutrition.

OVER-ARCHING THEMES

In all aspects of the fight against malnutrition, from identifying malnutrition through to delivering the best care for individual patients in a cost-effective way, several key themes emerge. These are that there must be multi-stakeholder involvement at all levels, that awareness, training and education are central to success, that audit and quality improvement activities should be included in any initiative that strives to tackle malnutrition and that good practice should be routinely shared.

	Specific Recommendations
Identifying malnutrition	• National nutrition policy should be in place that addresses under-nutrition as well as obesity and overweight • Routine screening for vulnerable groups should be built into national nutrition policies and quality standards with audit and quality control measures included • Validated screening tools should be used to identify patients with malnutrition or risk of malnutrition • Appropriate equipment (weighing scales, stadiometers) should be made available to enable screening to take place • Agreement should be made about who is responsible for performing screening for malnutrition or risk of malnutrition • Evidence-based guidance (including nutritional care plans) should be used by healthcare workers to take action following screening and for monitoring
Prevalence	• A commitment should be made to systematically measure the prevalence of malnutrition and risk of malnutrition and the results widely disseminated • A common approach should be taken to measuring and documenting malnutrition and risk of malnutrition
Causes	• Evidence based approaches for nutritional care plans should be used, taking into account the causes of malnutrition, the objectives of intervention, and also environmental and practical constraints
Consequences	• Awareness should be raised about the wide ranging negative consequences of malnutrition for patients, for healthcare providers and for society in general • Evidence based screening programmes should be used to ensure that malnutrition and risk of malnutrition is identified early and appropriate action is taken to minimise its consequences
Benefits of Medical Nutrition	• Evidence is available that demonstrates the benefits of medical nutrition (ONS, ETF and PN) in a wide range of patient groups. This should be translated into practice to ensure that patients who need nutritional intervention receive it in a timely and appropriate manner
Guidance	• Guidance on managing malnourished patients or patients at risk of malnutrition should reflect current evidence and should provide health care providers and practitioners with clear and practical advice about how and when to use different forms of nutritional intervention, including ONS, ETF and PN
Good practice	• Examples of good practice should be shared widely to facilitate the implementation of nutritional guidelines and ensure best use of resources.

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1.1 IDENTIFYING MALNUTRITION

Summary

'Malnutrition' can include both over-nutrition (overweight and obesity) as well as under-nutrition, but in the context of this report 'malnutrition' (and disease-related malnutrition) is used to mean **under-nutrition and nutritional risk**.

Due to inadequate nutritional intake to meet requirements which frequently occurs in acute or chronic disease, an individual may move from a good nutritional status to frank malnutrition in a matter of weeks, months or years. Severe malnutrition may be clinically obvious but as uncertainty exists in detecting lesser degrees of malnutrition screening for nutritional risk should be used **to identify those individuals who are at risk of adverse outcome and who might benefit clinically from nutritional support**.

A variety of **nutritional risk screening tools** have been developed to help identify adults and children who are malnourished or at risk of malnutrition and in most cases the tool prompts the healthcare worker to take action, i.e. to conduct or refer for in-depth nutritional assessment and to put in place a nutritional care plan to ensure that the patient's nutritional needs are met. Generally nutrition screening tools follow the basic principles of measuring weight/height and/or Body Mass Index (BMI), weight loss over a prior period of time and recent appetite/food intake and are thus **easy to implement**.

Validated tools provide a **reliable** way for healthcare professionals to identify patients who are malnourished or at risk of malnutrition. It is important that the validity of a nutritional risk screening tool is considered when selecting a tool, along with other considerations such as the intended purpose of the tool, reliability and practical aspects of implementation. ESPEN recommends the following tools for use in specific healthcare settings: the 'Malnutrition Universal Screening Tool' ('MUST') in the community, Nutrition Risk Screening (NRS-2002) for use in hospitals and the Mini Nutritional Assessment (MNA) in older people. In some countries national approaches have been developed, for example in the UK 'MUST' is often used in hospital and community settings to aid continuity of care. In practice the selection of a screening tool may vary from guidelines due to practical issues or local preferences. A number of tools have been developed for use in children and work is underway to assess the most suitable tool.

Different measurement approaches explain at least in part large differences in reported values for prevalence of malnutrition and risk of malnutrition. Nevertheless, all evaluations of prevalence point in the same direction and highlight the enormous dimension of the issue.

Malnutrition is more than just weight loss. Abnormalities or deficiencies of specific micronutrients (vitamins, minerals and trace elements) are frequently associated with malnutrition. However, micronutrient deficiencies will not be identified when screening for nutritional risk, but should be taken into consideration during nutritional assessment and when planning nutritional care.

Despite the availability of screening tools, **malnutrition still often goes undetected and thus untreated** in hospitals, care homes and in people living in their own homes all across Europe and other parts of the world. Often less than 50% of patients identified as malnourished receive nutritional intervention.

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Conclusion

Although a variety of practical, validated screening tools are available for the identification of malnutrition and risk of malnutrition in children, adults and older people they are not universally employed across healthcare systems. This means that malnutrition continues to go undetected in patients in hospital, in care homes and in patients living independently. The opportunity for early identification and appropriate management of malnutrition or risk of malnutrition is therefore often missed.

Recommendations

The MNI is committed to supporting efforts to raise awareness of malnutrition and to fight malnutrition.

On the issue of **identification of malnutrition** the MNI makes the following recommendations:

Recommendation	Issues to consider
National nutrition policy should be in place that addresses undernutrition as well as obesity and overweight	• Nutrition policy should cover all age groups across all healthcare settings and provide a framework for a consistent approach to standards and quality improvement in nutritional care
Routine screening for vulnerable groups should be built into national nutrition policies and quality standards with audit and quality control measures included	• Vulnerable groups include patients admitted to hospitals, care homes, and under the care of community/general practitioners • A programme of regular audit and quality control should be implemented to ensure that screening is undertaken
Validated screening tools should be used to identify patients with malnutrition or risk of malnutrition	• Selection of appropriate screening tools should take account of factors including the patient group, the setting, practical implementation and validity of the tool • Guidance from professional societies and national authorities should be taken into account when selecting a suitable tool. In addition the possibility that the use of one tool across healthcare settings may facilitate continuity of care and comparisons across patient groups and care settings should also be considered
Appropriate equipment (weighing scales, stadiometers) should be made available to enable screening to take place	• The equipment used for screening should comply with relevant national guidance • Equipment should be regularly calibrated in line with national guidance
Agreement should be made about who is responsible for performing screening for malnutrition or risk of malnutrition	• A healthcare worker with the right knowledge and skills is well placed to undertake screening, but agreement is needed on exact roles and responsibilities. Health-care workers need to know what is expected of them • **Training** is a critical component of ensuring that healthcare workers have the knowledge and skills to undertake screening, and when and how to act upon the results of screening • **Appropriate documentation** of the results of screening and action planned and taken is critical for continuity of care and for audit and quality control activities.

1.1.1 What is malnutrition and how is it measured?

In adults and older people

Malnutrition can be defined as a 'state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease'.[1; 2] Some definitions of malnutrition include over-nutrition (overweight and obesity) as well as under-nutrition[3], but in the context of this report 'malnutrition' is used to mean under-nutrition and nutritional risk. Malnutrition can occur due to a number of reasons alone or in combination, and is illustrated well in the ESPEN diagnoses tree of malnutrition which depicts the different types of malnutrition based on aetiology (Figure 1.1).[2]

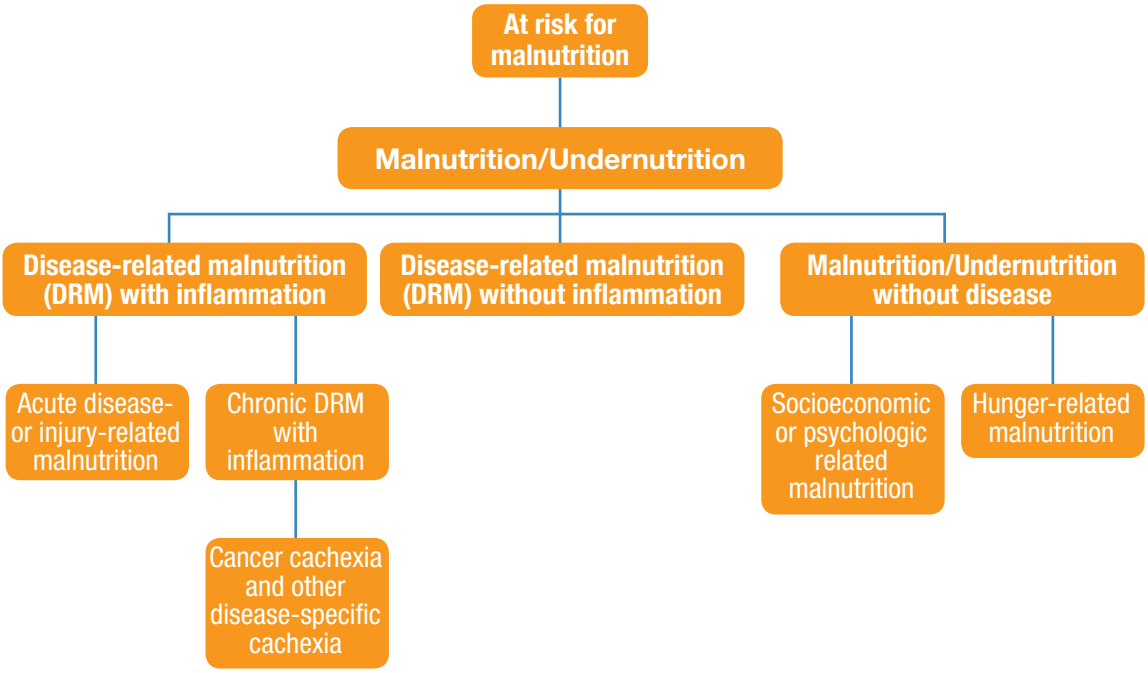

Figure 1.1 **ESPEN Diagnoses tree of malnutrition** (adapted from Cederholm et al. 2016)[2]

The presence and degree of malnutrition is established using 'nutritional assessment', a detailed, specific and in-depth evaluation undertaken by a competent health professional, which should be undertaken using a variety of measures and repeated at regular intervals to identify trends for an individual over time. A variety of methods of assessment are commonly used, ranging from simple 'eyeball assessment' to more complex measures, e.g. anthropometric or biochemical measures. No single measure should be used in isolation, and a number of important factors should be considered during nutritional assessment (see Table 1.1).[2; 4]

Table 1.1 **Factors that should be considered during nutritional assessment**
(adapted from Thomas 2007 and Cederholm et al 2016)[2; 4]

Clinical considerations	Impact of acute or chronic illness, surgery or treatment, e.g. medication
Physical state	Physical appearance (thin, pale, loose clothing), mobility, breathlessness, poor wound healing, oedema, weight loss
Social and psychological history	Impact of living conditions, loneliness and depression
Dietary aspects	Current intake, recent changes in intake, identifying factors which may affect food and fluid intake, nutritional requirements including energy, protein, fluid and micronutrient needs
Anthropometric measures	Body weight, height, adiposity (waist circumference, body mass index [BMI], skinfold thickness), muscle mass (mid-arm muscle circumference [MAMC], grip strength), estimates of water content and body composition
Biochemical and haematological markers	Detailed knowledge is essential as some markers are dynamic, changing on a daily basis, and influenced by disease and age. Useful for specific nutrients, e.g. vitamin B_{12} or iron deficiency in anaemia

In children

Inadequate growth in early childhood has been described as failure to thrive,[5] and more recently as faltering growth.[6] Under-nutrition is accepted as the primary cause of poor growth in infancy. Although no agreed consensus exists for the definition of faltering growth,[7] in practice, abnormal growth patterns such as a fall across centiles, plateauing or fluctuating weight should trigger further assessment.[6] Prompt identification of faltering growth is a prerequisite for effective management; infants and children who have faltering growth should receive immediate nutritional evaluation and intervention.[5] See footnote to Table A1.8, Appendix I for details of criteria for classification of malnutrition in children.

The general principles for nutritional assessment described in Table 1.1 also relate to children; however, extra factors to consider include feeding behaviour and feeding skill development, growth evaluation, including the determination of target height, family viewpoint regarding nutrition and feeding, and maternal nutritional status if feeding an infant.[4] UK and international charts are available for height, weight, head circumference, BMI and waist circumference. As growth is an important measure of health and well-being, the World Health Organization (WHO) published Child Growth Standards for infants and children up to the age of 5 years in 2006 and for 5-19 year olds in 2007. Based on the growth of healthy breastfed children in optimal conditions in 6 countries, these standards describe optimum growth rather than average growth. The standards have been implemented in a number of countries, including the UK in 2009.[8]

1.1.2 What is nutritional risk and how is it measured?

In adults and older people

Due to lack of adequate nutrition, acute or chronic disease and/or treatment, an individual may move from a good nutritional status to frank malnutrition in a matter of weeks, months or years. Severe malnutrition/emaciation may be clinically obvious, but as uncertainty exists in detecting lesser degrees of malnutrition (due to the lack of universally agreed criteria), the concept of 'risk' is useful.[9] Malnutrition risk is defined as 'a measure of the likelihood that malnutrition is present or likely to develop'[9] and is in itself a condition related to increased morbidity and mortality.[2] Therefore establishing malnutrition risk aims to identify those individuals who are at risk of adverse outcomes and who might benefit clinically from nutritional support.[10]

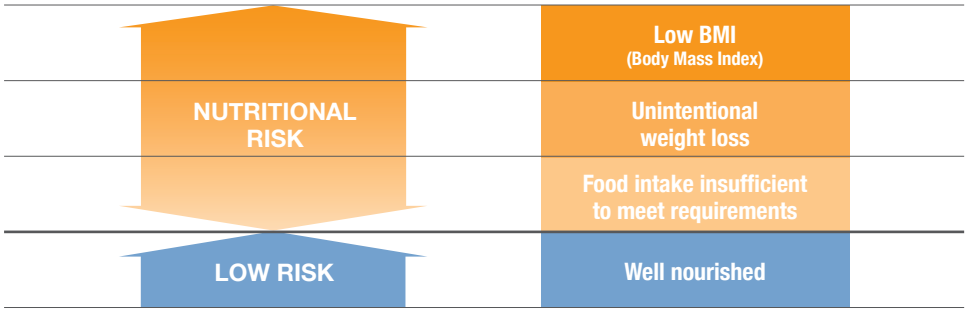

Figure 1.2 The concept of nutritional risk

Reflecting common practice, in this report the term 'malnutrition' is used synonymously with under-nutrition and nutritional risk.

Nutritional risk is of relevance because:

- it is widespread, particularly in patients admitted to hospital, residents in care homes, and people receiving community care;
- it has severe clinical consequences: weight loss, functional impairments, impaired quality of life, increased complications, and higher mortality;
- it results in economic consequences from increased consumption of healthcare resources due to management of complications, prolonged length of stay in hospital, increased readmission to hospital, need for community care, and thereby increased costs;
- it is frequently under-recognised and therefore under-treated;
- it is particularly common in the older person. Given that the population is aging (the number of older people in Europe aged 65–79 years will increase by 37.4% by 2030)[11] and that the problem is often unrecognised, this means that the costs to healthcare systems are likely to escalate at an unprecedented rate due to adverse clinical consequences.

Screening can be defined as 'an initial brief evaluation, which often precedes an in-depth and more accurate evaluation, of those considered to be at risk of a particular disease or condition'.[9] Table 1.2 summarises the main differences between nutritional screening and nutritional assessment.

Table 1.2 **Summary of the main differences between nutritional screening and nutritional assessment** (adapted from Elia 2003)[9]

Nutritional screening	Nutritional assessment
• Simple, quick, reliable, sensitive, reproducible	• Detailed evaluation of nutritional status and nutritional needs
• Identifies those likely to have or develop nutritional problems and classifies them, e.g. as medium- or high-risk	• Ideally performed in patients identified as medium- or high-risk through screening
• Typically based on current weight, history of weight loss and/or food intake/appetite/acute disease effect (i.e. severity of disease)	• Ideally performed by a dietitian/nutritionist or other trained healthcare professionals
• Able to be performed by other healthcare workers who have received appropriate training	• The results of nutritional assessment are used by healthcare professionals to establish the presence of and degree of malnutrition and to plan appropriate nutritional intervention
• Able to guide other healthcare workers who have received appropriate training to an appropriate course of action	

The act of regular nutritional screening applies a test to a whole population (e.g. on admission to hospital or a nursing home) to identify individuals who are 'at risk' of malnutrition to ensure that timely and appropriate nutritional care is provided. Figure 1.3 illustrates that nutritional screening is intended to identify individuals who are 'at risk' of malnutrition across the spectrum of nutritional status. An 'at risk' status may result from the effects of disease or treatment, or it may arise in a well-nourished individual due to an acute event such as sustaining an injury or undergoing emergency surgery that will result in no nutritional intake for a period of time. Individuals identified as high-risk are likely to be, but are not necessarily, frankly malnourished, although a more detailed nutritional assessment should be undertaken for 'at risk' individuals to establish the degree of malnutrition present, its causes, and the best course of action.

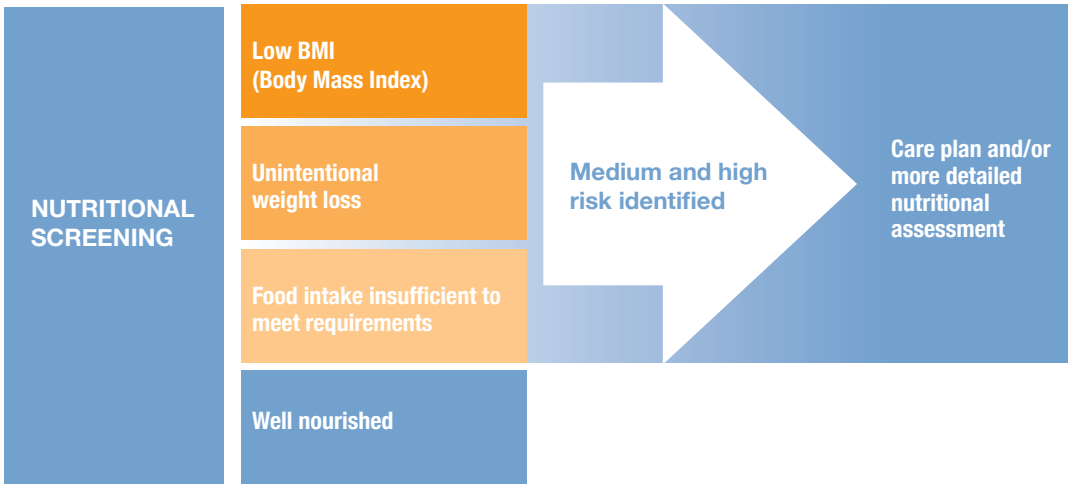

Figure 1.3 **Individuals identified as 'at-risk' of malnutrition through nutritional screening may have different degrees of malnutrition**

Different screening tests or tools use different criteria and/or cut-off points and/or weightings to detect nutritional risk. Furthermore, some tools have been developed for specific purposes or settings, or for use by specific healthcare workers.[9; 12] This means that not all individuals identified as 'at risk' are at the same point on the malnutrition spectrum (this is true even if a single tool is used). Table 1.3 shows some examples of commonly used screening tools designed for use in adults or older people and summarises their main components.

Table 1.3 Summary of components included in nutritional risk screening tools specifically designed for use in adults or older people

Reference	Tool	Age group & healthcare setting	Anthropo-metric measures	Weight loss	Nutritional intake	Other	Linked to action plan
Elia 2003[9]	'MUST'*	Adults Multiple care settings	✔ (BMI**)	✔	✔	Acute disease effect	Yes
Kondrup et al. 2003[13]	NRS-2002	Adults + option for ≥ 70 yrs Hospital	✔ (BMI)	✔	✔	Severity of illness, age	Prompts user to initiate a care plan
Rubenstein et al. 2001[14]	MNA-SF†	Older people Multiple care settings	✔ (BMI or calf circumference)	✔	✔	Mobility, acute disease/physical stress, neuropsyc-hological problems	Yes
Kruizenga et al. 2005[15]	SNAQ¥	Adults Hospital	-	✔	✔	Use of ONS or tube feeding	Prompts nutritional intervention
Ferguson et al. 1999[16]	MST	Adults Hospital	-	✔	✔	-	Yes
Jeejeebhoy et al. 1990[17]	SGA***	Adults Hospital	-	✔	✔	GI symptoms, functional capacity, underlying disease state, physical exam	No

*'Malnutrition Universal Screening Tool' ('MUST') – suitable for use across healthcare settings, see **http://www.bapen.org.uk/musttoolkit.html** for more information. **Alternative measures and subjective criteria can be used if unable to measure height/weight. †Mini Nutritional Assessment Short-form. MNA fulfils the function of both nutritional screening and assessment. See **www.mna-elderly.com** for more information. ¥SNAQ^{RC} available for use in older people in care homes or residential care and SNAQ^{65+} for patients in the community aged ≥ 65 years, see **http://www.fightmalnutrition.eu/malnutrition/screening-tools/** for more information. ***Subjective Global Assessment.

Use of specific screening tools varies by country, and the nutritionDay survey showed that screening was most often performed using locally-developed tools.[18] Results from the 2010 British Association for Parenteral and Enteral Nutrition (BAPEN) Nutrition Screening Week in the UK showed that among care homes and hospitals using screening tools, 'MUST' was the most common tool used to screen for risk of malnutrition, potentially facilitating continuity of care within and between care settings and the comparison of prevalence rates across countries and settings.[19] It is important that the validity of a nutritional risk screening tool is considered when selecting a tool, along with other considerations such as the intended purpose of the tool, reliability and practical aspects of implementation.[10; 12]

In children

Growth in infancy and childhood is most commonly assessed by measuring weight-for-height (WFH) and height-for-age (HFA).[20] Anthropometric measures are rapid, inexpensive and non-invasive. Malnutrition can also be assessed as thinness (low BMI for age), as described by Cole et al. in 2007, where the thinness cut-off linked to 17 kg/m^2 is close to the wasting cut-off based on -2 z-scores.[21] However, no single anthropometric measure provides enough information to make a full assessment of nutritional status.[20] The use of anthropometric measures alone may underestimate the problem of malnutrition in hospitalised children or children with specific underlying diseases. Anthropometric measures will identify patients who are malnourished but not those who are 'at risk' of developing malnutrition.[22] On the other hand, clinician evaluation alone has also been shown to be inadequate for accurate assessment of nutritional status and for identification of severe malnutrition.[23]

In an effort to overcome these issues multi-component screening tools have been developed to identify children at risk of malnutrition, who should then undergo further assessment.

Tools to screen for risk of malnutrition specifically developed for use in children are available (see Table 1.4), and they usually take account of nutritional intake, presence and severity of disease and weight loss, and in some cases they include anthropometric measures. In most cases, the results of screening are linked to a care plan, management pathway or recommendations for nutritional intervention.[24; 25; 26; 27; 28]

Table 1.4 Summary of components included in nutritional risk screening tools specifically designed for use in children

Reference	Tool	Age group	Anthropo-metric measures	Weight loss	Nutritional intake	Other	Linked to action plan
Gerasimidis et al. 2010[24]	Paediatric Yorkhill Malnutrition Score (PYMS)	1–16 years	✔ (BMI)	✔	✔	Acute admission or condition effect on nutrition	Yes
Hulst et al. 2010[25]	STRONG$_{kids}$ Screening Tool Risk of Nutritional Status and Growth	> 1 month	-	✔	✔	Subjective clinical assessment High-risk disease	Yes
McCarthy et al. 2012[26]	Screening Tool for the Assessment of Malnutrition in Paediatrics (STAMP)	2–17 years	✔ (Height, weight)	Compare with growth charts	✔	Diagnosis	Yes
Secker and Jeejeebhoy 2007[27]	Subjective Global Nutritional Assessment (SGNA) for children	31 days –17.9 years	History from parents	History from parents	History from parents	History of GI symptoms, and functional capacity	Not specified
Sermet-Gaudelus et al. 2000[28]	Paediatric Nutritional Risk Score	> 1 month	-	-	✔	Pain Pathological condition	Yes

Assessing nutritional status and nutritional risk in children with specific diseases

Specific growth charts have been developed to take account of the differences in expected growth in children with a variety of underlying diseases (e.g. cerebral palsy, Down's syndrome, Duchenne muscular dystrophy).[20] These growth charts can be used in some cases to ensure that a more appropriate assessment of nutritional status is undertaken; however, in cerebral palsy for example, the growth charts are used to plot current growth rather than optimal growth. Screening tools for use in children with specific conditions have also been developed, e.g. cystic fibrosis.[29]

Different measurement approaches explain at least in part large differences in reported values for malnutrition

- As described above, measuring frank malnutrition using nutritional assessment techniques and screening for nutritional risk are different; however, in the published literature, prevalence rates reported for 'malnutrition' are not always clearly separated in this way.

- The use of anthropometric measures alone may underestimate the extent of nutritional risk. Anthropometric measures will identify patients who are malnourished but not those who are 'at risk' of developing malnutrition.

- In a study of the prevalence of malnutrition in children on admission to hospital (n = 1571) using the PYMS tool, 46% of the patients at high risk of malnutrition had a normal BMI, illustrating the importance of using a malnutrition screening tool rather than BMI alone to assess malnutrition risk.[30] In the Dutch national survey among 424 hospitalised children the same message can be drawn: 8% of the children were scored as high risk, but of these children 47% were malnourished based on assessment of WFH and HFA.[25] In the Australasian Nutrition Care Day Survey undertaken in 2010 (acute care hospitals in Australia and New Zealand, n = 3122), 18% of the overweight/obese patients in the study (n = 299) (BMI > 25 kg/m^2) were assessed as malnourished (Subjective Global Assessment [SGA] B+C categories).[31]

- In children, although most reports include moderate and severe malnutrition when reporting prevalence figures, some reports include severe malnutrition alone, whilst others include mild malnutrition as well as moderate and severe malnutrition, leading to much higher figures. In other cases, details of the severity of malnutrition are not provided, making comparisons difficult (see Appendix I, Table A1.8).

- Some studies report either acute or chronic malnutrition or an overall figure which is either a simple addition of the two or reflects the use of a different method of screening or assessment which does not distinguish between acute and chronic malnutrition (see Appendix I, Table A1.8).

- It is interesting to note that some studies excluded patients who are likely to be at high risk of malnutrition, in particular studies in children:

  ~ Rocha et al. (2006) reported prevalence rates of between 6.9% and 18.7% (see Appendix I, Table A1.8 for details of classification) in children within 48 hours of admission to hospital. However, they excluded children with chronic liver or renal disease, surgical pathologies or cerebral palsy and children who were admitted to intensive care or oncology units during the study period;[32]

~ Hankard et al. (2001) reported a prevalence rate of 20% (BMI z-score below -2 SD, 12% when patients with anorexia nervosa were excluded) in children admitted to medical, psychiatric or surgical wards. The study design excluded patients receiving nutritional support, who represented 19% of the total number of patients admitted on the day of the survey. As these patients were receiving nutritional support, their nutritional status would be expected to be good if the treatment was adequate and effective; however, they would also most likely reflect the patients with a diagnosis which would place them most at risk of malnutrition.[33] Gerasimidis et al. excluded paediatric patients from cardiology, renal, orthopaedics and critical care;[24]

~ An Italian study of all children aged 1 month to 16 years admitted to a medical paediatric ward with Grade 1 conditions involving mild stress factors, such as admissions for diagnostic procedures, minor infection or minor surgery, reported a prevalence rate of 10.2% (BMI z-score below -2 SD). The study provides valuable data in this group of patients, but it should be used with care as patients with a hospital stay of > 72 hours and patients with chronic conditions were excluded.[34]

- Studies using nutritional risk screening tools specifically designed for adults and children or SGA report higher prevalence rates for malnutrition compared to studies that use anthropometric measures alone (see Section 1.2 – Prevalence of Malnutrition and Tables A1.1–A1.8 in Appendix I).

Where possible in this report, the term malnutrition is defined in relation to specific studies

Stratton et al. recommend that wherever the terms 'malnutrition' or 'at risk' of malnutrition are used, they should be defined or explained.[35] In practice, these terms and nutritional risk are often used interchangeably.

Where available, this report includes information on the type of screening test used, the criteria used to define nutritional risk/malnutrition, the patient groups and the clinical setting as reported in original texts to help to avoid confusion. In many cases, this information is included in the detailed tables in the Appendices.

Malnutrition is more than just weight loss

- Abnormalities or deficiencies of specific micronutrients (vitamins, minerals and trace elements) are frequently associated with malnutrition.[2] However, micronutrient deficiencies will not be identified when screening for nutritional risk, but should be taken into consideration during nutritional assessment and when planning nutritional care.

- Vitamin D deficiency is one of the most common nutrient deficiencies among older people.[36; 37] Low vitamin D levels (< 20 ng/ml) have been found in nearly 50% of independent community-dwelling older men and women.[38]

- Research findings in targeted population groups indicate that vitamin D deficiency is prevalent in 57% of medical inpatients, 49% of patients admitted to sub-acute rehabilitation facilities, and 23% (12% deficient, 11% severely deficient) of patients with gastrointestinal (GI) disease.[39; 40-41]

- Poor status of a range of micronutrients has been reported in the UK National Diet and Nutrition Survey (people aged 65 years and over), for example:[42]

  ~ 40% of older people (both free-living and institutionalised) had low biochemical status of riboflavin;

- ~ 40% of older people living in institutions and 15% of free-living older people had low status of vitamin C and folate;
- ~ 52% of older men and 39% of older women living in institutions had haemoglobin levels below the WHO cut-off for anaemia (13.0 g/dl for men and 12.0 g/dl for women);
- ~ 15% of older men and 7% of older women living in institutions had plasma zinc concentrations below 10 µmol/l indicating zinc deficiency.

- Plasma zinc and selenium levels below reference levels have been observed in hospitalised older patients with hip fractures and older people attending day care centres in the UK.[43]

Malnutrition still goes undetected and untreated across healthcare settings

Hospital inpatients

- As many as 40% of patients found to be at risk of malnutrition in a Danish hospital had not been screened for nutritional problems.[44]
- Rasmussen et al. (2004) found that nearly 40% of patients in Danish internal medicine, GI and orthopaedic surgery departments were at nutritional risk, and that two-thirds did not have a nutrition care plan or monitoring of dietary intake.[45]
- A prospective study of 395 newly admitted patients to general medical wards in a Dutch hospital revealed that nutritional assessment and intervention were not sufficiently applied by any professional (doctor, medical student, nurse) at any stage of the pre-, actual- and post-hospitalisation period.[46]
- A study in a major tertiary teaching hospital in Australia found that despite 30% of patients being identified as malnourished and 61% at risk, there was poor documentation by staff of two key risk factors (recent weight loss in 19% and appetite in 53% of cases), and even poorer evidence of referral for dietetic assessment in these cases (7% and 9% respectively).[47]
- A cross-sectional survey of 2,094 patients in 140 Belgian hospital wards for older people found a suboptimal implementation of nutritional care practices, such as:[48]
  - ~ 56% of wards did not undertake nutritional screening or assessment at admission;
  - ~ 86% of wards did not have a nutrition protocol;
  - ~ only 31% of wards used a standardised nutritional screening tool.
- In one UK hospital, only 69% of patients were screened for malnutrition on admission, with only 45.2% of high-risk patients appropriately referred to dietetic services. In almost 40% of high-risk cases, no action was taken.[49]
- In the 2011 UK Nutrition Screening Week Survey, most hospitals reported that in spite of a screening policy being in place (99%), weighing (assessment of body weight on admission) on all wards was carried out in only 67% of the hospitals surveyed, although this has improved from 49% in 2007 (Figure 1.4).[50]

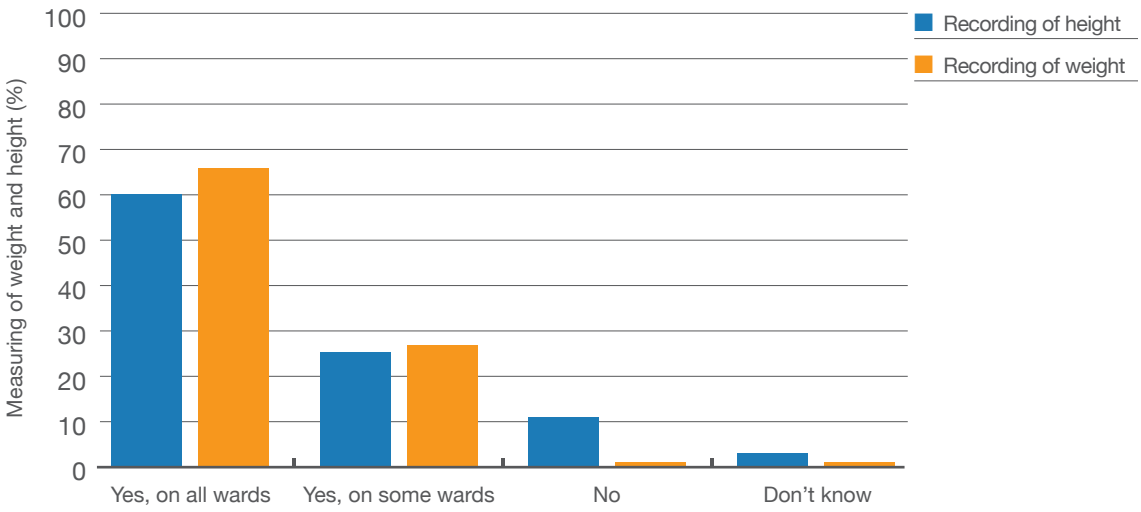

Figure 1.4 **Measurement of height and weight in UK hospitals participating in the National Nutrition Screening Week Survey in 2011** (adapted from Russell & Elia 2012)[50]

- A prospective cohort study of newly admitted adult patients (18–74 years of age) to an acute tertiary hospital in Singapore found that only 3 of the 235 malnourished patients (SGA B+C) were coded as such, illustrating that the majority of malnourished patients are either not recognised or that the presence of malnutrition is not documented.[51]

- An analysis of over 1.5 million patients from the Minimum Basic Data Set from Spanish hospitals identified only 1.4% with malnutrition, a much lower prevalence than in published studies within Spanish hospitals and hospitals in other countries across the world (see Table 1 in Appendix 1, Figure 1.8); the authors suggested that this low number was due to low communication of malnutrition in discharge reports.[52]

- A retrospective analysis of data from 2013 and 2014 from the department of internal medicine from a university hospital in France (8541 hospitalisations, mean age 72.8±16.5 years) revealed that although the practice of nutritional screening (using NRS-2002) significantly increased (16.5% in 2013 v. 41.9% in 2014 [$p<0.001$]) less than half of patients identified as 'at-risk' of malnutrition actually received any nutritional management and that the proportion of 'at-risk' patients who received nutritional intervention decreased from 2013 to 2014 (46.9% v. 40.3% [$p<0.05$]).[53]

The community

- In a multi-centre survey of hospital outpatients in the Netherlands (n = 2288; 9 hospitals), only 17% of severely malnourished patients and 4% of moderately malnourished patients were referred to a dietitian.[54]

- In a Dutch study, nutritional interventions were applied in fewer than half of the malnourished patients identified across hospitals, nursing homes and patients receiving care in their own home. In fact, only 20% of patients in their own home received appropriate nutritional care.[55]

- In a large international multi-centre study (n = 3248; 49 care homes), despite screening on admission (undertaken more frequently in German [94%] than Dutch [88%] and Austrian [86%] care homes), fewer than 50% of all of the residents identified as malnourished received nutritional interventions (Germany 46%, Austria 40% and the Netherlands 46%).[56]

- An audit of the use of ONS in care homes in the south of England (*n* = 1176, 43 care homes) found that most residents identified as at risk of malnutrition did not receive ONS in the 4 weeks prior to the audit and none were under the care of a dietitian (39% of residents malnourished [medium and high risk], 8.2% of all residents received ONS). Further work is needed to establish whether other forms of nutritional support are used.[57]

- A cross sectional study of nutritional care in 19 care homes (*n* = 703; mean age 84 [range 27-104 years]) in Peterborough in the UK showed that although 32% were found to be at risk of malnutrition ('MUST' 13% medium + 19% high risk) the majority (64%) of patients at high risk were not receiving any form of nutritional support including food fortification, ONS or dietetic care.[58]

- In a community hospital in Germany, 75% of patients who were judged by the attending physician to be malnourished did not receive nutritional support.[59]

- The medical records of malnourished patients in The Health Improvement Network (THIN) database (actual health record data from a representative range of National Health Service [NHS] General Practitioner [GP] practices across the UK) showed that only 35.5% of malnourished patients received some form of nutritional intervention (meaning that two–thirds received no intervention despite having been identified as malnourished).[60]

- In a study designed to describe the use of ONS in 926 nursing homes (n=23,689 residents aged ≥65 years) from 19 countries (96.3% from Europe, 3.7% from North America) participating in the nutritionDay project (cross sectional multicentre survey) only 42% of malnourished residents (nursing staff estimated nutritional status) received oral nutritional supplements (ONS) and only 1 in 3 (33%) of residents with low Body Mass Index and 1 in 5 (22%) of residents with previous weight loss received ONS.[61]

Malnutrition is often undetected and untreated in children

- Pawellek et al. (2008) found that almost 25% of children admitted to a paediatric hospital in Germany did not have combined height and weight data recorded, hampering efforts to identify children at risk of malnutrition.[62]

- A pilot study for The Children's Nutrition Survey examined the current nutrition and dietetic practices in paediatric centres across the UK and Ireland (*n* = 27; 7 specialist paediatric hospitals and 20 district general/single wards) and found that:[63]

  ~ most centres reported that they were not using a nutrition screening tool;

  ~ although the majority of centres measured weight on admission (> 85%), measurement of height was infrequently undertaken in hospitals with a nutrition support team/nutrition steering committee, and it appeared that it was not measured in hospitals without such a team (31% vs 0%) (see Figure 1.5).

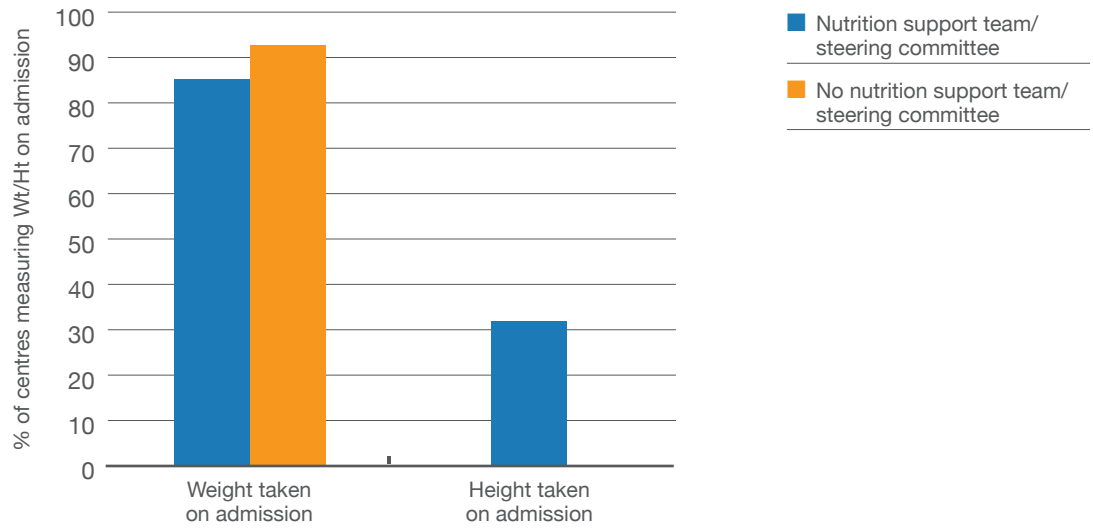

Figure 1.5 **Current nutrition-related practices in paediatrics throughout the UK and Ireland: results for measurement of weight and height on admission** (adapted from Carey et al. 2010)[63]

- In France, a study of the prevalence of malnutrition in hospitalised children aged between 2 months and 16 years (*n* = 280) showed that only 30% of malnourished children were identified.[64]
- Only 50% of children identified as malnourished in a cross-sectional survey in France had been referred to a dietitian on the day of the study.[33]
- A cross-sectional analysis undertaken at the time of enrolment of children and adolescents with Crohn's disease in a trial of initiating therapy with either thiopurine or infliximab established that 36% of severely underweight patients did not receive a multi-vitamin supplement, supplemental formula or tube feeding.[65]

Inconsistent nutrition-related practices are widespread in centres that care for children

- A pilot study for The Children's Nutrition Survey examined the current nutrition and dietetic practices in paediatric centres across the UK and Ireland (*n* = 27; 7 specialist paediatric hospitals and 20 district general/single wards) and found that:[63]
  - ~ less than half (48%) had a nutrition support team or nutrition steering committee;
  - ~ only 6 centres (22%) routinely included nutrition-related information in the discharge plan;
  - ~ audits of nutrition practices, implementation of referral criteria, and staff training on nutrition topics were not consistently undertaken across centres (see Figure 1.6).

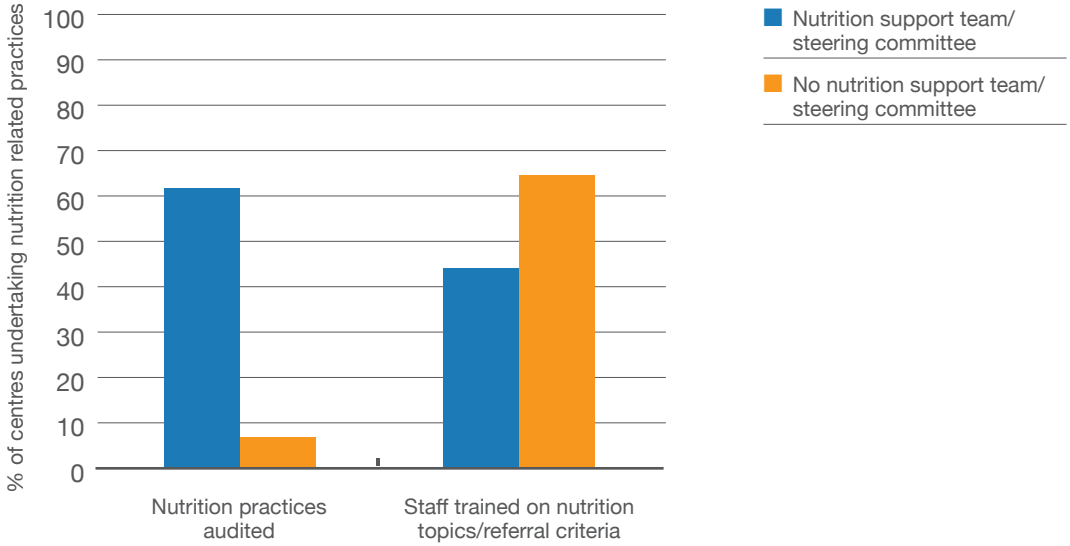

Figure 1.6 **Current nutrition-related practices in paediatrics throughout the UK and Ireland** (adapted from Carey et al. 2010)[63]

- A nationwide survey (USA) of 125 institutions (54% response rate) found no consistency in the provision of nutritional services in paediatric oncology, a group of patients at high risk of malnutrition. Many institutions fail to undertake nutritional assessments at critical time points during care, do not use screening tools to identify patients at risk of malnutrition, and have no criteria for intervention (see Figure 1.7).[66]

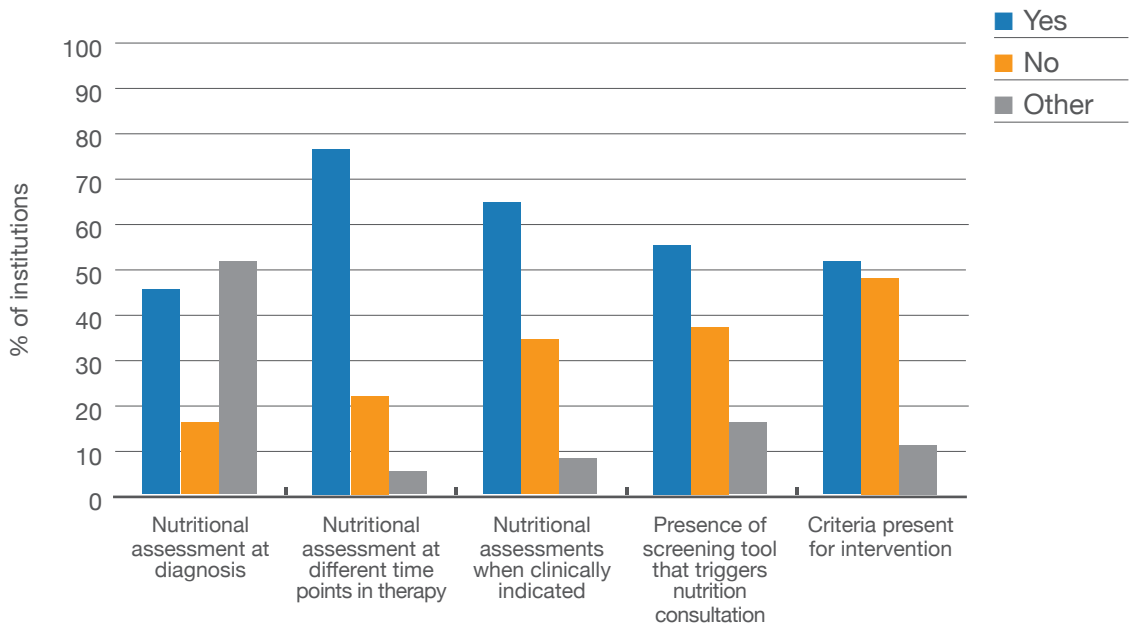

Figure 1.7 **Standards of nutritional care in paediatric oncology: results from a nationwide survey** (adapted from Ladas et al. 2006)[66]

Continuity of care

- The UK Nutrition Week Survey undertaken in winter 2010 also highlighted that although the results of screening were linked to a care plan in 9 out of 10 hospitals surveyed, less than half always or usually included nutritional information in discharge letters, potentially affecting continuity of nutritional care.[67]

1.2 PREVALENCE OF MALNUTRITION

Summary

Malnutrition is not a new problem and with an ageing population it continues to be a **major public health concern**. It is not confined to developing countries, but is **highly prevalent in the European healthcare system and in other developed regions**.

Based on work done in the UK (showing > 3 million adults are at risk of malnutrition) and extrapolated to the rest of Europe, an estimated **20 million adults are at risk of malnutrition in the European Union (EU) and 33 million adults are at risk across Europe**.

Malnutrition is prevalent across **all healthcare settings** particularly in patients in hospital and in institutions:

- Large-scale studies show that **about 1 in 4 adult patients in hospital** are at risk of malnutrition or are already malnourished.
- **More than 1 in 3 patients in care homes** are malnourished or at risk of malnutrition.
- As many as **1 in 3 older people living independently** are at risk.

Whereas many studies have addressed the prevalence of malnutrition in hospitals, the prevalence in the community setting has received less attention. Data from 2009 reveals that in the UK, 93% of the estimated 3 million people who are malnourished or at risk of malnutrition live in the community.

Malnutrition is prevalent **across all age groups**:

- In adults it is **particularly a problem in older people**. In the UK Nutrition Screening Week Survey in 2011, the risk was 30% greater in hospital patients aged 65 years and over than in those aged under 65 years (28% vs 21%, $p < 0.001$).
- **Almost 1 in 5 children** admitted to Dutch hospitals have acute or chronic malnutrition.

Malnutrition is common across a variety of **patient groups** e.g. **in patients with gastrointestinal, respiratory and neurological disease**. It is particularly prevalent in **people with cancer**, where rates of malnutrition have been found to be **twice as high** when compared with patients without cancer.

Conclusion

Many studies have been published in many different parts of the world using a variety of screening tools and techniques designed to estimate the prevalence of malnutrition and risk of malnutrition. The diverse methods that have been used at least partly explain the wide variability in reported prevalence rates. However, it is clear that all studies point to the same conclusion that malnutrition and the risk of malnutrition is very common in patients across the age range and across healthcare settings, and that it is of particular concern in older people.

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Recommendations

On the issue of **prevalence of malnutrition** the MNI makes the following recommendations:

Action	Issues to consider
A commitment should be made to systematically measure the prevalence of malnutrition and risk of malnutrition, and the results should be widely disseminated	• Measuring prevalence of malnutrition and risk of malnutrition is a key way of driving awareness of this important issue and calling for action, and should be considered in countries where this has so far not been done. The UK Nutrition Screening Week is an excellent example for countries to refer to
A common approach should be taken to measuring and documenting malnutrition and risk of malnutrition	• A common approach would be of great value to enable comparison of prevalence rates across healthcare settings and countries

Malnutrition is not a new problem

- A systematic analysis of a large number of studies reporting on malnutrition according to healthcare setting and clinical condition from as early as the 1970s revealed a prevalence of adult patients with a BMI of < 20 kg/m^2 of up to 60% in hospital and community settings across countries.[35]

- The analysis also showed that over 10% and up to 40% of children were at risk of malnutrition if WFH < 90% and HFA < 95% were used as the criteria.[35]

1.2.1 Hospital

One in four adult hospital patients is malnourished or at risk of malnutrition

- Despite differences in the age of subjects, there is consistent and overwhelming evidence that malnutrition is a widespread problem in hospitals across the world and that it is highly prevalent in affluent and developed societies (see Table A1.1 in the Appendix) (see Figure 1.8). Variation in prevalence figures may in part reflect the different methods that exist to detect malnutrition risk.

- Large-scale multi-centre surveys (n > 5000 in each study) show that about 1 in 4 (18–34%) adult hospital patients are malnourished or at risk of malnutrition[18; 50; 67-71] (see Table 1.5). In the winter 2010 UK Nutrition Screening Week Survey a prevalence of 34% was found in adult patients admitted to hospital; this higher figure may be related to a number of reasons, including a higher prevalence of malnutrition in patients with respiratory disease.[67]

- The nutritionDay Survey undertaken by 1,217 units from 325 hospitals in 25 countries (Europe and Israel; data collected on a single day in 2007 and 2008) included 21,007 adult patients and found that 27% of patients were classified as being at risk of malnutrition.[18] Similar results were found in the Australasian Nutrition Care Day Survey undertaken in 2010 (acute care hospitals in Australia and New Zealand, n = 3122), where 32% of adult hospital patients were found to be malnourished (combined number of malnourished patients identified by SGA [B+C categories] and BMI < 18.5 kg/m^2).[31]

- In smaller studies, rates of malnutrition and risk of malnutrition of up to 90% have been reported in adult hospital patients (see Table A1.1 in the Appendix) (see Figure 1.8).

Table 1.5 **Summary of large-scale studies of the prevalence of malnutrition and the risk of malnutrition in adult hospital patients** (*n* > 5000)

Country/ Region	Author (year)	Patients (*n*)	Timing of nutritional assessment/screening (data collection)	Prevalence %	Method of assessment/ screening
Europe and Israel	Schindler et al. (2010)[18]	21007	One day, cross-sectional (single day in 2007 & 2008)	**27**	Variety of tools used, including NRS-2002, 'MUST', national or local tools
Switzerland	Imoberdorf et al. (2010)[69]	32837	On day of admission	**18.2**	NRS-2002
The Netherlands	Meijers et al. (2009)[68]	8028	Cross-sectional, point prevalence on specified day	**23.8**	Based on BMI, weight loss and food intake*
UK	Russell & Elia (2012)[50]	7657	Within 72 hours of admission (spring 2011)	**25**	'MUST'
UK	Russell & Elia (2011)[67]	9669	Within 72 hours of admission (winter 2010)	**34**	'MUST'
UK	Russell & Elia (2009)[71]	5089	Within 72 hours of admission (summer 2008)	**28**	'MUST'
UK	Russell & Elia (2008)[70]	9336	Within 72 hours of admission (autumn 2007)	**28**	'MUST'

*See Table A1.1, Appendix I for further details of method

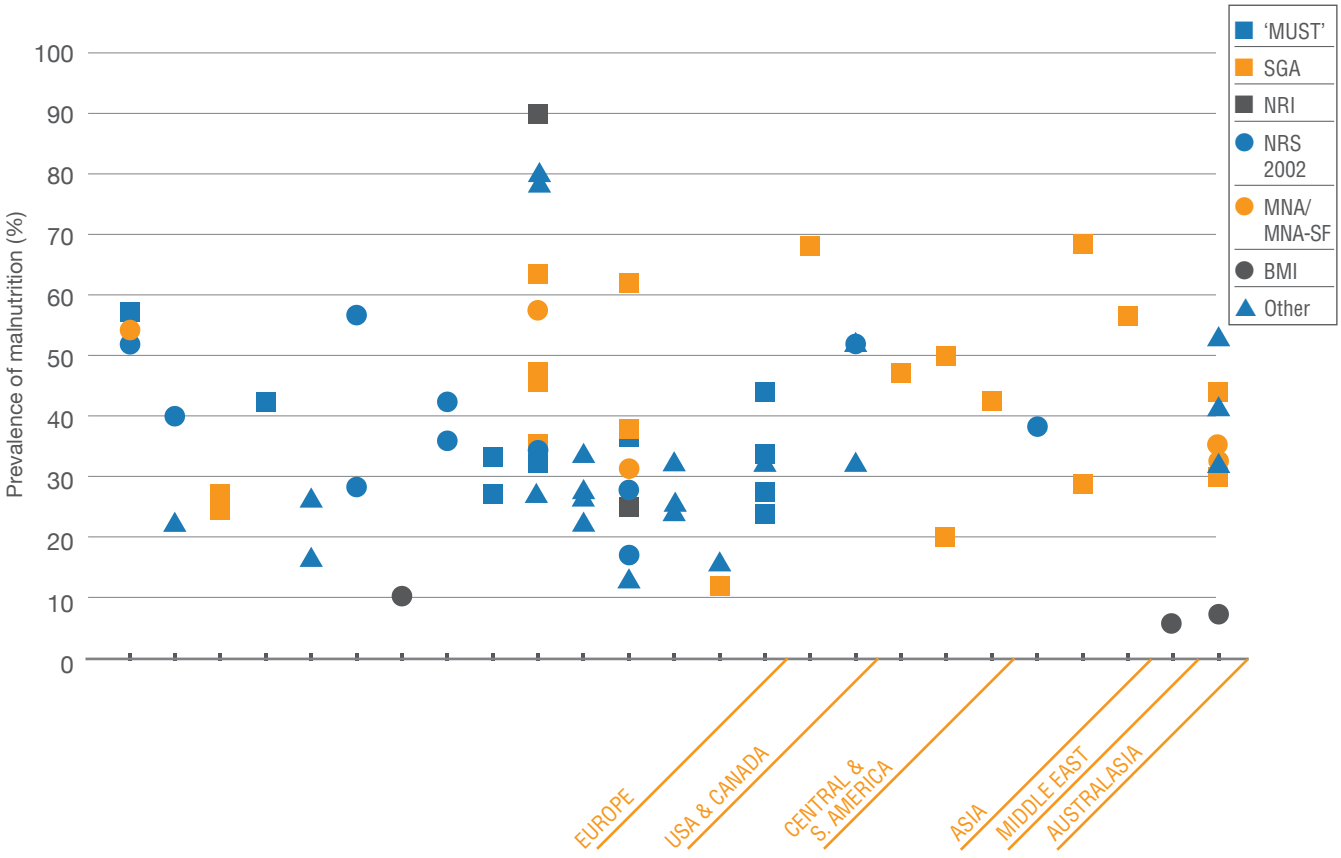

Figure 1.8 **Prevalence of malnutrition risk in adult hospital patients using different screening methods by country and world region**

(see Appendix I, Table A1.1 for full details)

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- Data from the Healthcare Cost and Utilisation Project (HCUP) statistical brief show that in 2013 nearly 2 million U.S. hospital inpatient stays involved malnutrition representing 7.1% of a total of nearly 28 million non-maternal and non-neonatal stays. The majority (63.9%) of the malnutrition-related stays were categorised as 'protein-calorie malnutrition'.[72]

Older people are at significantly higher risk of malnutrition

- Malnutrition affects all age groups but increasing age is associated with an increased risk of malnutrition.[50;67;69-71;73-81] Older people are vulnerable to malnutrition as they often have several co-morbidities that are often chronic and progressive.[82] In the UK Nutrition Screening Week Survey in 2011, the risk was 30% greater in patients aged 65 years and over than in those aged under 65 years (28% vs 21%, $p < 0.001$).[50]

One in three older people in hospital are malnourished or are at risk of malnutrition

- The prevalence of malnutrition and risk of malnutrition is high in older people in hospital (see Table A1.2 in the Appendix, Figure 1.9). In some studies, depending on the ward or method used, over 90% of older people were found to be malnourished or at risk of malnutrition.[47;48;59;83]

- Large-scale surveys ($n > 1000$) show that about 1 in 3 older people in hospital are malnourished (38.7%)[84] or are at risk of malnutrition (22–47.3%)[48;50;67;69-71;84] (see Table 1.6).

- In an Italian study, older hospital patients with mild cognitive impairment (MCI) ($n = 65$) and dementia ($n = 84$) were more likely to be malnourished than those with no cognitive impairment (NoCI) ($n = 439$) (dementia 59.5% vs NoCI 15%, $p < 0.001$ and MCI 44% vs NoCI 15%, $p < 0.001$).[85]

- A systematic review and meta-analysis of studies examining the prevalence of malnutrition in older people in the hospital setting ($n = 66$) (malnutrition was identified using the Mini Nutritional Assessment (MNA®) criteria), showed a prevalence of malnutrition (MNA <17 points) of 22% (95% CI, 18.9-22.5) and a prevalence of risk of malnutrition (MNA 17-23.5 points) of 45.6% (95% CI, 42.7-48.6). The authors highlighted that there was significant heterogeneity in individual study results.[86]

Table 1.6 **Summary of large-scale studies of the prevalence of malnutrition and risk of malnutrition in older people in hospital** (*n* > 1000; using a validated screening tool)

Country/ Region	Author (year)	Patients (*n*)	Timing of nutritional assessment/screening (data collection)	Prevalence %	Method of assessment/ screening
Europe†	Kaiser et al. (2010)[84]	1384	Not available	86 (47.3 at risk, 38.7 malnourished)	MNA
Belgium	Vanderwee et al. (2011)[48]	2094	Cross-sectional (between 16th May and 15th June 2007)	31.9	MNA-SF
Switzerland	Imoberdorf et al. (2010)[69]	See Table A1.2, Appendix I	On day of admission	22 (65–84 years) 28 (> 85 years)	NRS-2002
UK	Russell & Elia (2012)[50]	See Table A1.2, Appendix I	Within 72 hours of admission (spring 2011)	28	'MUST'
UK	Russell & Elia (2011)[67]	See Table A1.2, Appendix I	Within 72 hours of admission (winter 2010)	39	'MUST'
UK	Russell & Elia (2009)[71]	See Table A1.2 Appendix I	Within 72 hours of admission (summer 2008)	32	'MUST'
UK	Russell & Elia (2008)[70]	See Table A1.2, Appendix I	Within 72 hours of admission (autumn 2007)	30	'MUST'

†Retrospective pooled analysis of data from studies in older people in hospitals in Belgium, Switzerland, Germany, Italy and Sweden

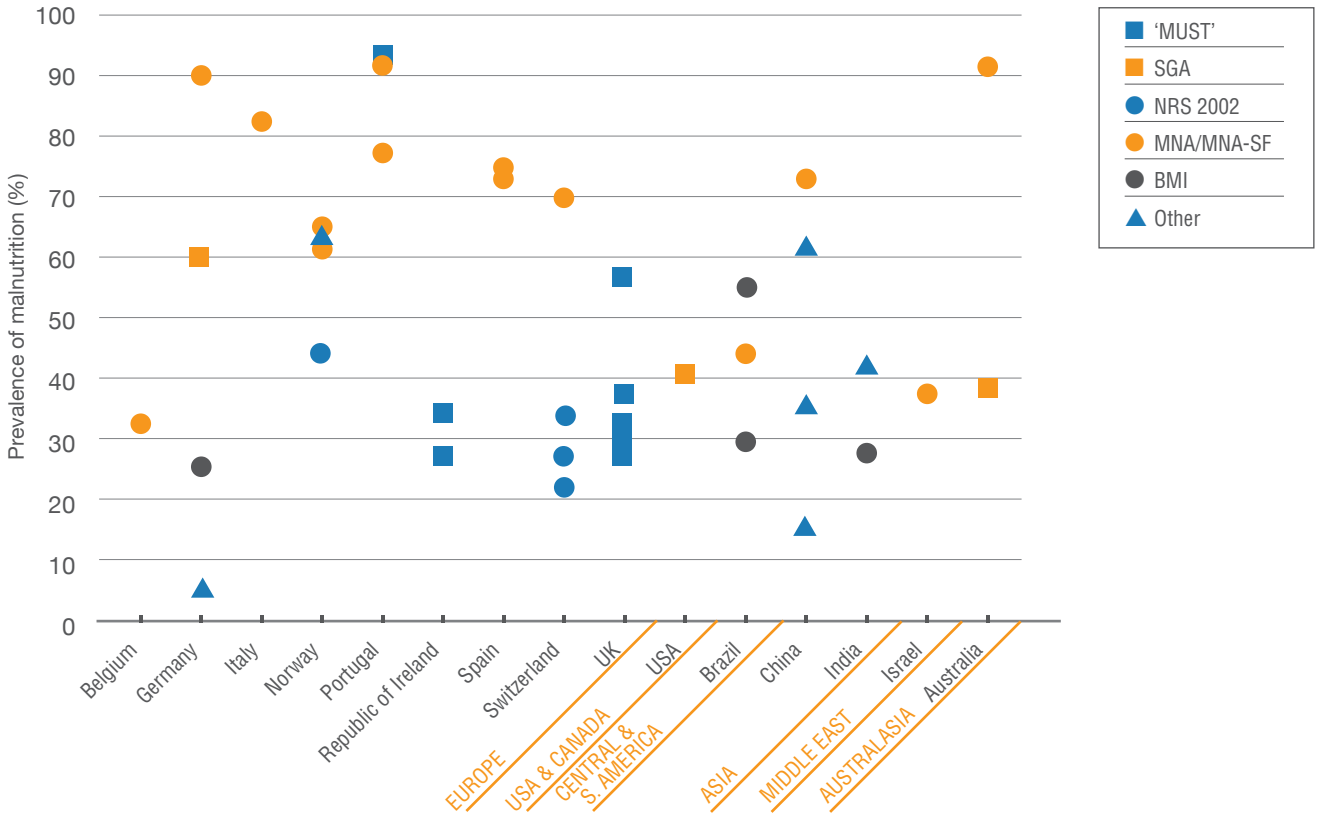

Figure 1.9 **Prevalence of malnutrition risk in older people in hospital using different screening methods by country and world region**

(see Appendix I, Table A1.2 for full details)

Malnutrition in children in developed countries

- Whilst childhood malnutrition is internationally recognised as a major public health problem in developing countries, especially those afflicted by poverty, war and famine, it is often assumed to be absent in affluent developed countries. Worldwide, under-nutrition is an underlying cause of 53% of all deaths in children younger than 5 years.[87] Underweight does exist in developed countries and it is projected to decrease from 1.6% in 1990 to 0.9% in 2015, a change of -41%.[88] However, although these figures appear low in comparison to developing countries, malnutrition and underweight is a significant problem in developed countries, particularly in children with underlying disease-related malnutrition, as illustrated by the high prevalence of malnutrition on admission to hospital.

Malnutrition and risk of malnutrition is common in children in hospital

- Malnutrition and risk of malnutrition has been reported in 2–85% of children in hospital (see Figure 1.10 and Table A1.8, Appendix I). The prevalence reported in the literature varies due to the different methods used for either screening for malnutrition risk or assessment of nutritional status, the criteria used to define malnutrition, how the results have been reported (whether they include mild, moderate and severe malnutrition or acute and/or chronic malnutrition), the type of population studied, and the disease spectrum of the subjects included or excluded from individual studies.

- Studies using nutritional risk screening tools specifically designed for paediatric populations or SGA report higher prevalence rates for malnutrition in children (18–85%)[24-28;89-90] compared to studies that use anthropometric measures alone, such as WFH, weight-for-age (WFA), % ideal body weight (IBW), BMI, TSFT and MUAC (2.5–52%)[32-34;62;64;90-99] (see Figure 1.10 and Table A1.8, Appendix I).

Data from large-scale national or regional surveys describing the prevalence of malnutrition risk in children on admission to hospital is emerging

- A large cross-sectional study (The Children's Nutrition Survey) undertaken in the UK and Ireland found a prevalence of malnutrition in children (mean age 5.7 years) of 11% (in terms of WFA ≤ 2 SD; timing of assessment not specified) ($n = 1003$). Thirty-one hospitals participated, 20 of which had nutrition support teams.[63]

- A prospective multi-centre cohort study investigating the prevalence of malnutrition risk in children on admission to hospital and the impact on outcomes is currently underway in 14 centres across 12 different European countries and it is being funded by ESPEN. The study also aims to arrive at an agreement on the preferred screening tool for identifying nutritional risk in children.

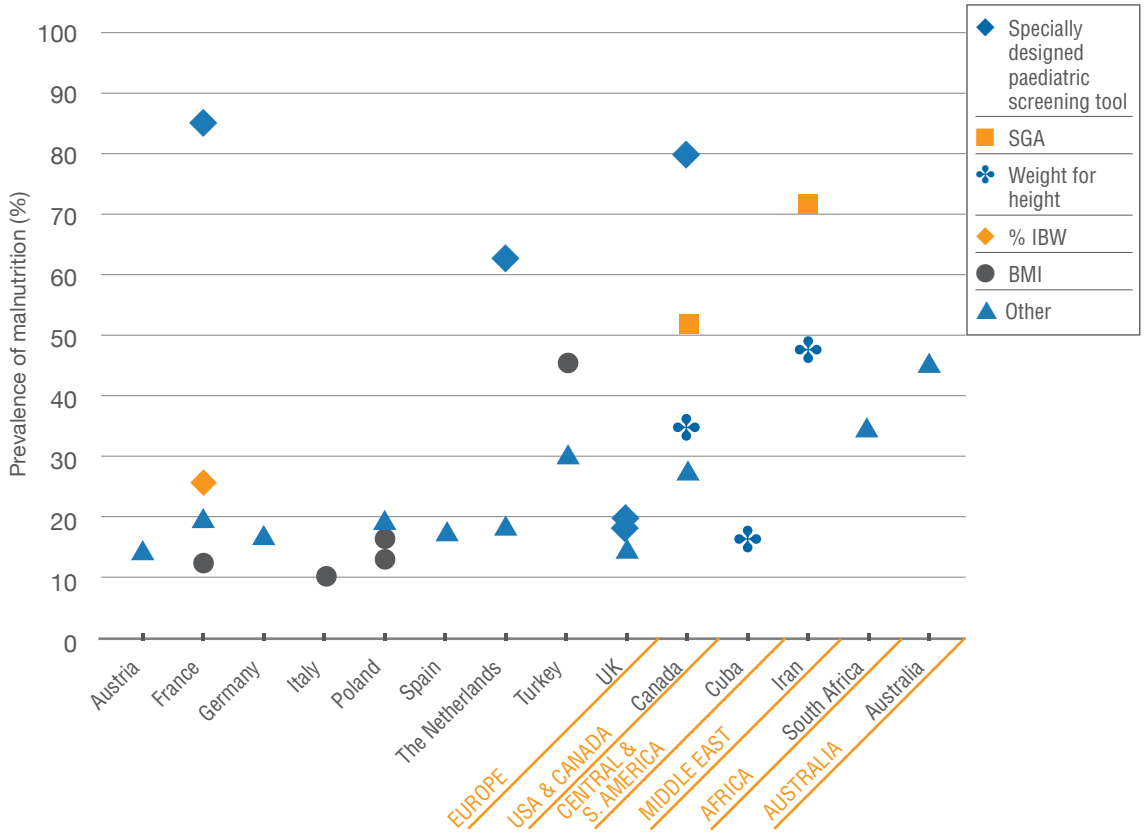

Figure 1.10 **Prevalence of malnutrition and risk of malnutrition in children in hospitals using different screening and/or assessment methods by country and region.**

(see Appendix I, Table A1.8 for full details)

Malnutrition and risk of malnutrition are common across a variety of hospital wards

- Malnutrition and risk of malnutrition are common across a variety of hospital ward types, with a particularly high prevalence in care of the elderly, oncology, respiratory, endocrine and gastroenterology wards/specialities (see Figure 1.11).[31;50;51;68;74]

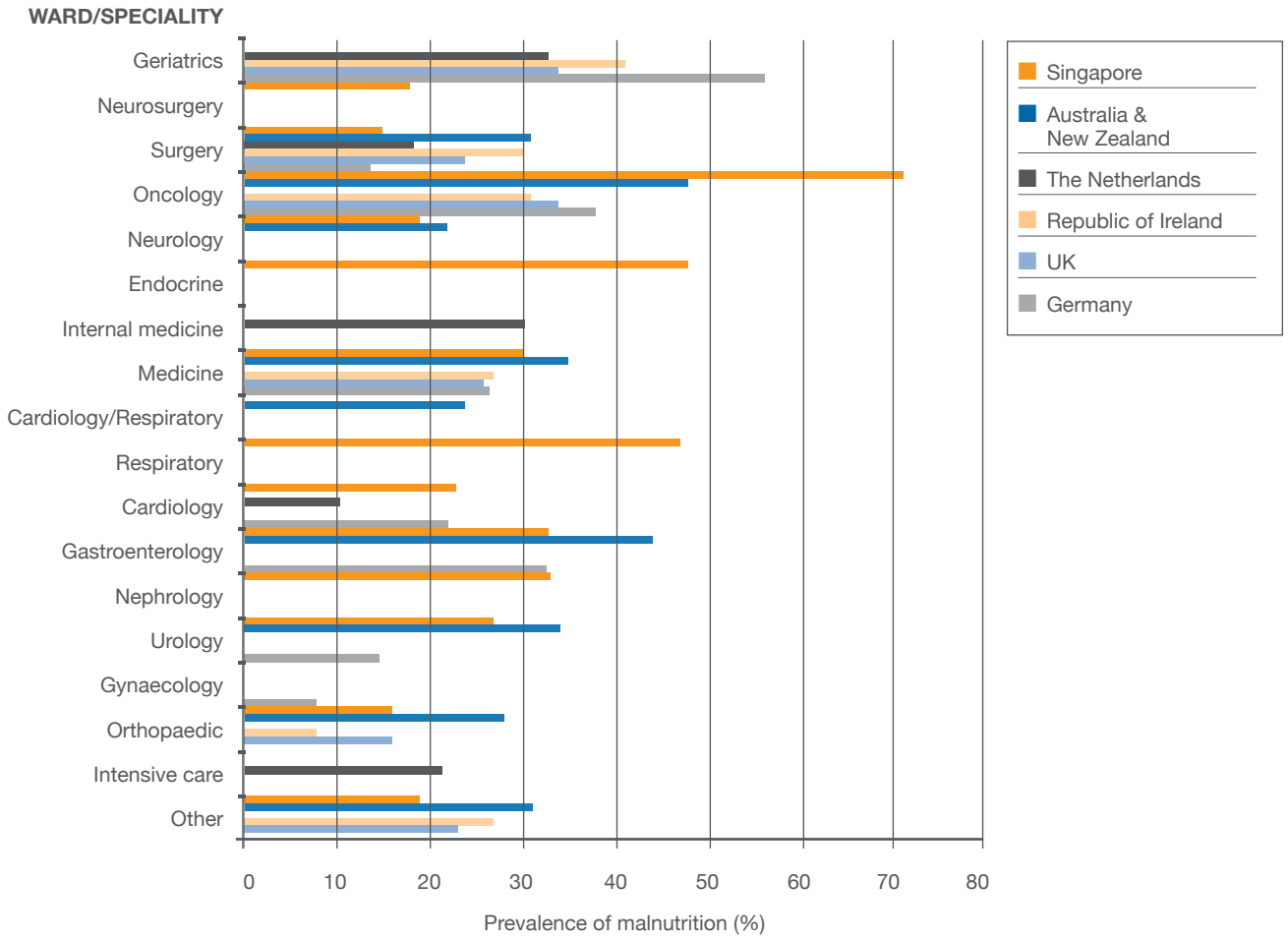

Figure 1.11 **Prevalence of malnutrition and risk of malnutrition according to hospital ward/primary admitting speciality**

(Singapore *n* = 818 [SGA B+C], Australia & New Zealand *n* = 3080 [SGA B+C & BMI], the Netherlands *n* = 8028 [defined by BMI, undesired weight loss, nutritional intake*], UK *n* = 7408 ['MUST' medium + high risk], Republic of Ireland *n* = 1090 ['MUST' medium + high risk], Germany *n* = 1886 [SGA B+C])[31;50;51;68;74]

(*see details in Table A1.1)

Malnutrition in children is more common in specialist wards and hospitals than in general units

- In hospitals in the Netherlands, a significantly higher rate of chronic malnutrition (HFA < - 2 SD) was found in children admitted to academic hospitals (14%) compared to general hospitals (6%), $p = 0.013$. This may reflect the nature of the cases seen at academic hospitals, where possibly more complex cases are managed.[92] Hulst et al. (2010) found that the distribution of risk categories differed between general and academic hospitals i.e.15% of children in academic hospitals were at high risk vs 5% in general hospitals ($p = -0.014$ for low vs high risk and $p < 0.001$ for moderate vs high risk).[25]

- Gerasimidis et al. (2011) found that a high risk of malnutrition was more prevalent in the specialist wards than the acute receiving wards of a tertiary paediatric hospital (18% in specialist vs 8.3% in acute receiving).[30]

Malnutrition and risk of malnutrition is prevalent in a wide variety of diseases in adults

- Recent large-scale multi-centre surveys consistently show that malnutrition risk is common across many diagnostic groups in hospitals, with a particularly high prevalence in patients with GI, respiratory and haematological disease and cancer (see Figure 1.12).[50;68]

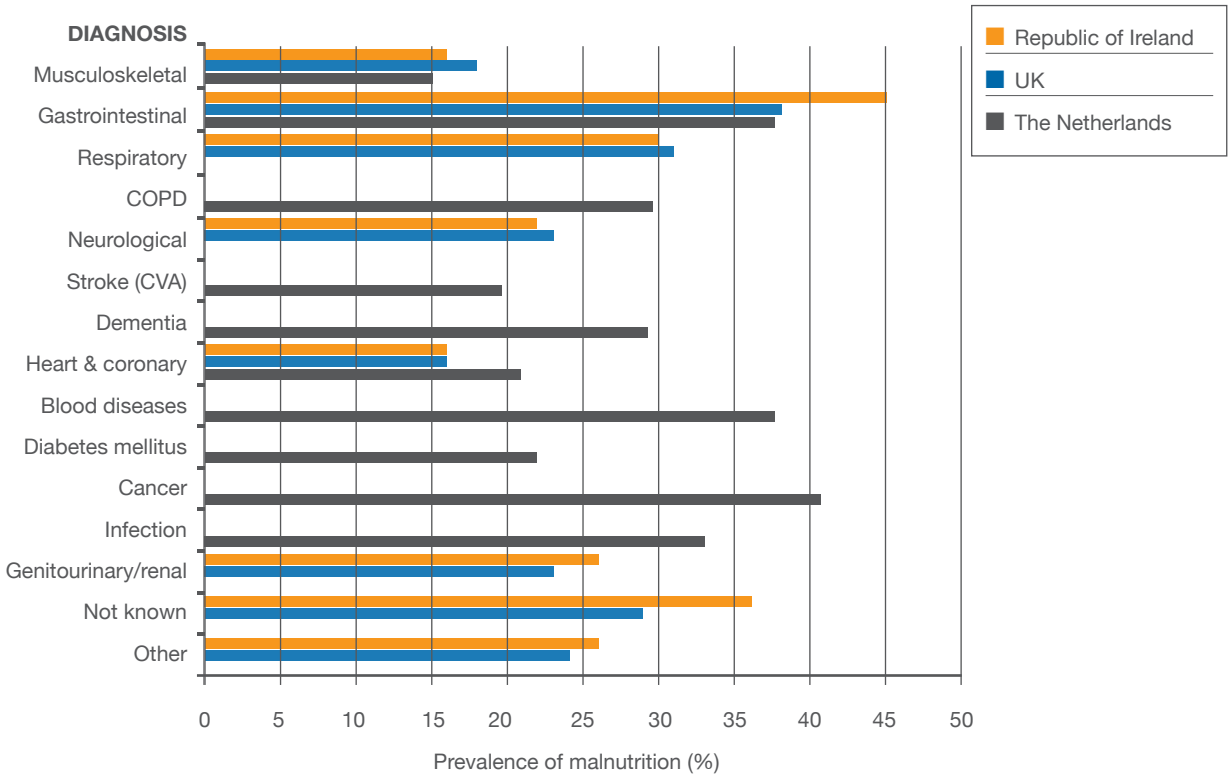

Figure 1.12 **Prevalence of malnutrition risk in hospital by diagnosis**
(Republic of Ireland *n* = 1102 ['MUST' medium + high risk], UK *n* = 7521 ['MUST' medium + high risk], the Netherlands *n* = 8028 [defined by BMI, undesired weight loss, nutritional intake*]).[50;68]
(*see details in Table A1.1)

Malnutrition is prevalent in a wide variety of diseases in children

- In a study of children (*n* = 475) on admission to a large tertiary care children's hospital in Germany, the greatest prevalence of malnutrition was found in patients with multiple diagnoses (42.8%), children with learning disabilities (40.0%), children with infectious diseases (34.5%), and children with cystic fibrosis (33.3%) (see Figure 1.13).[62] Note that the overall figures include mild, moderate and severe malnutrition.

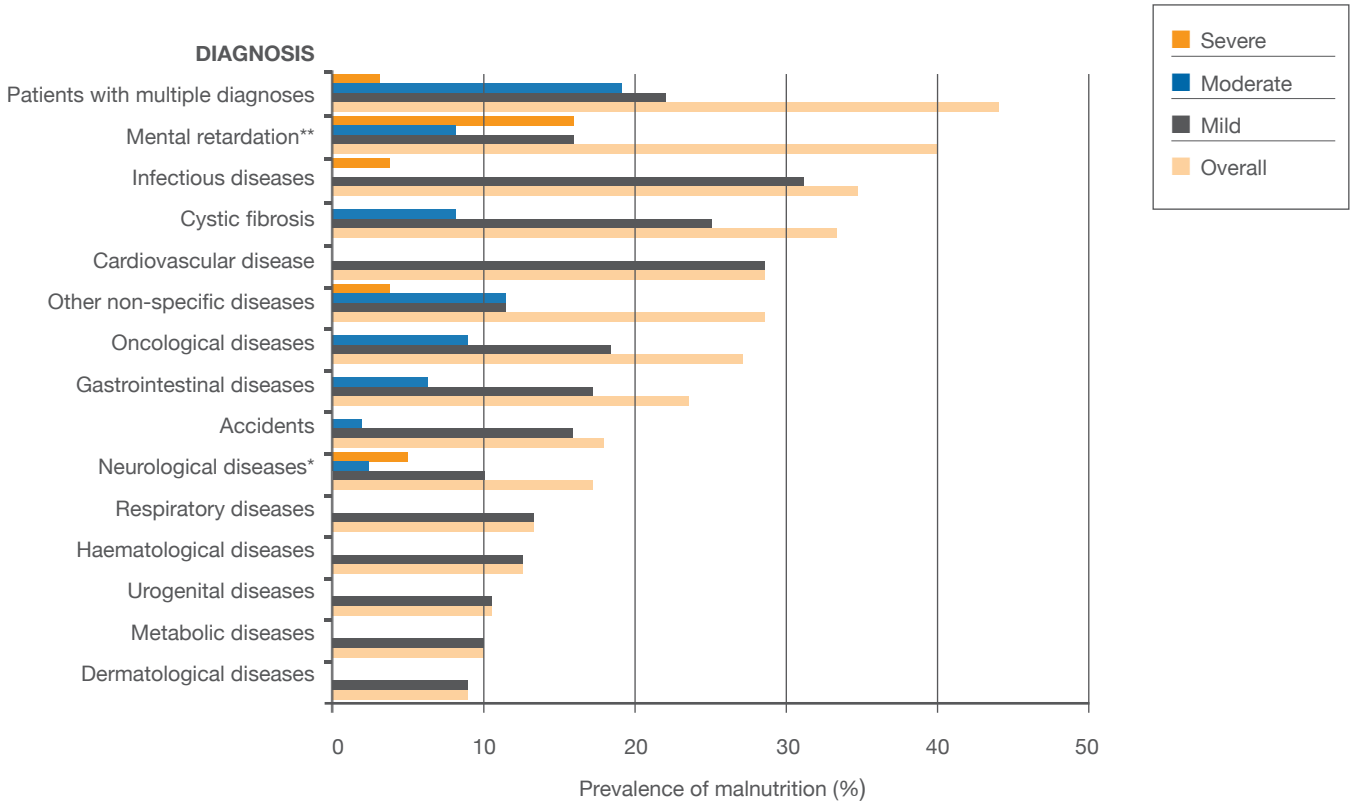

Figure 1.13 **Prevalence of malnutrition in children on admission to hospital in Germany by diagnosis and degree of malnutrition**

(*Includes mental retardation, **subgroup of patients with neurological diseases)[62]

- A nationwide prospective observational study of all newly admitted children to hospitals in the Netherlands (n = 424) found that almost 1 in 5 children had acute or chronic malnutrition. The study also showed that children with an underlying disease had a significantly higher overall prevalence of malnutrition and chronic malnutrition compared to children without an underlying disease (28% vs 15% and 18% vs 5% respectively [p = 0.004 and p < 0.001]).[92]

- The highest prevalence of acute malnutrition was found in children with GI disease (18%), and the highest prevalence of chronic malnutrition was seen in children with neurological disease (31%); the overall prevalence was around 19% (see Figure 1.14).[92]

- Using multiple logistic regression analysis that allowed for age, underlying disease, ethnicity and surgery, Joosten et al. (2010) showed that a significant relationship existed between the presence of malnutrition on admission and underlying disease (odds ratio [OR] 2.2, confidence interval [CI] 1.3–3.9; p = 0.005). For chronic malnutrition, both underlying disease and non-white ethnicity were significantly related to a higher prevalence of malnutrition (OR 3.7, CI 1.7–7.8; p = 0.001 and OR 2.8, CI 1.2–6.6; p = 0.016 respectively), but this was not the case for acute malnutriton.[92]

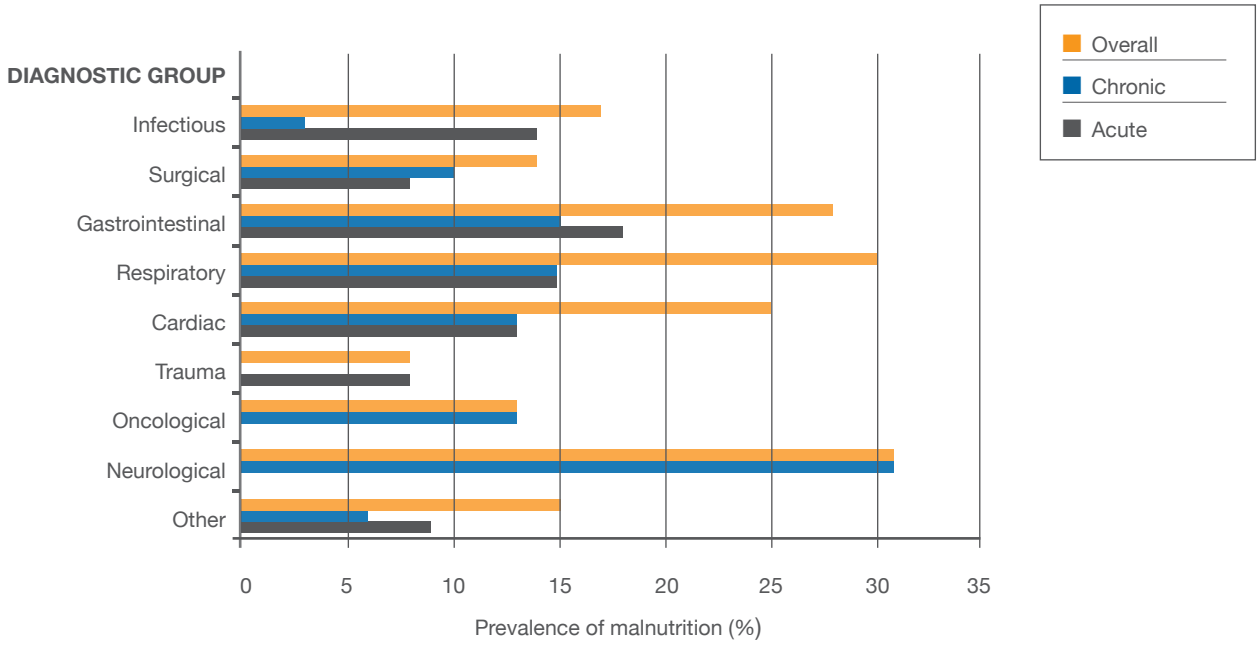

Figure 1.14 **Prevalence rates of malnutrition in children on admission to hospital in the Netherlands by diagnostic group and type of malnutrition**[92]

Deterioration in nutritional status during hospital stay can occur in both malnourished and well-nourished patients

- In a review by Stratton et al. (2003), deterioration in nutritional status during hospital stay was identified in a variety of patient groups e.g. general hospital/mixed diagnoses, paediatrics, stroke and surgical patients, with over 80% of patients in some studies losing weight during hospitalisation.[35]

- Table 1.7 shows the change in malnutrition risk (assessed using MNA) during hospital stay for older people admitted to medical and surgical wards in a non-teaching hospital in Portugal. A higher proportion of patients were at risk of malnutrition on discharge than on admission.[83]

Table 1.7 **Prevalence of malnutrition and risk of malnutrition in older people on hospital admission and discharge** (adapted from Cansado et al. 2009)[83]

	Surgical patients (*n* = 341)			Medical patients (*n* = 190)		
MNA Category	**Admission (%)**	**Discharge (%)**	***p****	**Admission (%)**	**Discharge (%)**	***p*****
Normal	21.9	22.8	NS***	8.4	4.2	0.05
Risk of malnutrition	51.3	43.4	0.05	48.9	44.7	0.07***
Malnourished	26.6	33.7	0.003	42.6	51.0	0.002

*p** indicates statistical differences for surgical patients on admission vs discharge
*p*** indicates statistical differences for medical patients on admission vs discharge
***NS: Not Significant

Weight loss can occur in children during hospital stay even when well-nourished on admission

- A study in Sao Paolo, Brazil of 203 children (average age 21.6±15.4 months; majority aged less than 24 months, *n* = 126, 62.2%) whose nutritional status was assessed within 48 hours of admission to hospital and again a maximum of 24 hours before discharge found that:[32]
  - ~ 51.6% of children lost weight during their hospital stay;
  - ~ malnourished children on admission remained malnourished on discharge;
  - ~ 9.2% of well-nourished children on admission developed mild malnutrition during their hospital stay.
- In a prospective study in France, Sermet-Gaudelus et al. (2000) found that 65% of children lost weight during their hospital stay and that weight loss was > 2% of admission weight in 45% of these children.[28]
- In a national screening survey in The Netherlands, 65% of children in hospital neither gained nor lost weight, but 3% of children experienced weight loss of more than 5% during their hospital stay.[92]

1.2.1 Community

Malnutrition is common in outpatients

- Between 7% and 16% of patients across hospital general outpatient departments have been found to be malnourished or at risk of malnutrition (see Table A1.3, Appendix 1).[54;100;101]
- The prevalence varies considerably depending on the department:
  - ~ a large multi-centre study in the Netherlands (*n* = 2288, 9 hospitals) found the highest prevalence of malnutrition in oral maxillofacial surgery outpatients (17%), although this could be an underestimate as no patients with head and neck cancer were present on the day of the survey (see Figure 1.15);[54]
  - ~ in a study of 1,000 outpatients with cancer in Italy, 39.7% were found to have experienced significant weight loss (≥ 10%) and 33.8% were found to be at nutritional risk.[102] A small study (*n* = 207) of medical oncology outpatients in a UK hospital found that the prevalence of risk of malnutrition ranged from 45% to 83% depending on the tumour site[103] (see Table A1.3, Appendix 1 for details);
  - ~ depending on the severity of disease, as many as 1 in 4 outpatients with Chronic Obstructive Pulmonary Disease (COPD) are malnourished or at risk of malnutrition;[104;105]
  - ~ about 1 in 3 adult gastroenterology outpatients have been identified as at risk of malnutrition;[106]
  - ~ a study of older people attending a geriatric medical outpatient clinic in Turkey found that 28% were at risk of malnutrition (using MNA).[107]
- A systematic review and meta-analysis of studies examining the prevalence of malnutrition in older people in outpatients (*n* = 37) (malnutrition was identified using the Mini Nutritional Assessment (MNA®) criteria), showed a prevalence of malnutrition (MNA <17 points) of 6% (95% CI, 4.6-7.5) and a prevalence of risk of malnutrition (MNA 17-23.5 points) of 30.9% (95% CI, 26.2-35.5). The authors highlighted that there was significant heterogeneity in individual study results.[86]

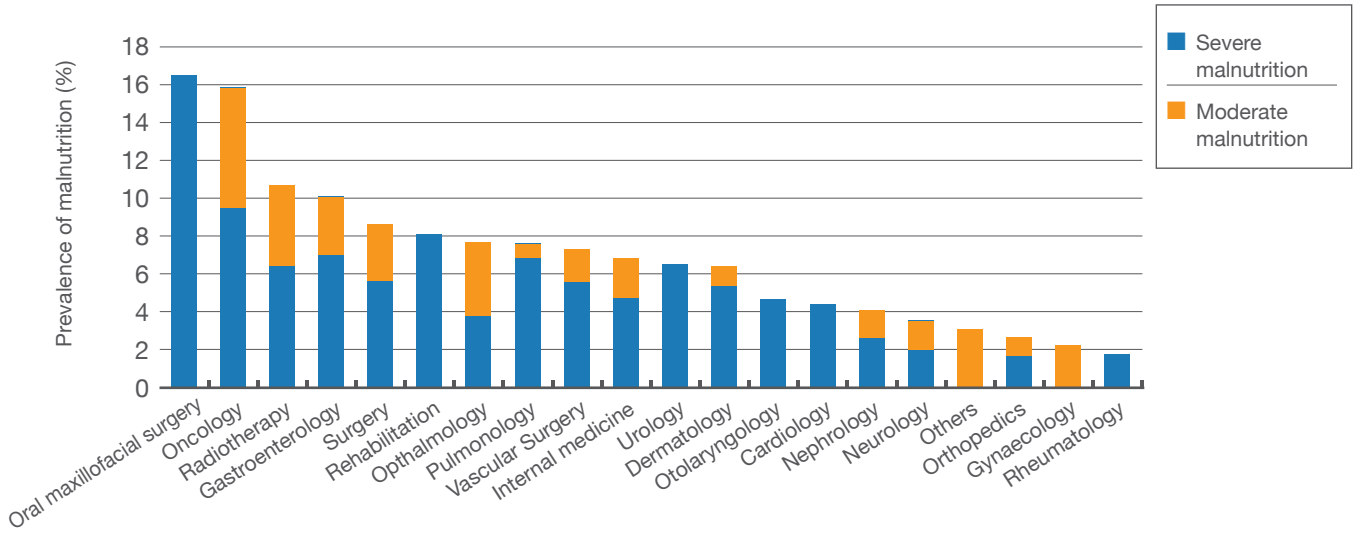

Figure 1.15 **Prevalence of malnutrition in outpatient departments in the Netherlands** (n = 2288).[54]
Others: psychiatry, radiology, geriatrics and physiotherapy (see Table A1.3, Appendix 1 for details)

Malnutrition is found to be common in people with intellectual disability and mental health problems

- In UK adults aged 20 years and over with intellectual disability, the prevalence of under weight (BMI ≤ 20 kg/m^2) has been shown to be 18.6%.[108]
- The UK Nutrition Screening Week Survey 2011 found a prevalence of malnutrition risk in patients in mental health units (n = 543) of 19% (Table A1.7, Appendix 1).[50]
- In Taiwan, a study by Tsai et al. found that the prevalence of malnutrition and malnutrition risk (using MNA-Taiwan version) in patients in mental health units differed with different diagnoses as follows:[109]
  - ~ 12.5% in patients with bipolar disorder;
  - ~ 21.1% in patients with schizophrenia;
  - ~ 55.6% in patients with major depression.

More than 1 in 3 patients in care homes are malnourished or at risk of malnutrition

- Estimates using a variety of methods in different types of care homes (majority of participants were older people) suggest that between 9% and 97% of residents in long-term care facilities are at risk of malnutrition or already malnourished (see Figure 1.16) (Table A1.4, Appendix 1). Figures at the lower end of this prevalence range are reported in studies where prevalence of malnutrition or malnutrition risk was assessed either by using a healthcare professional's subjective assessment or BMI;[110;111;112] both of these methods are known to underestimate the prevalence of malnutrition risk. An exception was residential homes in the Republic of Ireland which reported a prevalence of malnutrition risk using 'MUST' of 9% and 0% in 2010 and 2011, which contrasts starkly with the results for the UK for the same years (30% and 41% respectively).[50; 67] There may be differences between the two countries in the type of residents cared for in these facilities; however, it must also be noted that in the Republic of Ireland the sample sizes were small, with very low numbers of patients participating per care home (2010: n = 143 [17 care homes], 2011: n = 29 [6 care homes]), meaning that the results may not be representative of the actual level of malnutrition risk in residential homes in the Republic of Ireland.

Prevalence figures at the upper end of the range are reported in studies where MNA or MNA-SF was used.[110;113-120] In many of these studies, the subjects differed in terms of age, type of care home, and underlying condition, and some included small sample sizes (see Table A1.4, Appendix I).

- Based on large studies (n > 1000) using a validated screening tool (MNA or 'MUST'), more than 1 in 3 patients (30–53.4%) living in care homes are at risk of malnutrition[57;70;84;110;121] (see Table 1.8).

Table 1.8 **Summary of large-scale studies of the prevalence of malnutrition and risk of malnutrition in patients in care homes** (n > 1000; using a validated screening tool; majority of participants were older people)

Country/ Region	Author (year)	Patients (n)	Timing of nutritional assessment/screening (data collection)	Prevalence %	Method of assessment/ screening
International†	Kaiser et al. (2010)[84]	1586	Not available	67.2 (53.4 at risk, 13.8 malnourished)	MNA
Finland	Suominen et al. (2009)[110]	1043	All patients during 2 weeks in September 2003	97.4 (40.7 at risk, 56.7 malnourished)	MNA
Hungary	Lelovics et al. (2009)[121]	1381	Timing of assessment not clear	38.1	'MUST'
UK	Parsons et al. (2010)[57]	1176	Timing of assessment not specified	39	'MUST'
UK	Russell et al. (2008)[70]	1610	Restricted to adults admitted within the previous 6 months	30	'MUST'

†Retrospective pooled analysis of data from studies in older people in nursing homes in Switzerland, Germany, Spain, France, The Netherlands, the United States and South Africa

- Studies in the UK using 'MUST' show that the risk appears to increase with increasing dependency (35–46% in nursing homes vs 22–36% in residential homes) (see Table A1.4, Appendix 1). In a study of the prevalence of risk of malnutrition in a Primary Care Trust in England (n = 703), a significantly higher prevalence was found in nursing care compared with residential care (38% vs 25%, p = 0.001).[58] The prevalence of malnutrition (using SGA) was found to be higher in residents receiving a higher level of care in aged care facilities in Australia (OR 2.9 [95% CI 1.7–5.2; p < 0.001]).[122]

- A systematic review and meta-analysis of studies examining the prevalence of malnutrition in older people in a variety of community care facilities (malnutrition was identified using the Mini Nutritional Assessment (MNA®) criteria), showed a high prevalence of malnutrition (see Table 1.9).[86]

Table 1.9 **Prevalence of malnutrition in older people in a variety of community care facilities[86]**

Setting	Studies (n)	Malnourished (MNA <17 points) % (95% CI)	At risk of malnutrition (MNA 17-23.5 points) % (95% CI)
Nursing home	44	17.5 (14.3-20.6)	48 (44.2-51.8)
Long-term care	23	28.7 (21.4-36.0)	49 (43.6-54.4)
Rehabilitation and sub-acute care	15	29.4 (21.7-36.9)	48.5 (42.4-54.6)

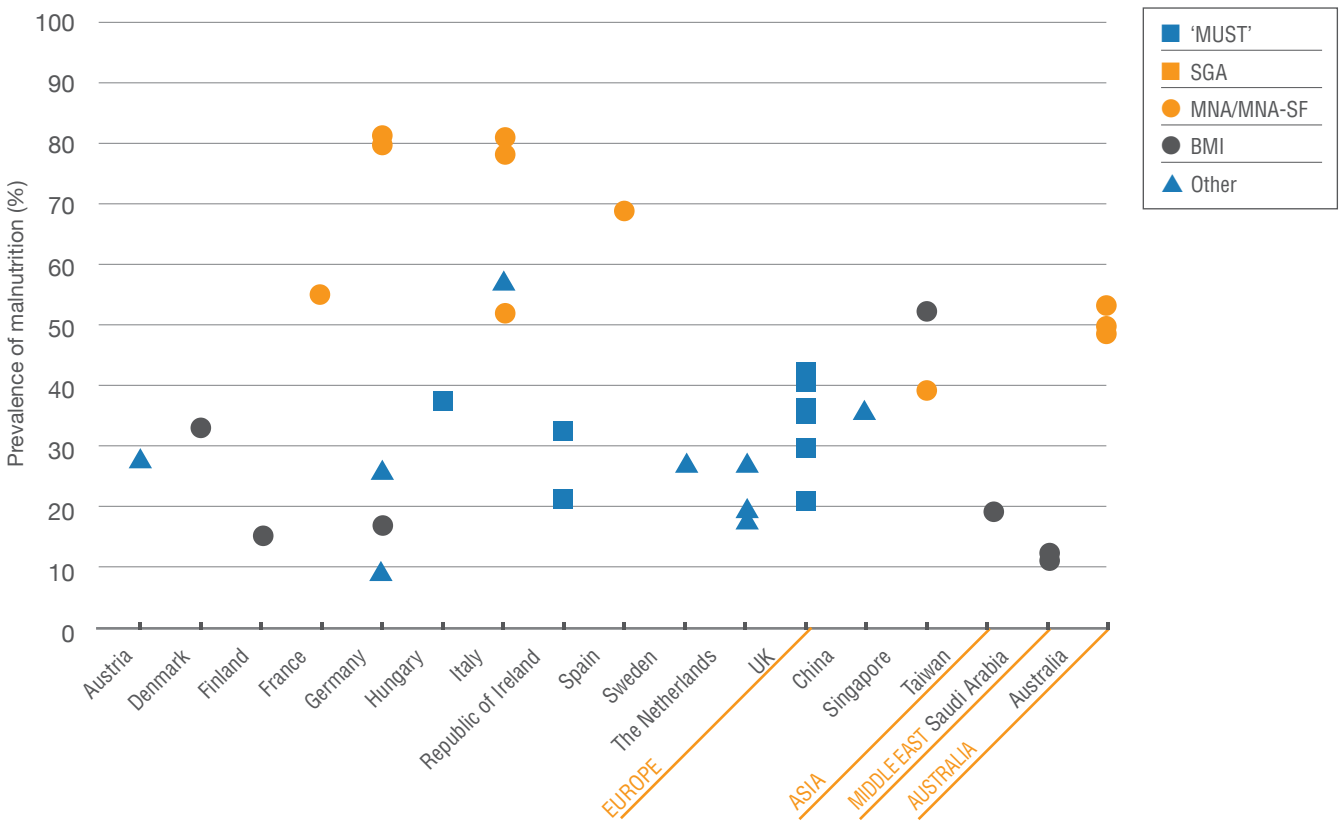

Figure 1.16 **Prevalence of malnutrition risk in care homes using different screening methods by country and world region**

(see Appendix I, Table A1.4 for full details)

As many as 1 in 3 older people living independently face the same risk

- Malnutrition is not just found in older people (the age of subjects differs in different studies but in general, people aged over 60 years or 65 years are included) in hospitals and care homes; free-living older people are also at risk of malnutrition. As with other settings, the prevalence varies depending on the method used (2–52%) (see Table A1.6, Appendix 1) and the type of subjects studied, including disease status. Special efforts should be made to identify these people since they may not all be in regular contact with health or social care professionals, meaning that malnutrition could easily be missed.

- A large pooled analysis of previously published datasets of community-dwelling older people (n = 964, > 65 years of age) from 5 different countries (Switzerland, France, Japan, Sweden and South Africa) using MNA found that 31.9% of participants were at risk of malnutrition and 5.8% were malnourished.[84]

- Prevalence of risk of malnutrition of 12–14% (using 'MUST') has been found in residents in sheltered accommodation in the UK (see Table A1.5, Appendix 1) and 31–37% in recipients of meals on wheels in the UK and Ireland (using 'MUST' and MNA) (see Table A1.6, Appendix 1).[123-125] Prevalence of malnutrition or risk of malnutrition of up to 90% using MNA has been found in older people resident in serviced flats in Sweden and Finland.[126-128]

- A systematic review and meta-analysis of studies examining the prevalence of malnutrition in older people in the community (n = 58) (malnutrition was identified using the Mini Nutritional Assessment (MNA®) criteria), showed a prevalence of malnutrition (MNA <17 points) of 3.1% (95% CI, 2.3-3.8) and a prevalence of risk of malnutrition (MNA 17-23.5 points) of 26.5% (95% CI, 22.4-32.7). The authors highlighted that there was significant heterogeneity in individual study results.[86]

- There are few studies to date on the risk of malnutrition in patients attending general practices (family doctors), although emerging data indicates that the prevalence of malnutrition risk in older community-dwelling Dutch people attending general practices for influenza vaccination (identified using SNAQ) is 12%, and 10.8% in adults (mean age 41.8, SD±18.3) attending GP practices in areas with a high Multiple Deprivation Score in the UK (identified using 'MUST').[129;130]

Risk of malnutrition is associated with level of dependency

- A systematic review and meta-analysis of studies examining the prevalence of malnutrition in older people according to healthcare setting (n = 240) (malnutrition was identified using the Mini Nutritional Assessment (MNA®) criteria), showed that across all healthcare settings both the presence of malnutrition and the risk of malnutrition were directly correlated with the level of dependence associated with the care setting (p<0.001).[86]

Malnutrition is common in patients with cancer

- When considering the issue of malnutrition in cancer, it is important to note that the terms malnutrition and cachexia are often used interchangeably due to differing definitions of cancer cachexia.[131] In addition, it can be difficult to separate the effects of cachexia and the effects of cancer treatment as a cause of malnutrition.[131] The approach used in a recent review of the effect of malnutrition on cancer patients by Henry (2011) will be employed here, i.e. 'the term "malnutrition" is used to describe the changes in nutritional status observed in cancer patients'.[131]

- A number of definitions of cancer cachexia have been proposed[132-134] and a practical, easy-to-use classification of cancer cachexia has been developed (defined as ≥ 10% weight loss associated or not with anorexia, early satiation and fatigue; weight loss of < 10% is defined as pre-cachectic).[135]

- Cancer is a chronic condition often identified late and it involves complex treatment regimens. Nutrition and malnutrition are often not seen as important by healthcare professionals and weight loss is incorrectly viewed as inevitable by patients and their families.

- In practice, the need to identify patients who are at nutritional risk or who are malnourished is an important aspect of good patient care, since cancer-related weight loss affects patients' physical activity, morbidity, response and tolerance to treatment, survival, and quality of life.[136]

More than 1 in 3 patients with cancer are malnourished and they are at higher risk of malnutrition than other patient groups

- In a prospective observational multi-centre study conducted in French cancer centres (n = 1545 inpatients and patients admitted for 1 day [outpatients], median age 59.3±13.8 years, 23.4% aged ≥ 70 years), the overall prevalence of malnutrition was reported to be 30.9% (with 18.6% of cases classed as moderate malnutrition and 12.2% as severe).[137] Table 1.10 shows the prevalence of malnutrition according to tumour type.

- In a study of 1,000 outpatients with cancer in Italy, 39.7% were found to have experienced significant weight loss (≥ 10%) and 33.8% were found to be at nutritional risk.[102] A small study (n = 207) of medical oncology outpatients in a UK hospital found that the prevalence of risk of malnutrition ranged from 45% to 83% depending on the tumour site[103] (see Table A1.3, Appendix 1).

- Not unexpectedly, the rate of malnutrition is more than twice as high in patients with malignant disease (n = 54) than in patients with non-malignant disease (n = 448) (50.9% vs 21.0%, p < 0.0001, assessed using SGA).[138] The 2010 UK Nutrition Screening Week Survey similarly demonstrated a significantly increased risk of malnutrition in those with a cancer diagnosis (44% vs 32% without cancer, p < 0.001).[67]

Table 1.10 **Prevalence of malnutrition in expert cancer centes in France by tumour type** (adapted from Pressoir 2010)[137]

Tumour type	Overall prevalence of malnutrition %	Moderate malnutrition %	Severe malnutrition %
Breast	18.3	11.2	7.1
Head and neck	45.6	22.5	23.1
Colorectal	31.2	22	9.2
Haematological	34.2	26.3	7.9
Upper digestive	49.5	26.3	23.2
Gynaecological	32	16.4	15.6
Lung	40.2	21.9	18.3
Other*	27	18	9

*Prostate, urinary, brain, thyroid, testicular and kidney cancers; trunk and limb sarcomas; melanoma; other thoracic or abdominal cancers; unclassified tumour.

Definitions of malnutrition used

	Age ≤ 70 years of age	Age > 70 years of age
Moderate malnutrition	Weight loss over last 6 months ≥ 10% or BMI < 18.5 kg/m²	Weight loss over last 6 months ≥ 10% or BMI < 21 kg/m²
Severe malnutrition	Weight loss over last 6 months ≥ 15% or BMI < 16 kg/m²	Weight loss over last 6 months ≥ 15% or BMI < 18 kg/m²

Patients with advanced cancer have a higher prevalence of weight loss and malnutrition

- As may be expected, studies confirm a higher prevalence of patients with weight loss and malnutrition with more advanced stages of disease. A Brazilian study showed prevalence of malnutrition across different cancer types according to stage, with 23% in Stages I–II, 21.9% in Stage III, rising to 62% in Stage IV cancers.[139]
- In a study of patients with locally advanced or metastatic cancer in Spain (n = 781, median age 62 years [range 19–92]) using a Patient-Generated Subjective Global Assessment (PG-SGA), more than 50% of patients with cancer were found to have moderate or severe malnutrition.[140]
- Sixty-eight percent of patients receiving palliative home care services in the Stockholm region were found to be at risk of malnutrition (based on modified NRS-2002), with prevalence ranging from 52% to 76% depending on the tumour site.[141]
- A study describing a retrospective review of presenting symptoms in 1,539 lung cancer patients also showed prevalence of weight loss at presentation (see Table 1.11).[142]

Table 1.11 **Prevalence of malnutrition in lung cancer patients according to cancer type and stage** (adapted from Chute et al. 1985)[142]

Cancer type	Stage	Prevalence of malnutrition % (assessed by weight loss)
Small-cell lung cancer	Limited disease	35
	Extensive disease	52
Squamous cell lung cancer	Stage I	36
	Stage II	44
	Stage III	52
Adenocarcinoma lung cancer	Stage I	14
	Stage II	33
	Stage III	49
Large-cell lung cancer	Stage I	13
	Stage II	52
	Stage III	45

1.3 CAUSES OF MALNUTRITION

Summary

Poor food and nutrient intake due to disability and disease are at the heart of the cause of malnutrition; here are some examples:

- patients with **cancer** may have altered taste, nausea and anorexia due to their medical treatment
- patients with **stroke or other neurological conditions** may have swallowing difficulties or problems with self-feeding for example, poor oral-motor function in cerebral palsy
- breathlessness in **severe respiratory disease** can make eating difficult
- patients with **severe dementia** may forget to eat or even forget how to eat
- poor dentition and swallowing problems are a particular problem in **older people**

Inadequate food intake is common in patients in hospital including in children and older people and in patients in the community. More than 50% of patients in hospital don't eat the full meal they are given and 30% of nursing home residents eat less than half their lunch.

As a result energy, protein and micronutrient intake (vitamins, minerals and trace elements) is compromised and often fails to meet recommendations or estimated requirements, which may be increased in disease. Identification of and addressing where possible the underlying causes of malnutrition will help ensure maximal effectiveness of nutritional support.

Many other factors at organisational or institutional level exacerbate the problem of malnutrition such as:

- **lack of nutritional policies and equipment** for screening
- **lack of a clear description of responsibilities** for health authorities, institutions and healthcare workers
- **lack of nutritional knowledge** due to inadequate training
- **poor documentation of nutrition related information**
- **lack of adequate nutrition care planning and lack of monitoring**

Conclusion

The causes of inadequate food intake to meet nutritional requirements in disease and disability are multi-factorial. They include patient-related factors as well as organisational and institutional factors. Therefore a multi-disciplinary approach is needed to identify and implement appropriate and effective solutions. All stakeholders need to be involved from national and professional bodies (to set national nutritional policy/quality standards) to the patient and carer. Awareness of the issue of malnutrition and education on how to manage it are vital components in achieving success in the fight against malnutrition.

Recommendations

On the issue of **causes of malnutrition** the MNI makes the following recommendation:

Action	Issues to consider
Evidence based approaches for nutritional care plans should be used, taking into account the causes of malnutrition, the objectives of intervention and also environmental and practical constraints	• Identification of and addressing, where possible, the underlying causes of malnutrition will help ensure maximal effectiveness of nutritional support • The actions taken to address a patient's nutritional needs should be evidence based and should also be tailored to each individual patient, taking account of their individual circumstances and wishes

The effects of disease and treatment on food and thus energy and nutrient intake are key factors in the development of malnutrition in adults and children

- Table 1.12 summarises the causes of nutritional inadequacy in various diseases.
- For children with faltering growth, contributing factors include not only underlying medical conditions, but also factors such as parental attitude and cultural beliefs, child management/coercive behaviour, maternal influences/family difficulties, poverty, neglect, and abuse. Progression through weaning, appetite, feeding difficulties, excess fluid, and dental caries are also important considerations.[6]

Table 1.12 **Diseases associated with malnutrition and causes of nutritional inadequacy** (adapted from Gibbons and Fuchs 2009)[143]

Disease or risk factor	Cause of inadequacy
Short bowel syndrome	• Nutrient loss from malabsorption
Cystic fibrosis	• Nutrient loss from malabsorption caused by pancreatic insufficiency • Increased energy expenditure from chronic lung disease • Decreased oral intake as a result of recurrent respiratory infections and altered taste
Inflammatory bowel disease	• Increased energy expenditure from chronic inflammatory process/ cachexia • Nutrient loss from malabsorption • Decreased oral intake as a result of abdominal pain, diarrhoea, anorexia and cachexia
Chronic liver disease	• Nutrient loss from malabsorption • Inappropriate substrate use • Increased metabolic needs • Decreased oral intake as a result of abdominal pain, altered taste, cachexia (if prominent underlying inflammatory component)
Chronic kidney disease	• Decreased oral intake as a result of altered taste, anorexia, nausea, cachexia (if underlying inflammatory component) & dietary restrictions • Altered energy expenditure resulting from metabolic disturbances (uraemia, acidosis)
Heart disease	• Decreased oral intake caused by fatigue and shortness of breath
Cancer	• Increased energy expenditure from cachexia • Decreased oral intake as a result of gut mucosal injury, altered taste and cachexia • Nutrient loss from malabsorption caused by gut mucosal injury
Neurological diseases	• Feeding difficulties related to oral dysfunction, abnormal movement and reflexes, sensory and perceptual difficulties, posture, and communication. Swallowing problems/dysphagia
Acute metabolic stress, e.g. burns, trauma, surgery	• Inability to eat and drink (e.g. ventilated, nil by mouth) • Increased metabolic needs • Increased losses e.g. exudate, fistula
Unknown causes	• Fussy eating/swallowing difficulties • Non-organic faltering growth

Poor food intake due to disease or disability leads to inadequate energy and nutrient intake

- Poor food intake may occur for a variety of reasons associated with disease and disability in adults and children, and it may be physical or psychological in origin (see Figure 1.17). Patients with cancer may have altered taste, nausea and anorexia due to treatment, whilst patients with stroke or other neurological conditions may have swallowing difficulties or problems with self-feeding, for example, poor oral-motor function in cerebral palsy. Breathlessness in severe respiratory disease can make eating difficult. Patients with severe dementia may forget to eat or even forget how to eat.

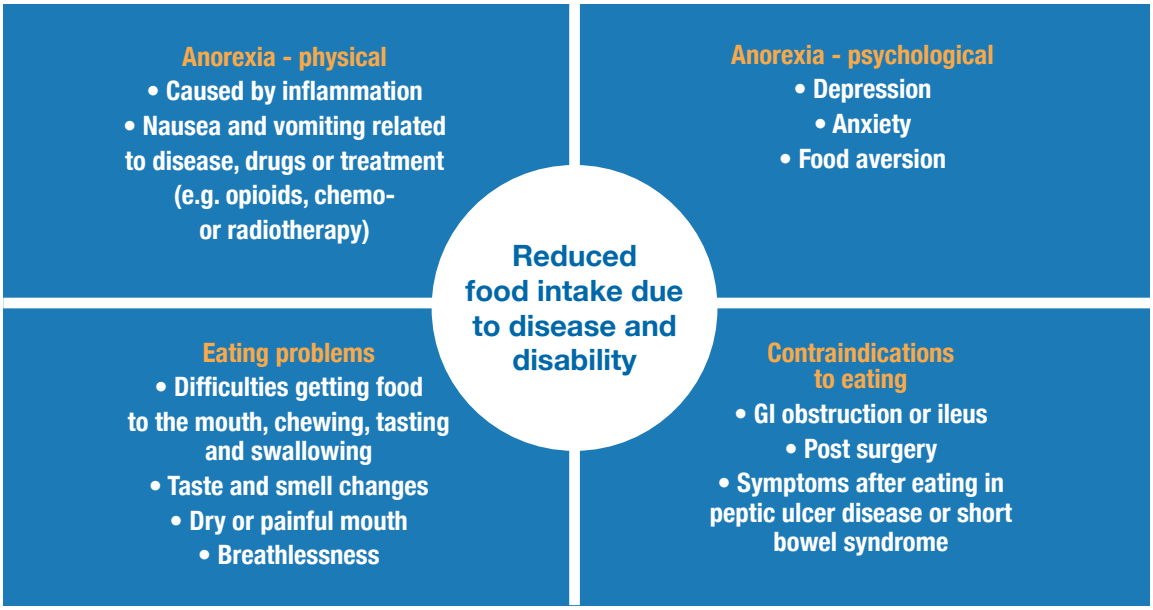

Figure 1.17 Causes of reduced food intake associated with disease and disability[35]

1.3.1 Hospital

(H)

Inadequate food intake is common in adult and older patients in hospital

- Inadequate food intake is common in hospitals despite adequate food provision.[144-146]

- The nutritionDay Survey conducted in European hospitals in 2006 (748 wards from 256 hospitals in 25 countries, total *n* = 16455) showed that less than half of all patients finished their meals. The most frequent reason cited by patients for eating less or nothing was 'not being hungry' (43%).[147] In the Australasian Nutrition Care Day Survey undertaken in 2010 (acute care hospitals in Australia and New Zealand, *n* = 3122), on average 1 in 2 malnourished patients (55%) ate ≤ 50% of the food offered and 1 in 3 well-nourished patients (33%) consumed ≤ 50% of the food offered during the survey.[31]

- In a longitudinal observational study of 100 older (mean age 81.7 years [SD ± 7.2]) inpatients in an inner-city hospital elderly care unit in the UK, patients were judged to be eating inadequately in 67% of assessments (285 out of 425) carried out during the study period of 4 weeks.[148]

- A cross-sectional observational study in Sweden found eating difficulties to be common in hospital patients (49%). Patients with a low BMI had significantly more eating difficulties than patients with a normal or high BMI.[149]

Inadequate food intake is also of concern in children in hospital

- A small Swedish survey of 21 children (median age 14.5 years [range 11–17]) receiving chemotherapy for cancer reported that the causes of poor food intake in children with cancer range from primary changes in taste to the effects of the disease itself, treatment or the environment. The frequency of eating problems is presented in Figure 1.18, with responses shown separately for children, their parents and nurses. Whilst the results show that significant eating problems occur, it is interesting to note that parents generally report these problems more frequently than the children themselves.[150]

- Access to food may also pose a challenge in meeting the nutritional needs of children in hospital. A survey of current practice in children's cancer care in the UK found variable facilities for preparation and storage of food and drink for patients. Kitchen facilities were available at 90% of centres; however, there were restrictions in some centres, e.g. no microwave, only a toaster and kettle, no raw food allowed. Two centres had a chef available to cook on demand for children. Most centres (90%) had storage facilities for snacks and over 80% allowed food to be brought in from home.[151]

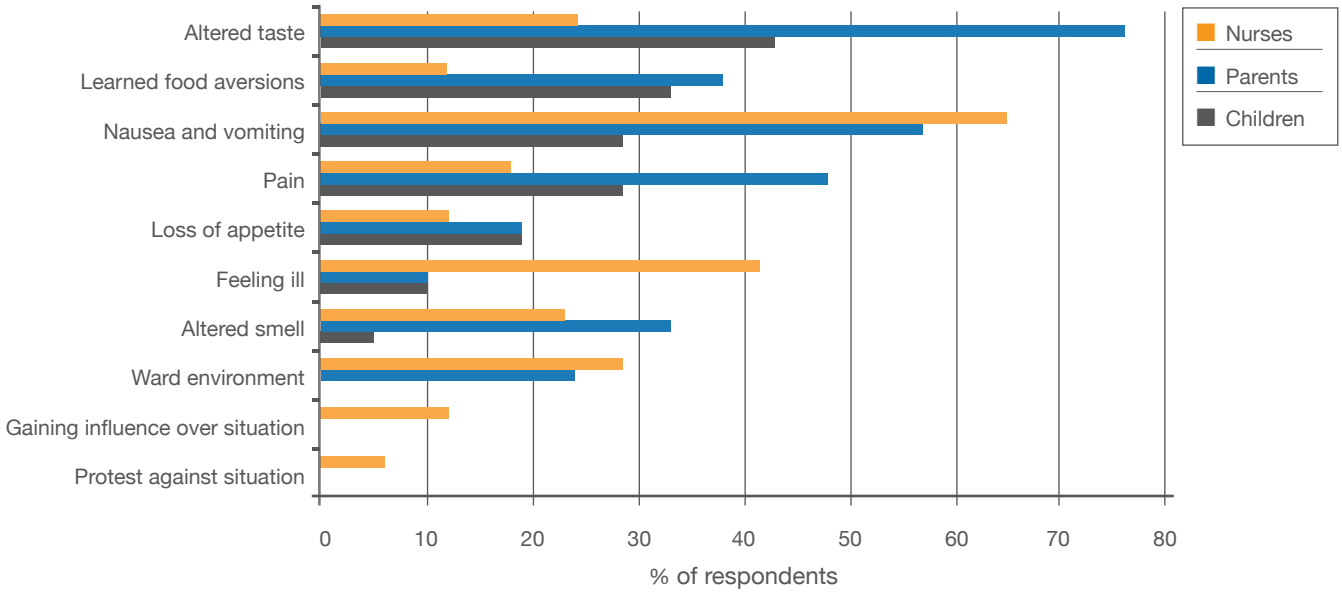

Figure 1.18 **Causes and frequency of eating problems among 21 children undergoing chemotherapy for cancer: responses of children, parents and nurses.[150]**
(Note that an individual may contribute to more than 1 category)

Energy intake is compromised and fails to meet recommended intake levels in adult hospital patients

- Stratton et al. (2003) collated studies that measured food intake in a variety of patient groups and demonstrated that in hospital patients, energy intakes fell consistently short of requirements across a spectrum of diseases.[35]

- In the European nutritionDay Survey (data collected during the 1-day cross-sectional Nutrition Days in 2007 and 2008), data on energy goal and intake was available for 12,398 patients, 47% of whom consumed less energy than their estimated requirements (defined as ≥ 1500 kcal/day for most patients).[18]

- In a prospective cohort study of older medical hospital patients (n = 134) in a large teaching hospital in Australia, almost two-thirds of patients (59%) did not consume enough dietary intake to meet estimated resting energy requirements, and only 8% of patients had sufficient energy intake for estimated total energy expenditure.[152]

Energy intake may be compromised in children in hospital

- A study of children aged > 6 months admitted to medical or surgical wards for > 48 hours in France (*n* = 183) found that 67% of malnourished and 70% of non-malnourished patients had an energy intake of less than 75% of the recommended daily allowance.[33]

- Campanozzi et al. (2009) found that of 496 children aged 1 month to 16 years admitted to medical paediatric wards with mild clinical conditions, 50.4% had a food intake of < 50% of the recommended dietary allowance.[34]

Protein intake is compromised in hospital patients, particularly in older people

- Older people and people with compromised health have difficulty meeting recommended intakes for protein, particularly hospitalised older people and orthopaedic patients.[35;43;144;153] When compared with typical daily intakes in the healthy population, it is clear that protein intake in a variety of patient groups is severely compromised.[35]

- Data on dietary intake retrospectively extracted from dietetic records of 610 undernourished adult patients (identified using SNAQ) admitted to a general hospital for > 4 days in The Netherlands in 2008 showed that more than half of the patients (58.4%) did not meet predefined requirements for either protein or energy.[154]

Micronutrient intake is compromised in adult hospital patients

- Hospital patients, particularly older hospital patients, have lower than recommended intakes of a range of vitamins and minerals. In female orthopaedic inpatients, median intakes of vitamin D, magnesium, potassium and selenium were found to be even below the lower reference nutrient intake.[iii,153] Compared with day centre visitors, hospitalised hip fracture patients had significantly lower micronutrient intakes, e.g. 29% lower vitamin B_6, 23% lower selenium, 21% lower iron, 20% lower calcium and 20% lower magnesium.[43]

1.3.2 Community

Inadequate food intake is common in patients in the community

- A cross-sectional observational study in Sweden found eating difficulties to be common in special accommodation residents, i.e. nursing home-type care (56%). Patients with a low BMI had significantly more eating difficulties than patients with a normal or high BMI.[149]

- In a large survey (nutritionDay in 2007) of Austrian and German nursing home residents (*n* = 1922), 1 in 3 residents ate ≤ 50% of their lunch on the day of the assessment.[111]

Energy intake is compromised and fails to meet recommended intake levels in community patients

- Stratton et al. (2003) collated studies that measured food intake in a variety of patient groups; in community patients, energy intake was better than in hospital patients but still of concern in a number of patient groups.[35]

- In community-based older people with medium and high risk of malnutrition (identified using 'MUST'), total daily energy intake was found to be significantly lower than the national average for older people (1368 [SD 513] kcal vs 1628 [SD 464] kcal, z-score $p < 0.004$).[155]

- A cross-sectional study of nutrient intake in older serviced house residents in Finland (*n* = 375) found that 46% consumed less energy than recommended, with 13% receiving less than 1,200 kcal/day.[126]

[iii]Lower reference nutrient intake (LRNI): an amount of a nutrient sufficient for only the few people in a group who have low needs

Protein intake is compromised in patients in the community

- In a study of the nutritional status of older people in low-level care facilities in Australia (semi-independent ambulatory residents; similar to residential care homes in the UK) (n = 95, mean age 85.8±6.6 years), 3-day weighed food intake showed that 30% of residents consumed less than the estimated average requirement (EAR) for protein (i.e. 46 g/day). However, when intake was compared with a requirement of 1 g/kg/day of protein, 77% of residents were found to have an inadequate intake.[156]

- A cross-sectional study of nutrient intake in older serviced house residents in Finland (n = 375) found that 47% received less than 60 g of protein/day and 11% received less than 40 g/day.[126]

Micronutrient intake is compromised in patients in the community

- Low intakes (below reference values) of some but not all micronutrients are evident in a substantial proportion of free-living and institutionalised older adults and in those at risk of malnutrition.[157;158] Over 80% of older adults have intakes below the reference nutrient intake (RNI) for potassium, magnesium, copper and vitamin D (see Figures 1.19 and 1.20).

- Even in well-nourished, apparently healthy free-living older people consuming adequate macronutrients, lower than recommended micronutrient intake is prevalent and this increases significantly with age.[159]

- Assessment of energy and nutrient intakes in 52 Swedish nursing home residents showed that of 16 micronutrients considered, males had a mean intake below the Swedish Nutrition Recommendations (SNR) for 9 nutrients and females for 8 nutrients. Intakes of vitamin D, vitamin E, folic acid and selenium were very low, reaching only 40–60% of the SNR.[160]

- Lower than recommended intakes of fibre, vitamin E, vitamin D and folic acid were found to be particularly common in all age groups of residents in serviced housing in Finland. The proportions of residents failing to meet these nutrient requirements were 98%, 98%, 83% and 86% respectively.[126]

- In community-based older people with medium and high risk of malnutrition (identified using 'MUST'), mean total daily intake for micronutrients such as magnesium, iron, zinc, selenium, iodine, vitamin A and folate was found to be below the RNI and the national average daily intake in older people.[155]

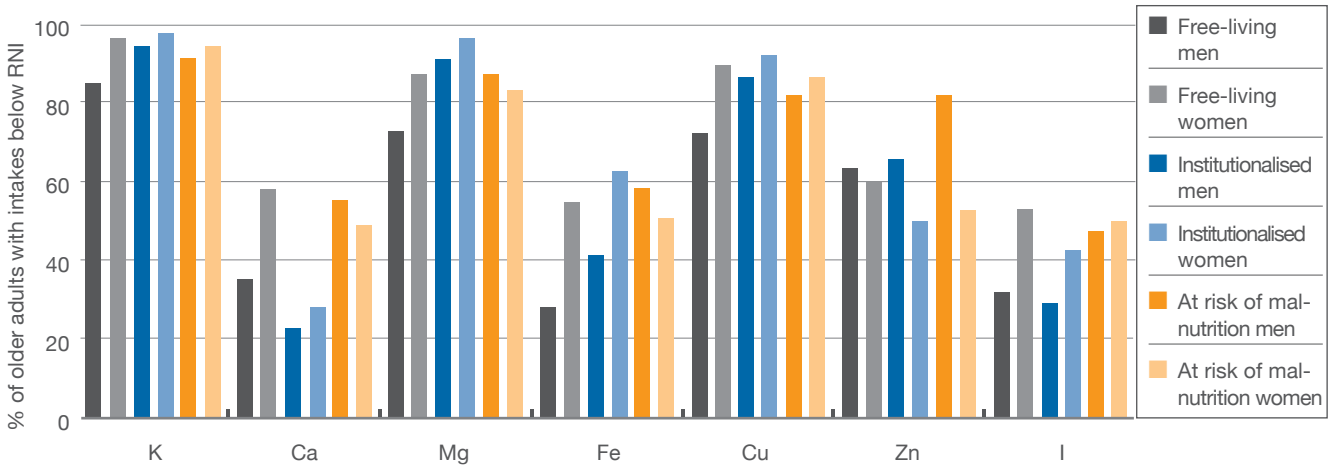

Figure 1.19 **Percentage of older adults in the UK with mineral intakes below the RNI** (adapted from Stratton 2007).[157]

RNI for men and women aged ≥ 50 years. Number of patients varies according to micronutrient and group (male and female): free-living (n = 540–735), institutions (n = 93–319), at risk of malnutrition (all settings n = 55–80)

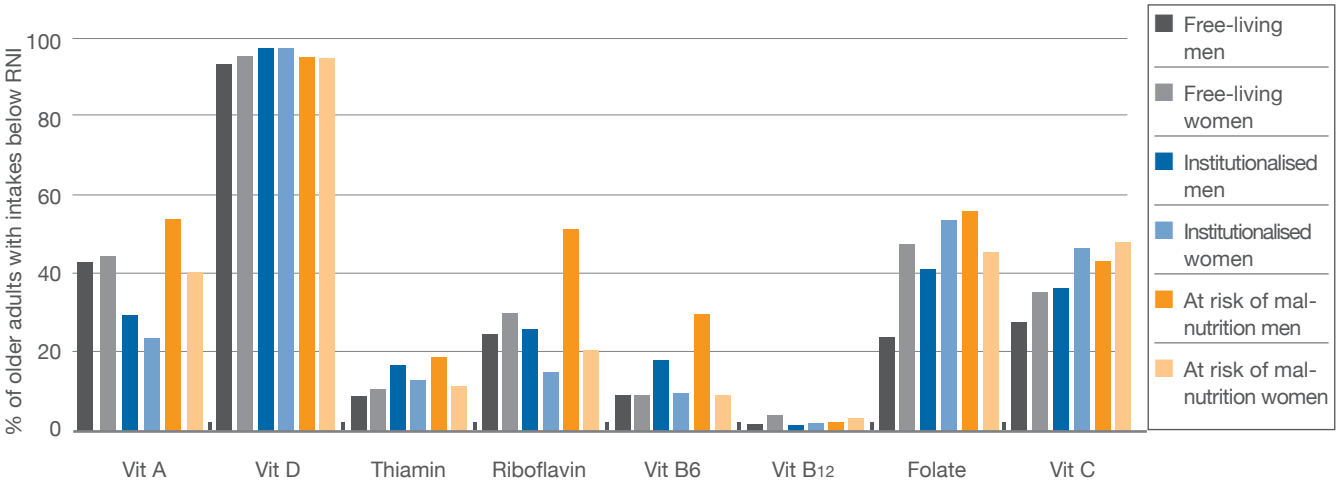

Figure 1.20 **Percentage of older adults in the UK with vitamin intakes below the RNI** (adapted from Stratton 2007).[157]

RNI for men and women aged ≥ 50 years. Number of patients varies according to micronutrient and group (male and female): free-living (*n* = 540–735), institutions (*n* = 93–319), at risk of malnutrition (all settings *n* = 55–80)

Energy and nutrient intake is compromised in children with a variety of conditions

- Two recent reviews of growth, nutritional issues and management in children with neurological impairment and cerebral palsy both identified poor food intake and inadequate energy intake as factors in the development of malnutrition and poor growth in this patient group.[161;162] Poor oral-motor function impairs the ability to consume sufficient energy and nutrients to sustain adequate growth.[162]

- Eating problems are commonly reported in children with motor disability (20%), with an adverse impact on intake of some but not all nutrients:[163]

  ~ energy intake 76% of recommendations;
  ~ vitamin D intake 76% of recommendations;
  ~ iron intake 87% of recommendations;
  ~ fibre 52% of recommendations.

- Sullivan et al. (2002) assessed the macro- and micronutrient intake (using a 24-hour recall and a 3-day diet diary) of a group of neurologically-impaired children with motor and feeding problems and found that:[164]

  ~ 59% of the group with severe disabilities consumed below 80% of the EAR vs 16% of the group with moderate disabilities;
  ~ generally, children met their protein requirements;
  ~ nearly half of the children did not meet the RNI for iron;
  ~ half of the children with severe disabilities failed to meet at least 81% of the RNI for potassium, iron, copper, magnesium and zinc;
  ~ low intakes of selenium, vitamin A, niacin and folate were also seen in the groups with moderate and mild disabilities.

- A review of nutrition in children with chronic renal failure (CRF) and on dialysis by Rees and Shaw (2007) described energy intakes below recommended intakes, deteriorating intake with severity of CRF, and decreased intake over time. Low intakes of calcium, zinc and vitamins were also reported.[165]

- Children (10–16 years of age) with active Crohn's disease (CD) and children with CD in remission have been shown to have energy intakes significantly lower than estimated energy requirements ($p = 0.001$ and $p = 0.03$ respectively) and lower than recommended intakes of calcium and iron.[166]

There are multiple inter-related causes of malnutrition in cancer

- The possible causes of malnutrition in cancer patients are summarised in Table 1.13, but many of the factors listed in Figures 1.17 and 1.21 are also involved in the development of malnutrition in cancer patients. The causes are multi-factorial and they can be related to the effects of the tumour and/or treatment and the psychological effects of living with cancer.[131]

Table 1.13 **Possible causes of weight loss and malnutrition in cancer patients** (adapted from Henry 2011)[131]

CAUSES
• Catabolic effects of the tumour/abnormal metabolism of nutrients
• Inadequate intake due to tumour-induced anorexia
• Reduced food intake secondary to treatment side effects such as nausea, vomiting, stomatitis, constipation and malabsorption
• Obstruction from tumour or as a consequence of treatment, e.g. dysphagia secondary to cancer of the oesophagus, bowel obstruction secondary to disease, and dysphagia as a consequence of radiotherapy to the pharynx
• Pain, anxiety and depression

There are numerous reasons why food and thus energy and nutrient intake are poor in disease

- Energy and nutrient intake are affected by factors arising from the patient's condition and situation, healthcare workers' knowledge and action, institutional organisation, eating difficulties, inadequate provision of energy and nutrients, lack of guidance for staff, poor knowledge of nutrition, and failure to follow nutritional policies (see Figure 1.21).[35;44;45;63;66;140;148;149;152;167-172]

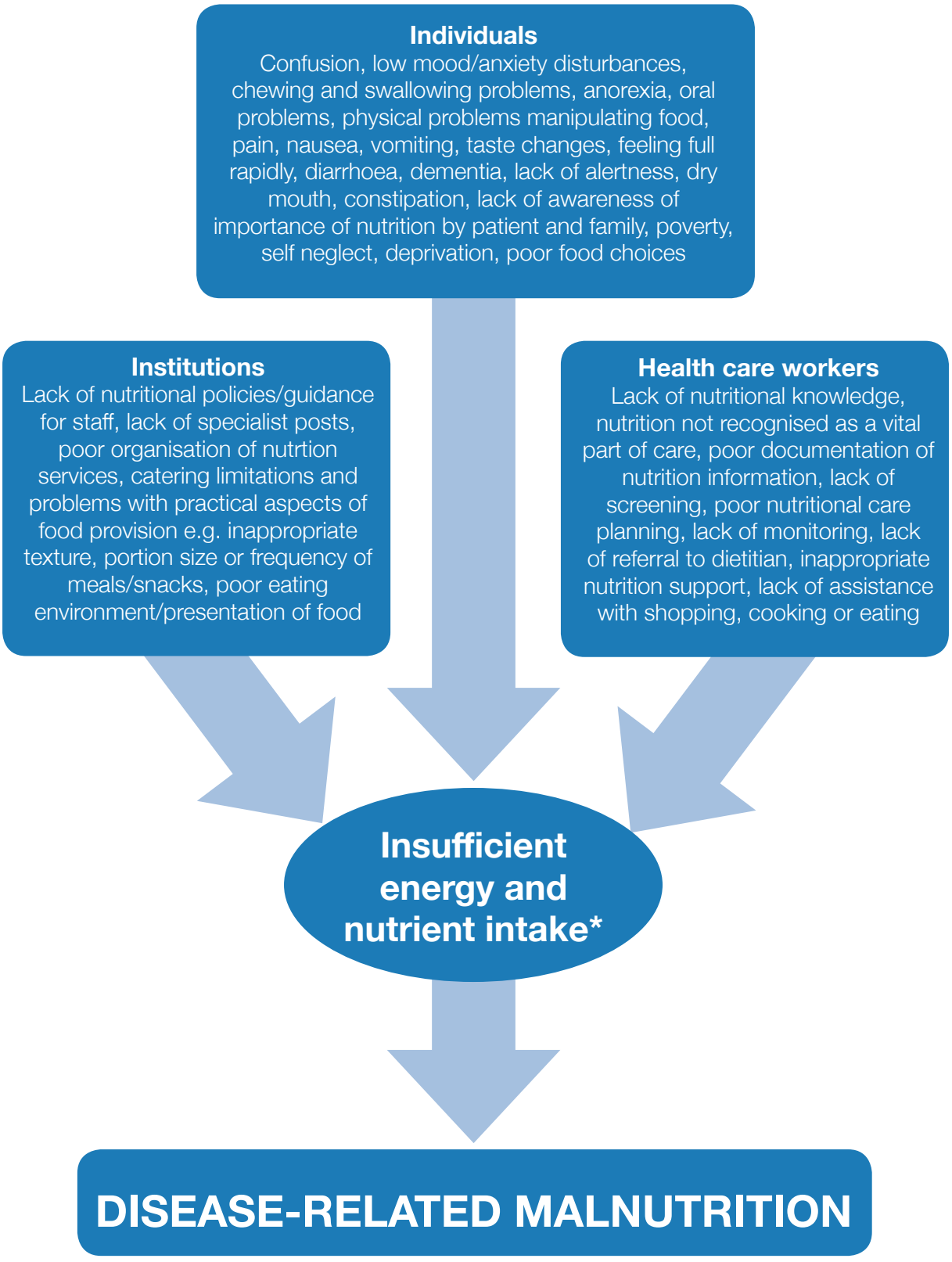

Figure 1.21 **Factors leading to insufficient energy and nutrient intake in adults as a cause of disease-related malnutrition** (adapted from Stratton et al. 2003)[35]

*Requirements for some nutrients may be increased due to malabsorption, altered metabolism and excess losses

1.4 CONSEQUENCES OF MALNUTRITION

Summary

Malnutrition leads to **far-reaching physical and psycho-social consequences** such as impaired immune response, impaired wound healing, reduced muscle strength and fatigue, inactivity, apathy, depression and self-neglect. **Malnutrition is also associated with poorer quality of life**. In children, growth and development is adversely impacted by malnutrition. Malnutrition has a particularly high adverse impact in the older person impairing function, mobility and independence.

These effects in turn contribute to increased morbidity and mortality. Malnourished hospital patients experience significantly higher complication rates than well-nourished patients (30.6% vs 11.3%) and the risk of infection is more than three times greater. Significantly higher mortality rates have been found in 'at-risk' hospital patients compared with 'not-at-risk' patients (12% vs 1%).

It is thus unsurprising that malnutrition is associated with increased healthcare resource use across all age groups such as increases in length of hospital stay, increased readmissions and more care needed after discharge. Average length of hospital stay may be increased by 30% in malnourished patients. In community patients malnourished patients visit family doctors more often and have more frequent hospital admissions than well-nourished patients.

As a result of increased morbidity and healthcare resource use malnutrition is costly to the individual, to society and to the economy. The estimated cost of managing patients at risk of malnutrition in the EU is €120 billion and €170 billion across Europe. This estimate is based on economic evidence from the UK undertaken in 2005 showing costs for managing patients at risk of malnutrition exceed €15 billion. A recent update puts the figure at £19.6 billion for England alone so it is highly likely that the figures above are now a very conservative estimate of the true cost of malnutrition in Europe.

The extra cost of treating a patient with malnutrition is 2-3 times greater than for a non-malnourished patient.

Conclusion

The adverse consequences of malnutrition arising as a result of disease and disability are far-reaching at both the individual and the societal level. Failure to address malnutrition risk appropriately puts unnecessary additional pressure on already constrained healthcare systems and leads to sub-optimal quality of care. The application of evidence-based nutritional screening programmes should help to address this.

Recommendations

On the issue of **consequences of malnutrition** the MNI makes the following recommendation:

Action	Issues to consider
Awareness should be raised about the wide ranging negative consequences of malnutrition for patients, for healthcare providers and for society in general **Evidence based screening programmes should be used to ensure that malnutrition and risk of malnutrition is identified early and appropriate action is taken to minimise its consequences**	• Education and training activities can be used to ensure that healthcare workers are fully aware of the negative consequences of malnutrition and what action to take to avoid these. Extra efforts need to be made to ensure that this message is heard and understood by all stakeholders including policy makers, healthcare providers, patients and carers. Malnutrition should not be accepted as an inevitable consequence of disease or ageing

Malnutrition adversely impacts on every organ system in the body, with potentially serious consequences (see Table 1.14).[82]

- Restricted recent dietary intake has been shown to affect metabolic, psychological and physical function in the presence and absence of disease, and in surgical patients to reduce collagen deposition, with implications for effective wound healing.[35]

Table 1.14 **Key physical and psychosocial effects of malnutrition** (adapted from Elia and Russell 2009)[82]

Effect	Consequences
Impaired immune response	Impaired ability to fight infection
Reduced muscle strength and fatigue	Inactivity, and reduced ability to work, shop, cook and self-care. Poor muscle function may result in falls, and poor respiratory muscle function may result in poor cough pressure - delaying expectoration and recovery from chest infection
Inactivity	In bed-bound patients, this may result in pressure ulcers and venous blood clots, which can break loose and embolise
Impaired temperature regulation	Hypothermia
Impaired wound healing	Increased wound-related complications, such as infections and un-united fractures
Impaired ability to regulate salt and fluid	Predisposes to over-hydration or dehydration
Impaired psycho-social function	Apathy, depression, introversion, self-neglect, hypochondriasis, loss of libido and deterioration in social interactions

1.4.1 Functional consequences

Malnutrition has functional consequences in adults and older people

- Malnutrition is associated with decreased muscle function and impaired functional status. In adult hospital patients, decreased hand-grip strength is a predictor of loss of functional status.[173] Reduced muscle strength and fatigue can lead to falls, reduced ability to self-care, and poor recovery from chest infection.[82]

- Low plasma vitamin D levels (< 20 ng/ml) have been associated with poorer physical performance and a greater decline in physical performance than with plasma vitamin D levels of at least 30 ng/ml.[38] In addition, low plasma vitamin D concentrations have been associated with a greater risk of future nursing home admission, and they are independently associated with an increased risk of falling in older people, particularly in those aged 65–75 years.[174;175]

- The clinical criteria for frailty ('shrinking' [i.e. unintentional weight loss/sarcopenia], weakness, poor endurance and low activity) are associated with chronic under-nutrition resulting in loss of weight and muscle mass and poor muscle function.[176] Without appropriate intervention, frail older people are likely to experience functional limitations and disability, increased morbidity and use of healthcare resources, and mortality.[138]

- A review of the links between nutrition and frailty suggested that loss of appetite, weight loss, sarcopenia, low energy and protein intake, low intake and blood levels of vitamins (B,C,D,E, folate), antioxidants (carotenoids) and trace elements (selenium and zinc) influence the development or aggravation of frailty.[177]

- Maintaining function in older people is considered a high priority by the WHO to help to prevent decline and institutionalisation (see Figure 1.22).

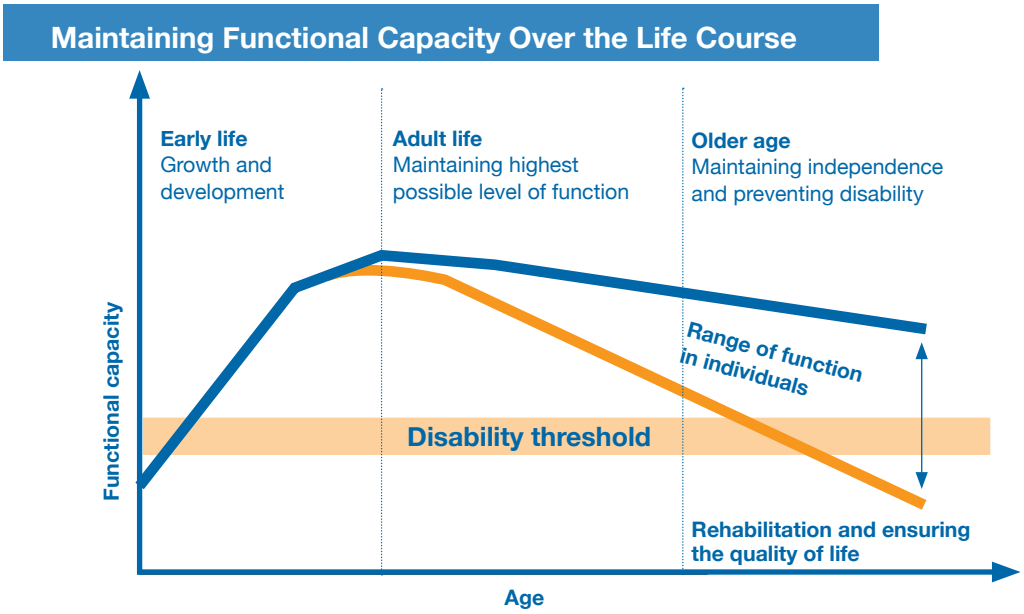

Figure 1.22 **Maintaining functionality and independence[178]**

Malnutrition is associated with impaired function in children and adults with cystic fibrosis

- Using the German Cystic Fibrosis Quality Assurance (CFQA) patient registry, cross-sectional and longitudinal analyses were undertaken in 3,298 patients aged > 2 years to investigate the relationship between malnutrition (stunting and/or wasting in children, BMI < 19 kg/m^2, weight < 80% or height < 90% of the median normal value for sex and age in adults) and lung function. The study found that:[179]

  ~ patients with malnutrition had significantly worse lung function;
  ~ malnourished adolescents had a serious decline in lung function compared with their well-nourished counterparts;
  ~ a fall in weight or height of ≥ 5% predicted within 1 year was associated with decrease in lung function; patients with improved nutrition showed constant or improved lung function.

Malnutrition is associated with impaired quality of life

- Malnutrition has been shown to impair quality of life (QOL) in free-living older people and in patients with cancer, hip fracture and COPD. Poor QOL is also reported in malnourished surgical patients, patients with end-stage renal disease undergoing haemodialysis and in general admissions to the acute hospital setting.[35]

1.4.2 Clinical consequences

1.4.2.1 MORTALITY

Malnutrition is associated with increased mortality in adults and older people

- A comprehensive review of studies addressing the associations between malnutrition and mortality showed that malnourished patients have a higher mortality rate than well-nourished patients. This effect was seen in a wide variety of patient groups and in younger patients:[35]
  - ~ general hospital admissions, medical and surgical patients;
  - ~ older people in a variety of care settings, e.g. hospital, intensive care, medical units, rehabilitation and long-term care;
  - ~ patients with stable COPD or acute exacerbations;
  - ~ patients with Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS);
  - ~ patients with cancer;
  - ~ patients with renal failure prior to dialysis or receiving dialysis;
  - ~ patients following stroke;
  - ~ patients in the community with chronic respiratory, GI, neurological or cardiovascular disease or cancer.

- In a large (n = 5051, mean age 59.8 years [±0.3 SEM]) multi-region (12 countries; Western Europe = 4, Eastern Europe = 5 and Middle East = 3), multi-centre (26 hospital departments; surgery, internal medicine, oncology, intensive care, gastroenterology and geriatrics) study, death was more frequent in 'at risk' patients than 'not at risk' patients (12% vs 1%, $p <$ 0.001), i.e. mortality was 12 times higher in 'at risk' patients (see Figure 1.23).[180]

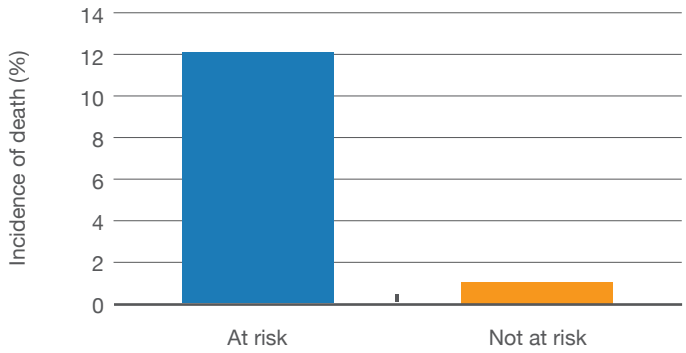

Figure 1.23 **Increased frequency of death in at risk patients vs not at risk patients ($p < 0.001$)** (adapted from Sorensen et al. 2008)[180]

- A prospective cohort study of newly admitted adult patients (18–74 years of age) to an acute tertiary hospital found that the mortality rate was higher in malnourished patients (SGA B+C) than in well-nourished patients at 1 year (34.0% vs 4.1%), 2 years (42.6% vs 6.7%) and 3 years (48.5% vs 9.9%, $p < 0.001$ for all). Malnutrition was a significant predictor of mortality (adjusted hazard ratio [HR] of 4.4 [95% CI 3.3–6.0], $p < 0.001$) (see Figure 1.24).[51]

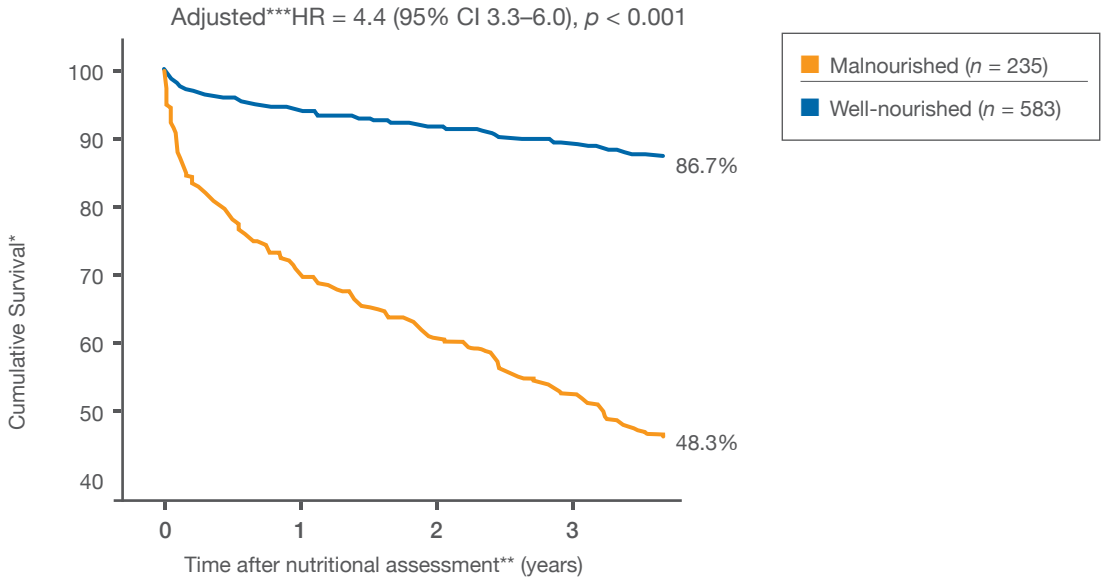

Figure 1.24 **Cumulative survival in well-nourished and malnourished patients (*n* = 818).** (adapted from Lim et al. 2012)[51]

HR: Hazard Ratio. *Survival and mortality data from Singapore Death Registry. **Assessment with Subjective Global Assessment within 48 h of hospital admission. ***Adjusted for ethnicity, age and gender.

- A survey of outpatients with COPD found that those at risk of malnutrition (medium and high risk using 'MUST') were more likely to die within 6 months than patients not at risk (6-month mortality rate 16.3% vs 5.8%, $p = 0.023$).[181]
- In a study that analysed the medical records of randomly selected malnourished patients with 996 matched (for age, gender and GP practice) non-malnourished patients in the UK, malnutrition remained an independent predictor of mortality after adjustment for age and co-morbidity.[60]
- Two-year mortality in nursing home residents in Sweden was found to be 52%. Male gender and low body weight were associated with increased risk of mortality.[160]
- DRM has been found to double the risk of mortality in hospital patients and to triple mortality in older patients in hospital and after discharge (see Figure 1.25).[182;183]

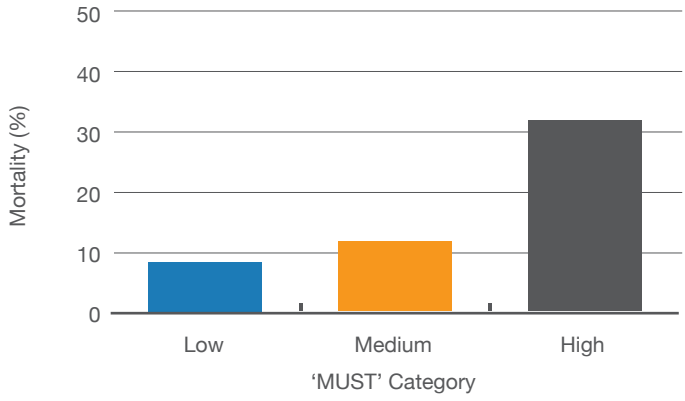

Figure 1.25 **Significant increase in in-hospital mortality with increasing malnutrition risk category** ($p = 0.01$) (adapted from Stratton et al. 2006)[182]

Malnutrition is associated with increased mortality in children

- Although data demonstrating that malnutrition has an adverse impact on morbidity and mortality in paediatrics is limited, it is clear from extrapolation of studies in adults and from studies in children in developing countries that malnutrition is associated with a greater risk.[184]
- A study of children operated on for congenital heart defects who died > 30 days after surgery showed that a decrease in WFA during the first months after surgery was strongly related to late mortality.[185]
- A prospective study of children aged 1–18 years newly diagnosed with cancer in low income countries in Central America showed that significantly higher mortality rates were related to degree of malnutrition (using percentile BMI for age, MUAC, TSFT and albumin) (14.0% vs 16.8% vs 20.5% for adequately nourished, moderately depleted and severely depleted children respectively [total 18.4%, $p = 0.006$]). Event-free survival at 2 years from diagnosis was significantly different in the 3 groups (65% vs 57.3% vs 48.4%, $p < 0.001$).[186]

1.4.2.2 COMPLICATIONS

Malnutrition is associated with increased morbidity in adults and older people

- The risk of infection is more than three times greater among hospitalised malnourished patients than well-nourished patients.[187]
- In a large ($n = 5051$, mean age 59.8 years [±0.3 SEM]) multi-region (12 countries; Western Europe = 4, Eastern Europe = 5 and Middle East = 3), multi-centre (26 hospital departments; surgery, internal medicine, oncology, intensive care, gastroenterology and geriatrics) study, the rate of complications was 3 times greater in at risk patients than not at risk patients (30.6% vs 11.3%, $p < 0.001$) (see Figure 1.26).[180]

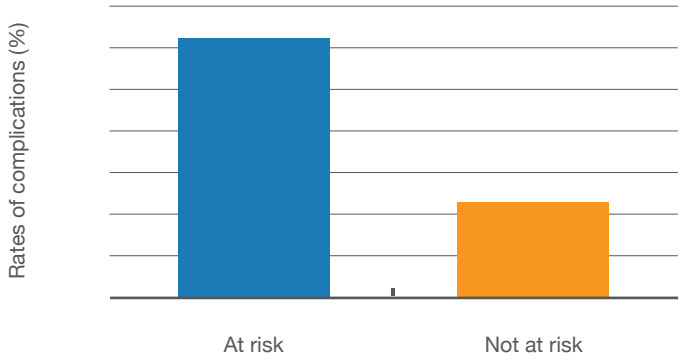

Figure 1.26 **Increased rate of complications in at risk patients vs not at risk patients** ($p < 0.001$) (adapted from Sorensen et al. 2008)[180]

- Older women with weight loss have increased rates of hip bone loss and the risk of subsequent hip fracture is twice greater.[188]

Malnutrition is associated with increased morbidity in children

- In a study of children aged 31 days to 17.9 years (n = 175) who required major abdominal or non-cardiac thoracic surgery on a non-emergency basis, malnourished children had a higher rate of infectious complications compared to well-nourished children (p = 0.042).[27]
- A prospective cohort study of 385 children admitted to a tertiary paediatric intensive care unit at a teaching hospital in Brazil found that malnutrition on admission (using z-score of WFA in infants < 2 years of age and z-score of BMI in children aged ≥ 2 years based on WHO child growth standard curves) was associated with greater length of mechanical ventilation in a multiple logistic regression model (OR 1.76, 95%; CI 1.08–2.88, p = 0.024).[189]
- A prospective study of children aged 1–18 years newly diagnosed with cancer in low income countries in Central America showed that frequency of abandonment of therapy was related to degree of malnutrition (using percentile BMI for age, MUAC, TSFT and albumin) (6.1% vs 12.5% vs 14.0% for adequately nourished, moderately depleted and severely depleted children respectively [total 11.9%, p < 0.001]).[186]

Malnutrition has an adverse impact on growth and development in children

- Poor weight gain or weight loss is one of the first indicators of malnutrition in children with acute malnutrition presenting with decreased WFH but normal HFA.[190]
- Nutritional imbalances that are sustained for any appreciable length of time adversely affect growth in terms of height.[190]
- Development is rapid in childhood, particularly in early childhood, and adverse effects of malnutrition on learning, behaviour and cognition in children have been described.[35]
- A review and meta-analysis showed that failure to thrive in infancy is associated with adverse cognitive outcomes in children identified in primary care (pooled effect size weighted standardised mean difference -0.30; 95% CI -0.18 to -0.42) and in children identified in hospital or specialist clinics (-0.85; 95% CI -0.41 to -1.30). The large difference in effect size may be related to the fact that cases with more developmental delay are more likely to be referred to hospitals or specialist clinics.[191]
- A small-scale study (n = 20, age groups 5–7 years and 8–10 years) from India designed to investigate the effect of stunting and/or wasting (as a result of chronic protein-energy malnutrition) on the nature of cognitive development and the rate of cognitive development found that malnourished children performed poorly compared with well-nourished children in tests of cognitive flexibility, attention, working memory, visual perception, verbal comprehension and memory. Stunting in particular may be responsible for the lack of age-related improvement in malnourished children for tests of design fluency, working memory, visual construction, learning or memory.[192]
- Early infancy may be a critical period for the effect of under-nutrition on cognitive development. The Avon Longitudinal Study of Parents and Children (ALSPAC) in the UK (n = 5771) found that early growth faltering (defined as < 5th percentile for weight gain in the first 8 weeks) was associated with a total intelligence quotient (IQ) that was significantly lower by an average of -2.71 points at 8 years of age.[193]
- Infants (n = 130) with faltering growth (defined as sustained WFA < 5th percentile or weight-for-length < 10th percentile) recruited from primary care clinics in low-income urban areas in the US were compared with infants with adequate growth and were shown to be more vulnerable to short stature, poor arithmetic performance and poor work habits at 8 years of age, illustrating the possible longer-term effects of early failure to thrive, although other factors could be involved.[194]

Malnutrition may affect the ability to withstand cancer treatment

- Nutritional risk (using NRS-2002) has been shown to be an independent predictor of postoperative complications in colorectal cancer patients.[195]
- Malnutrition has similar effects on patients with cancer as it has on patients without cancer, such as effects on GI integrity, adverse impact on respiratory and cardiac muscle function, recovery from surgery, wound healing, psychological and immune function.
- Treatment effects may also contribute, including the use of chemotherapy agents, irradiation and immunosuppressive medications, and surgery. Studies have demonstrated that malnourished patients receiving chemotherapy have more pronounced treatment-related side effects and breaks from treatment to manage these, e.g. stomatitis.[196]
- Malnutrition in cancer is associated with poor response to therapy, increased susceptibility to treatment-related adverse events, as well as poor outcome and QOL.[197]

1.4.3 Economic consequences

1.4.3.1 HEALTHCARE RESOURCE USE

- Malnutrition is associated with increased morbidity in both acute and chronic disease, e.g. poor wound healing and postoperative complications such as acute renal failure, pneumonia and respiratory failure. The increased morbidity results in increased health care needs, resulting in increased costs (see Figure 1.27).[198]

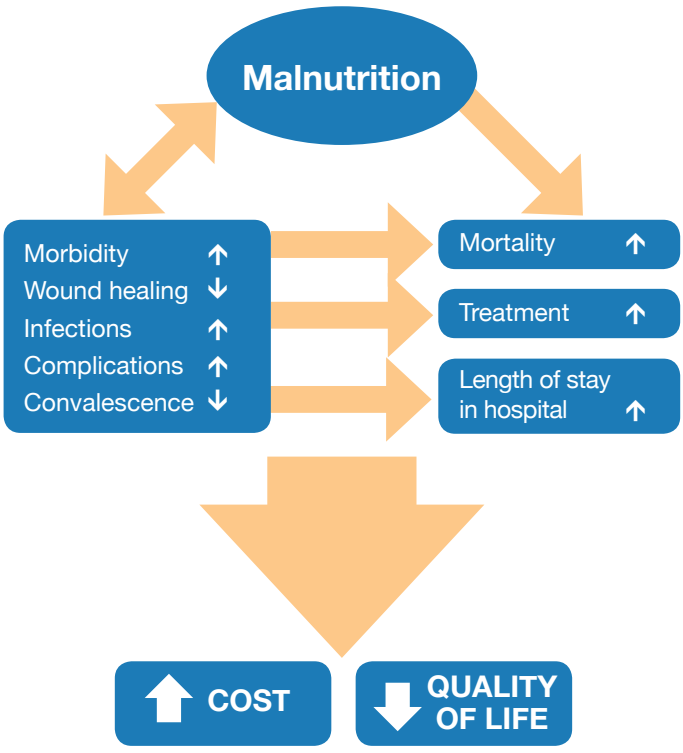

Figure 1.27 **Prognostic impact of malnutrition** (adapted from Norman et al. 2008)[198]

Malnutrition increases use of healthcare resources by adult and older hospital patients

- In prospective and several large retrospective evaluations, studies demonstrate that adults and older patients in hospital (with a variety of conditions) use significantly more healthcare resources than well-nourished patients in terms of (see Table 1.15):

  ~ increases in length of hospital stay;
  ~ increases in readmission rates;
  ~ delays in returning home.

- A case control study undertaken in adults (mean age 73.7 years) found that patients at risk of malnutrition on admission (according to NRS ≥3) had a significantly longer length of hospital stay. Patients that became at risk of malnutrition during their hospital stay also had a significantly longer length of hospital stay (Figure 1.28).[199]

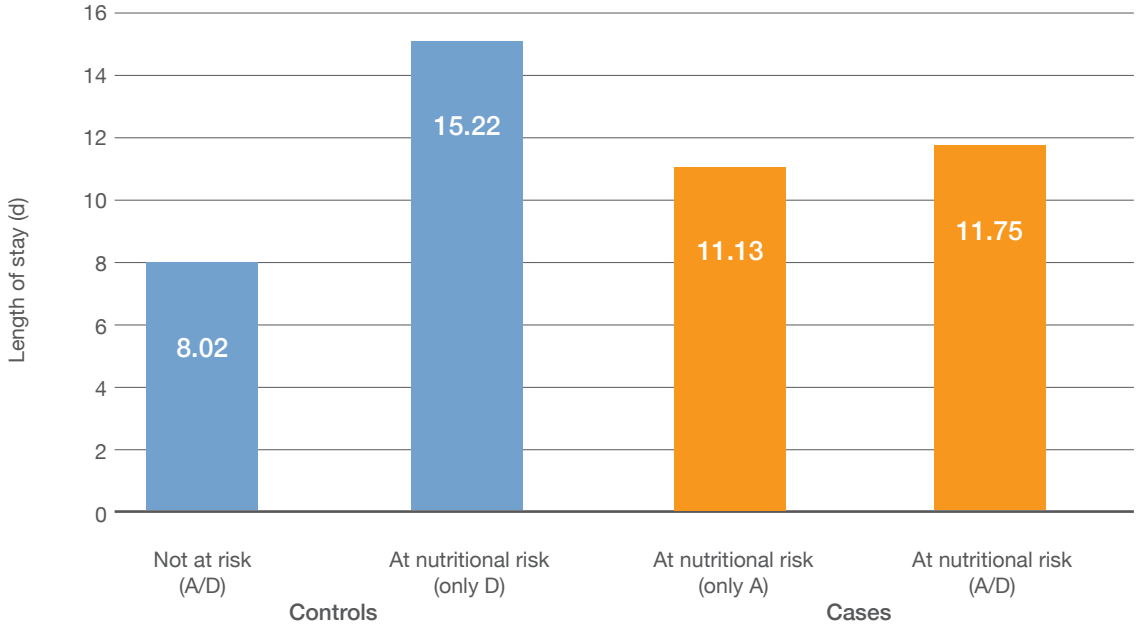

Figure 1.28 **Days of hospital stay according to the presence of nutritional risk at admission and discharge.** A, admission; D, discharge. (adapted from Leon-Sanz et al, 2015)[199]

Malnutrition increases use of healthcare resources by adults and older people in the community

- Similarly, in prospective evaluations and 1 large retrospective evaluation, studies demonstrate that adults and older patients (with a variety of conditions) use significantly more healthcare resources than well-nourished patients in terms of (see Table 1.16):

  ~ increases in the number of diagnosed diseases;
  ~ increases in the number of visits to family doctors;
  ~ increases in hospital admissions and readmissions;
  ~ increases in length of hospital stay.

Malnutrition in children is associated with an increased length of hospital stay

- A number of studies have demonstrated that malnourished children have a longer hospital stay compared with well-nourished children (see Table 1.17). This increase in use of healthcare resources is likely to increase the cost of care of malnourished children.

- Abdelhadi et al conducted a large retrospective analysis of over 6 million hospitalised children aged ≤17 years and found that LOS among children with a coded diagnosis of malnutrition (CDM) was significantly longer than those without a CDM (Figure 1.29). In addition, they found that discharge home with care was 3.5 times more common among malnourished patients (10.9% vs 3.1%, $p<0.001$).[200]

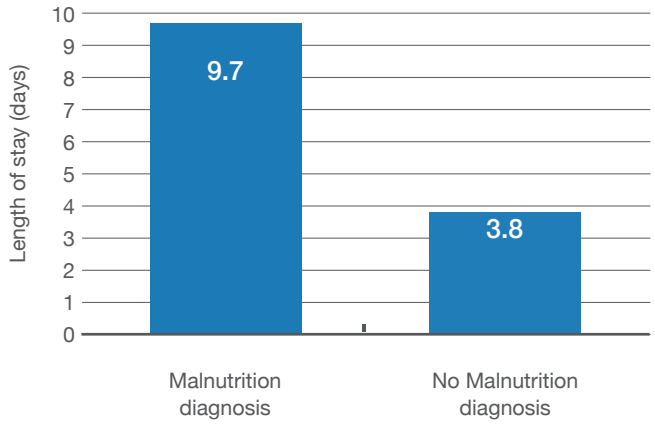

Figure 1.29 **Hospital length of stay of children ≤17 years with a coded diagnosis of malnutrition vs. those without** (adapted from Abdelhadi et al, 2016)[200]

Table 1.15 Examples of significantly increased use of healthcare resources by patients identified as malnourished or at risk of malnutrition compared with non-malnourished patients – hospital

Country/ Region	Study	Population (*n*) Study design	Method	Malnutrition/risk	Outcome
Brazil	Leandro-Merhi et al. (2011)[201]	Adults and elderly, surgical (*n* = 350) Prospective evaluation	SGA for adults, MNA for elderly	Adults: 19.3% slightly malnourished, 0.8% at risk Elderly: 11% malnourished, 32.9% at risk	• ↑LOS (malnourished 10.1±8.7 vs at risk of malnutrition 7.5±6.5 vs well-nourished 5.7±5.8 moderate days, *p* = 0.0005)
Canada	Curtis et al. (2016)[202]	Adult patients ≥18 years admitted to surgical or medical wards (*n* = 958) Multi-center Prospective cohort study	SGA	10.8% severely malnourished 33.5% moderately malnourished 55.7% well nourished	• Severely malnourished LOS 34% longer than well-nourished (p=0.000) with medical stays increased by 53% (*p* = 0.001) • Moderately malnourished LOS 18% longer than well-nourished (*p* = 0.014) with medical stays increased by 23% (*p* = 0.014) and surgical stays increased by 32% (*p* = 0.015)
Europe	Pernicka et al. (2010)[203]	Adults (*n* = 1,346 pairs case/controls) Retrospective evaluation	BMI + weight loss	7% malnourished	• ↑LOS (mean LOS 15.1 [95% CI 14.1–16.0] in malnourished cases vs 12.2 [95% CI 11.4–13.0] in non-malnourished controls)
France	Melchior et al. (2012)[204]	Colorectal cancer patients undergoing surgery (*n* = 453). Post-hoc analysis of prospective study	See details*	26.7% malnourished 73.3% well-nourished	• ↑LOS (malnourished 19.6 days vs. well-nourished 16.2 days; *p*= 0.017).
France	Nitenberg et al. (2011)[205]	Adults, post-surgical colorectal cancer (*n* = 762) Post-hoc analysis of prospective data	See details*	Not reported	• ↑LOS (mean LOS was 3.1 days longer in malnourished patients than in well-nourished patients, *p* = 0.004) • delays returning home (69.6% of malnourished patients referred to another facility compared with 54.2% of well-nourished patients, *p* = 0.027)

Table 1.15 Continued

Country/ Region	Study	Population (*n*) Study design	Method	Malnutrition/risk	Outcome
France	Grigioni et al. (2010)[206]	Adults (*n* = 354) Prospective evaluation	BMI/weight change/ albumin	29.5% moderate/severe malnutrition	• ↑LOS (11.7 days vs 7.9 days, $p < 0.001$)
France	Pressoir et al. (2010)[137]	Adults cancer (*n* = 879) Prospective evaluation	See details**	10.8% severely malnourished 33.5% moderately malnourished 55.7% well nourished	• ↑LOS (median 19.3±19.4 days vs 13.3±19.4 days, $p < 0.0001$)
Germany	Thomas et al. (2016)[207]	Surgical patients (*n* = 1244) Prospective observational study	NRS 2002	24.1% moderate to serious risk (NRS ≥3) 23% slight risk (NRS 1-2)	• ↑LOS (at risk 17.93 days ±19.66 vs. not at risk 9.42 days ± 10.05, $p < 0.001$)
Germany	Pirlich et al. (2006)[74]	Adults (*n* = 1,886) Prospective evaluation	SGA	27.4% malnourished (17.6% moderate and 9.8% severe)	• ↑LOS (average difference 4.6 days or 42%, $p < 0.001$)
Singapore	Lim et al. (2012)[51]	Adults (*n* = 818; 530 matched for DRG group) Prospective evaluation	SGA	29% malnourished (25% moderate and 4% severe)	• ↑LOS (mean 6.9±7.3 days vs 4.6±5.6 days, $p = 0.001$, DRG matched, adjusted) • readmission within 15 days of index admission (RR 1.9; CI 1.1–3.2)
Spain	Álvarez Hernández et al. (2015)[208]	Adults with dysphagia (*n* = 352) Observational study	NRS 2002 tool	45.6% malnourished on admission (NRS≥3) 54.6% ≥70 years malnourished on admission 25.5% <70 years malnourished on admission	• ↑LOS (malnourished 11.53 ± 7.10 days vs. well-nourished 8.80 ± 6.06 days, $p < 0.001$)

Table 1.15 Continued

Country/ Region	Study	Population (*n*) Study design	Method	Malnutrition/risk	Outcome
Spain	Gastalver-Martín et al. (2015)[209]	Adults Prospective observational study	NRS-2002 and SNAQ	33% malnourished on admission (NRS ≥3 or SNAQ ≥2) 30% malnourished on discharge (NRS ≥3 or SNAQ ≥2) 19% malnourished on admission and discharge (NRS ≥3 or SNAQ ≥2)	• LOS 14.00 days ± 10.44 (malnourished on admission) vs. 11.96 days ± 6.34, $p = 0.602$ (well-nourished on admission) • ↑LOS 19.96 days ± 14.01 (malnourished on discharge) vs. 14.68 days ± 8.38 (well-nourished on discharge), $p = 0.005$ • ↑LOS 24.44 days ± 17.49 (malnourished throughout hospital stay) vs. 14.69 days ± 7.99 (well-nourished throughout hospital stay), $p = 0.014$
Spain	Leon-Sanz et al. (2015)[199]	Adults Case-control study	NRS 2002	24.4% malnourished on admission (NRS ≥3) 22.6% malnourished at discharge (NRS ≥3)	• ↑LOS for patients at risk (11.5 days ± 7.5 vs 8.5 days ± 5.8, $p< 0.001$) • ↑LOS for patients that became at risk during hospitalisation vs. those not at risk during hospital stay (15.2 days ± 9.2 vs. 8 days ± 5.2, $p< 0.001$)
Spain	Marco et al. (2011)[52]	Internal medicine ($n = 1,567,659$) Retrospective evaluation	Diagnostic codes for malnutrition	1.4%†	• ↑LOS (18.1 vs 9.8 days, $p< 0.001$)
Spain	de Luis & Lopez Guzman (2006)[210]	Adults, internal medicine ($n = 213$) Prospective evaluation	MNA	23.9% (MNA < 17) 50.2% at risk (MNA 17–24)	• ↑LOS (increase of 2.6 days for each decrease of 1 kg of body weight, decrease of 3.2 days for each 1 point increase in MNA score)

Table 1.15 Continued

Country/ Region	Study	Population (*n*) Study design	Method	Malnutrition/risk	Outcome
Spain	Planas et al. (2004)[211]	Adults (*n* = 400) Prospective evaluation	SGA	46% malnourished	• ↑LOS (overall population 7.5±5.4 days vs 5.0±5.1 days; scheduled admissions 7.1±6.2 days vs 4.8±4.4 days, both $p < 0.05$) • ↑readmission rate (total – overall 30.1% vs 15.1%, scheduled 32.8% vs 15.9%, cancer 39.7% vs 21.4%, all $p < 0.05$; non-elective – overall 20.7% vs 13.2%, scheduled 21.4% vs 12.8%, cancer 29.3% vs 17.2%, all $p < 0.05$)
UK	Gomes et al. (2016)[212]	Stroke patients (*n* = 342) Prospective study	'MUST'	64% at low risk 7% at medium risk 29% at high risk of Malnutrition	• ↑LOS across malnutrition risk categories (median (range)): Low – 14 days (2-173) Medium – 19 days (3-165) High – 48 days (2-194) ($p<0.001$)
UK	Slee et al. (2016)[213]	Older (frail) adults	'MUST' and MNA-SF Albumin <30g/l (severe)	High risk 14% Medium risk 9% Low risk 77% MNA-SF Normal 9% MNA-SF At risk 45% MNA-SF Malnourished 46% Albumin <30g/l (severe) 42% Albumin 30-34.9 g/l (moderate) 29% Albumin >35 g/l (low/absent) 29%	• ↑LOS for albumin <30g/l (severe malnutrition) 25 days ± 21.6 vs. albumin >35g/l (no malnutrition) 14.1 days ± 9.5, $p < 0.05$

Table 1.15 Continued

Country/ Region	Study	Population (*n*) Study design	Method	Malnutrition/risk	Outcome
US	Weiss et al. (2016)[72]	All non-maternal and non-neonatal hospital inpatient stays (*n* = 27.6 million) Descriptive summary report of Heathcare Cost and Utilisation Project (HCUP) administrative health care data from the National (Nationwide) Inpatient Sample (NIS)	Malnutrition was identified using a broad set of diagnostic codes that included the following six categories: - Postsurgical nonabsorption - Nutritional neglect - Cachexia - Protein-calorie malnutrition - Weight loss or failure to thrive - Underweight	1.95 million hospital stays involved malnutrition i.e. 7.1% of the 27.6 million total	• ↑LOS across all six types of malnutrition compared with average length of hospital stay overall: - All 2013 non-maternal/non-neonatal 4.9 days vs. - Postsurgical non-absorption 9.6 days - Nutritional neglect 9.2 days - Cachexia 7.5 days - Protein-calorie malnutrition 10.7 days - Weight loss or failure to thrive 6.5 days - Underweight 6.0 days

SGA Subjective Global Assessment; MNA Mini Nutritional Assessment; BMI Body Mass Index; NRS Nutritional Risk Screening; SNAQ Short Nutritional Assessment Questionnaire; 'MUST' Malnutrition Universal Screening Tool'; MNA-SF Mini Nutritional Assessment Short Form; LOS Length of stay. *Malnutrition defined as weight loss greater than 10% of usual body weight in the 6 months pre-surgery and/or Body Mass Index (BMI) lower than 18.5 (patients under 70 years) or 21 (patients over 70 years). **See Table 1.10 for definitions of malnutrition used by Pressoir et al, (2010). † Low due to low communication of malnutrition in discharge reports.

Table 1.16 Examples of significantly increased use of healthcare resources by patients identified as malnourished or at risk of malnutrition compared with non-malnourished patients – community

Country/ Region	Study	Population (*n*) Study design	Method	Malnutrition/risk	Outcome
Israel	Feldblum et al. (2009)[214]	Older people (*n* = 204) Prospective evaluation	MNA	38.7% at risk (MNA < 24)	Healthcare use before index hospital admission: • ↑no. diagnosed diseases (mean 7.4±0.21 vs 5.9±0.16, $p = 0.001$) • ↑no. family physician visits (mean 7.7±0.95 vs 3.7±0.75, $p = 0.001$) • ↑no. hospital admissions before current admission (mean 1.7±0.19 vs 1.1±0.15, $p = 0.02$) Healthcare use after index hospital admission: • ↑LOS (current event) (mean 7.14±0.8 days vs 5.0±0.4 days, $p = 0.01$) • ↑LOS (in following 3 months) (mean 2.8±0.54 days vs 1.4±0.29 days, $p = 0.03$)
UK	Guest et al. (2011)[60]	Adult malnourished (*n* = 1,000) Retrospective analysis	BMI < 18.5 kg/m^2 + clinical indicators		• ↑no. GP visits in 6 months (mean 18.9 in malnourished cases vs 9.12 in non-malnourished controls, $p < 0.001$) • ↑no. hospital admissions in 6 months (13% vs 5%, $p < 0.05$) • ↑LOS (6.24 days vs 3.26 days, $p < 0.001$)
UK	Cawood et al. (2010)[215]	Adult outpatients (*n* = 194) Prospective evaluation	'MUST'	18% at risk (12% medium, 6% high)	• ↑LOS (all hospital admissions: low risk 0.90±3.9 days vs medium risk 2.04±4.9 days vs high risk 4.92±8.1 days, $p = 0.007$) • ↑no. hospital admissions in 6 months (12.6% vs 26.1% vs 66.7%, $p = 0.000$) • ↑no. emergency admissions in 6 months (5.0% vs 8.7% vs 41.7%, $p = 0.000$) • ↑no. planned admissions in 6 months (7.5% vs 21.7% vs 25.0%, $p = 0.025$)
UK	Collins et al. (2010)[181]	Adult COPD outpatients (*n* = 205) Prospective evaluation	'MUST'	23.9% at risk (medium + high)	• ↑no. emergency and elective admissions per patient in 6 months (low risk 0.65±1.1 vs medium + high risk 1.10±2.0, $p = 0.043$) • ↑no. emergency admissions per patient in 6 months (low risk 0.48±0.9 vs medium + high risk 0.92±1.8, $p = 0.023$)

COPD Chronic Obstructive Pulmonary Disease; MNA Mini Nutritional Assessment; BMI Body Mass Index; 'MUST' Malnutrition Universal Screening Tool'; LOS Length of stay.

Table 1.17 Summary of studies showing increased length of hospital stay in malnourished children or children at risk of malnutrition*

Country/ Region	Study	Population (*n*) Study design	Method of assessment/screening	Outcome
Brazil	Fernandez et al. (2008)[98]	Children aged < 3 years (*n* = 67) Prospective evaluation	Gomez score (WFA)	Linear regression analysis showed an association between longer hospital stay and no weight gain (r^2 = 0.11, *p* = 0.005)
Canada	Groleau & Babakissa (2008)[89]	Children aged 0–18 years (*n* = 173) Prospective evaluation	A variety of methods (see Table A1.8, Appendix I)	Length of stay was significantly correlated to nutritional status (r = -0.268, *p* < 0.05)
Canada	Secker & Jeejeebhoy (2007)[27]	Children aged 31 days – 17.9 years scheduled for surgery (*n* = 175) Prospective evaluation	Subjective Global Nutritional Assessment (SGNA)	Postoperative stay was more than twice as long for severely malnourished (19.0±58.8 days) vs well-nourished children (5.3±5.4 days) and moderately malnourished children (8.4±11.1 days) (*p* = 0.002) (remained significant when extreme outlier removed from the analysis) When taken together, moderately and severely malnourished children had a 55% longer hospital stay than well-nourished children
The Netherlands	Hulst et al. (2010)[25]	Children aged > 1 month, admission to paediatric ward and expected stay at least 1 day (*n* = 424) Prospective evaluation	STRONG$_{kids}$	After adjustment for a variety of clinical factors including younger age, presence of underlying disease, non-surgical reason for admission and non-Caucasian ethnicity, increase in nutritional risk category was significantly related to a longer length of hospital stay (*p* = 0.017)
The Netherlands	Joosten et al. (2010)[92]	Children aged > 1 month, admission to medium care unit and expected stay at least 1 day (*n* = 424) Prospective evaluation	Acute malnutrition = WFH < -2 SD Chronic malnutrition = HFA < -2 SD	Median duration of hospital stay of children with acute malnutrition was significantly longer vs non-malnourished children (median 4 [range 1–44] days vs 2 [1–24] days, *p* = 0.001)
US	Abdelhadi et al. (2016)[200]	Hospitalised Children (≤17 years) (*n* = 6,280,710) Retrospective analysis using patient-level data on hospital inpatient stays	ICD-9-CM and ICD-10-CM codes that related to malnutrition	LOS among children with a CDM was significantly longer than those without a CDM (9.7days vs. 3.8 days) Discharge with home care was 3.5 times more common among malnourished patients (10.9% vs 3.1%, *p* < 0.001)

*See Table A1.8, Appendix 1 for details of prevalence of malnutrition and risk of malnutrition. WFA weight for age; WFH weight for height; HFA height for age. ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification

1.4.3.2 FINANCIAL COSTS

Malnutrition increases healthcare costs

The financial burden of malnutrition is, increasingly, being defined and recognised. Historically much of the data on the costs of malnutrition has arisen from the UK from work undertaken by the British Association of Enteral and Parenteral Nutrition (BAPEN), with the first report on the costs of malnutrition being published in 2005.[216] The reports from BAPEN have been used by other workers to help estimate the cost of DRM in their own countries or for Europe as a whole.[217-219]

Increases in health and social care budgets together with improvements in defining and recording costs have led to an updated version of the report which aims to provide more accurate assessment of the costs of malnutrition.[220] The latest report is specific to England rather than the UK as a whole. This is because, as the four devolved nations of the UK (England, Scotland, Wales, and Northern Ireland) have been developing their own distinct healthcare systems using specific budgets allocated to their countries, it has become increasingly difficult to use a common framework to establish the cost of malnutrition in the UK as a whole.

Increasingly, data on the costs of malnutrition is available in other countries. Some of this data has been generated by prospective studies that measure the direct costs of hospital admissions for a malnourished vs. a well-nourished patient. Other estimates are made based on economic models that look at disease prevalence, malnutrition prevalence within disease states and financial data on the cost of treating the disease. However, what is clear from all of these reports and studies is that the financial burden of DRM is significant both at an individual level and at a population level.

The costs of DRM have increased and the cost of treating a malnourished patient is 2-3 times greater than for a non-malnourished patient

- The public health and social care expenditure associated with malnutrition in adults and children in England in 2011–12, identified using the 'Malnutrition Universal Screening Tool' ('MUST'), was estimated to be £19.6 billion, or about 15% of the total expenditure on health and social care.[220]
- Previous BAPEN reports have suggested that malnutrition accounted for >10% of the total costs in the UK.[216; 221] However, according to the latest report the estimated cost of disease-related malnutrition appears to have increased considerably over time:
  - >£7.3 billion in the UK in 2003
  - >£13 billion in the UK in 2007
  - £19.6 billion in England in 2011–12

  This is thought to be due to a striking increase in the budget for health and social care between 2003 and 2012 and the fact that the previous costs were based on minimum estimates. The current BAPEN report involves a more complete analysis of all the major services and associated costs providing a better estimate of the costs of disease related malnutrition.[220]
- Total expenditure of £19.6 billion is made up of £15.2 billion expenditure on healthcare costs and £4.4 billion relating to social are costs (Figure 1.30).

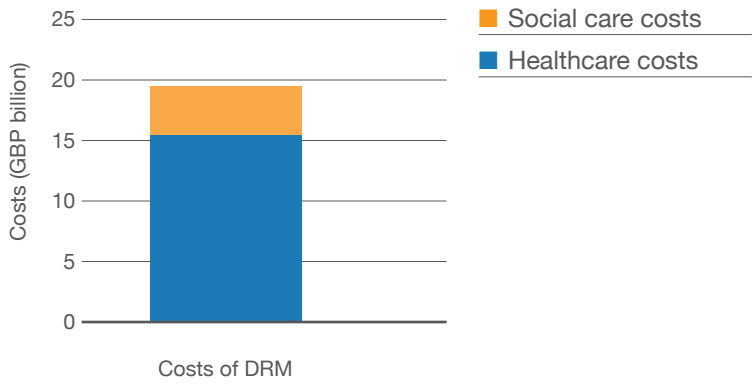

Figure 1.30 **The cost of disease-related malnutrition in England 2011-2012.** (adapted from Elia M, 2015)[220]

- The distribution of expenditure in the malnourished population is broadly similar to that of the general population, although a greater proportion is distributed towards secondary care and to older subjects (≥65 years) in the malnourished population (Figure 1.31).

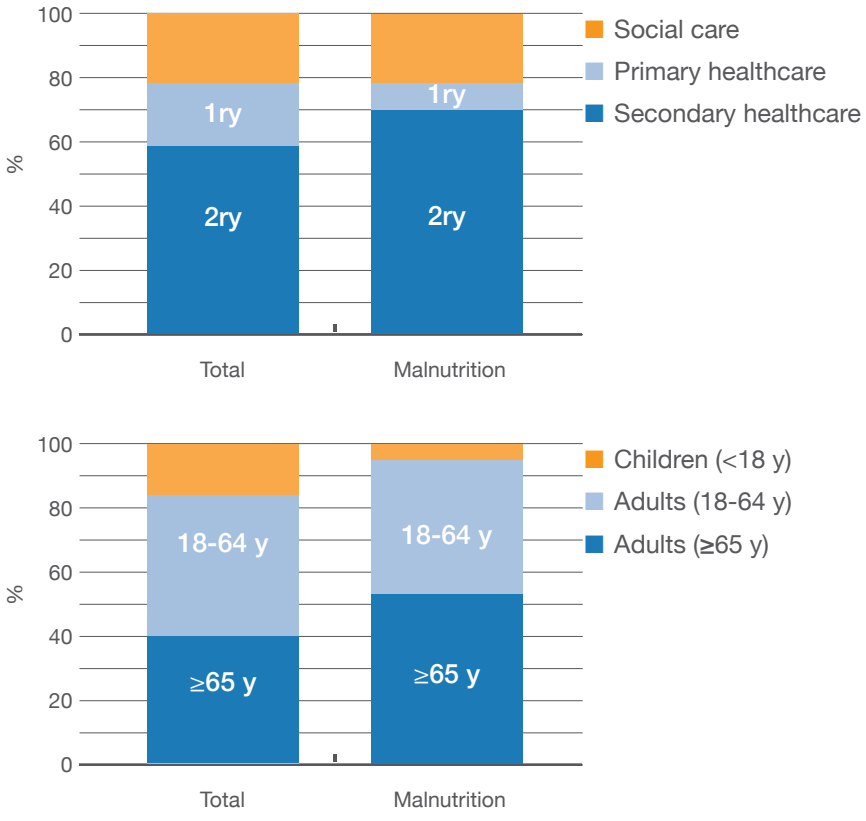

Figure 1.31 **The distribution of total public health and social care expenditure in England (£127.5 billion) and in the subgroup of individuals with malnutrition (£19.6 billion) according to type of care (upper chart) and age category (lower chart) (base case analysis).** 1ry = primary care; 2ry = secondary care. (adapted from Elia M, 2015)[220]

- The extra (incremental) cost of treating malnutrition was calculated as being 2–3 times greater than for a non-malnourished subject (Figure 1.32).

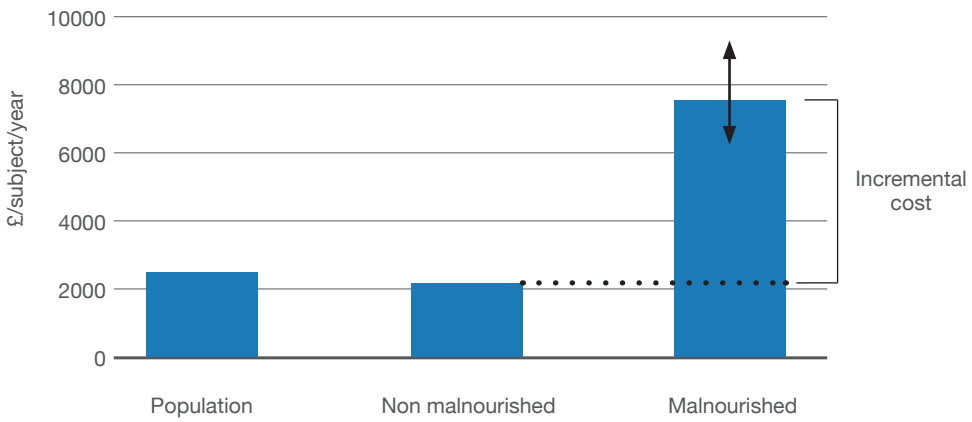

Figure 1.32 **Public expenditure on health and social care per subject in the general population, per subject without malnutrition and per subject with malnutrition (medium + high risk according to 'MUST').** The top of the bars represent the values calculated assuming that 5% of the population is malnourished or at risk of malnutrition. The tip of the upper arrow heads above the bar for the malnourished represents the value calculated assuming that 4% of the population is malnourished and the tip of the lower arrowhead assuming that 6% of the population is malnourished. No arrowheads are shown for the non-malnourished because the base case value was affected by only about ± 1% (adapted from Elia M, 2015).[220]

- In comparison, estimates of the direct NHS costs of treating overweight and obesity, and related morbidity in England have ranged from £479.3 million in 1998 to £4.2 billion in 2007,[222] significantly lower than the costs associated with DRM.

Data on the cost of malnutrition in Europe and beyond are now available

- Increasingly, more data is now available on the financial burden of malnutrition in many other countries. Estimates for Europe alone suggest that the cost of DRM is €170 billion[218] or €120 billion[219] in the EU. This estimate is based on health economic evidence from the UK showing that the costs for managing patients at risk of malnutrition exceed €15 billion.[221] The recent update by BAPEN puts the figure at £19.6 billion for England alone so it is highly likely that the figures above are now a very conservative estimate of the true cost of malnutrition in Europe.
- In a Spanish study hospitalization costs were calculated, based on a patients' nutritional status throughout their hospital journey. The highest costs were seen in subjects that were both malnourished on admission and at discharge and hospitalisation costs increased generally for **any** patient that was malnourished on discharge.[209] (Figure 1.33)

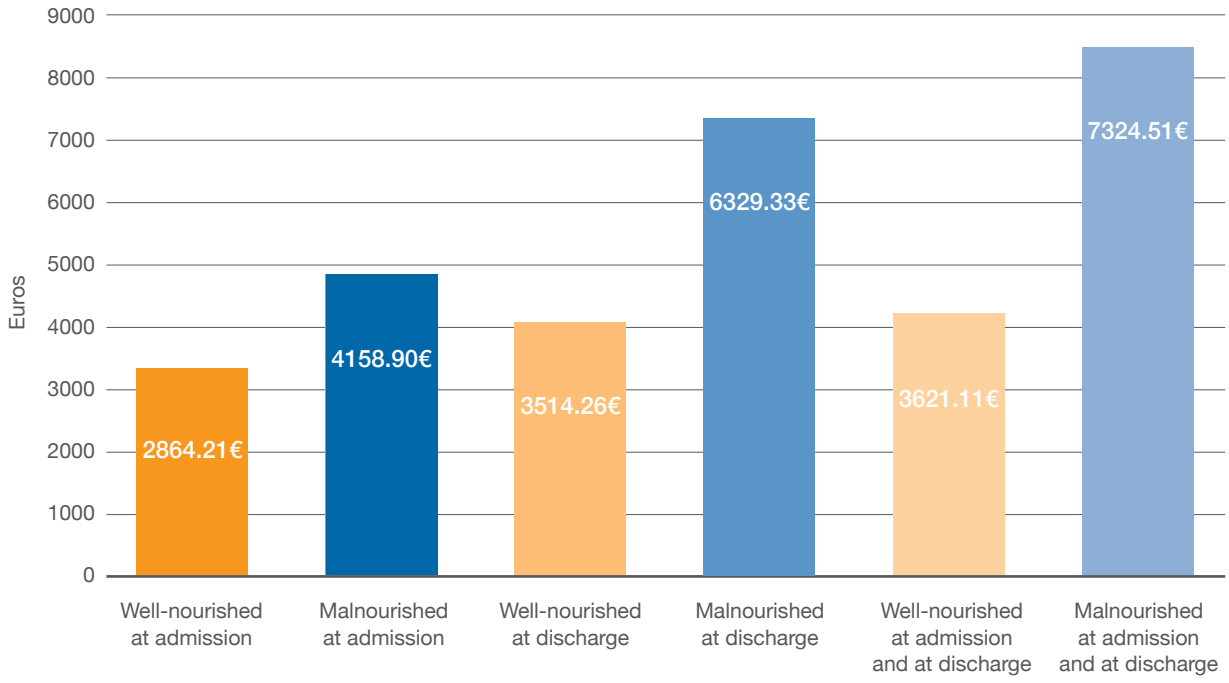

Figure 1.33 **Hospitalisation cost comparisons of subjects according to their nutritional status on admission and/or discharge** (adapted from Gastalver-Martin et al. 2015).[209]

- More recently estimates have been made to quantify the cost of malnutrition in the community with a study based on an economic model in the US estimating the annual cost at $156.7 billion or $508 per US resident,[223] whilst a Spanish study estimated that the cost of treating a malnourished patient was over 3.5 times higher than a well-nourished patient in a community setting.[224]

As the volume of evidence on the costs of DRM has increased over recent years, relevant studies have been summarised in Table 1.18 according to the following categories:

- o across healthcare settings
- o hospital
- o community
- o children

Data are also now available for the costs of DRM in children

Up until recently, data on the cost implication of malnutrition in children has been lacking. However, a recent report from BAPEN provides financial estimates of the burden of malnutrition in the pediatric population in England:[220]

- It is estimated that around 6% of the total public expenditure on malnutrition in health and social care is spent on children in England. This equates to around £1.2 billion[220]
- This estimate of the cost of malnutrition in children has been made based on the assumption that malnutrition affects 15% of children admitted to a typical hospital in England and that it prolongs length of hospital stay by 1.3 times, as for adults[220]
  - o malnutrition accounted for 18.7% of costs, when calculated using the same procedures as for adults;
  - o in relation to outpatients it was assumed that 7.5% of attendances and costs were due to malnutrition;

- it was assumed that malnutrition accounted for only 3% of the costs of the children's social services, including those for looked-after children.

In addition to these estimates, a study using US data from 2010 of hospitalised children showed that:[200]

- Hospitalisation costs were US$ 55,255 for children with a malnutrition diagnosis vs. US$17,309 without;
- Hospitalized children with a diagnosis of malnutrition were also less likely to have a routine discharge and almost 3.5 times more likely to require post-discharge home care, suggesting higher costs in the community too.

Table 1.18 Studies and reports relating to the costs of disease related malnutrition.

Country	Author (year)	Patient group	Healthcare setting	Study design	Method used to calculate costs	Cost of DRM per patient	Total cost of DRM per annum
Across health care settings							
China	Linthicum et al. (2015)[225]	Covers all ages and genders with a range of 15 diseases	Unclear	Economic model based on population surveys, current literature and census information	Adapted WHO model that quantifies the health burden of DRM (does not include direct medical costs)	NR	US$66 billion ($25.2 billion associated with ≥60years)
Croatia	Benkovic V et al. (2014)[226]	Adults >20 years with a range of diagnoses	Across healthcare settings	Economic model based on national data	Direct costs estimated from disease treatment costs, disease prevalence and undernutrition incidence	€1640.48 per person	€97.35 million for the range of diagnoses specified
Germany	Cepton Report[227]	Adults (unclear)	Across healthcare settings	Economic model	Only direct costs considered	NR	€9 billion (additional costs due to malnutrition in 2003)
Ireland	Rice and Normand (2012)[217]	Adults (age NR)	Across healthcare settings	Economic model based on national data	Costs based on DRM prevalence and official costs of healthcare utilisation using an adapted BAPEN model	Additional cost of €5357 per patient	€1.4 billion (in 2007)
The Netherlands	Kok (2014)[228]	Adults ≥ 20 years	Hospital, nursing home and residential care	Economic model based on national data	Costs based on DRM prevalence and healthcare costs (as part of a societal cost-benefit analysis)	NR	€1.8 billion (in 2011) made up of: Hospital: €1.1 billion Residential care and nursing homes: €523million Cost of the value of life: €244 million
The Netherlands	Freijer et al. (2013)[229]	Adults >18 years with a range of disease categories	Across healthcare settings	A cost of illness study using only direct healthcare costs	Formula developed based on disease category costs, prevalence of malnutrition in disease category and increased costs of managing malnourished patients	€135 per capita in 2011 (per head of population based on a population of 14 million)	€1.9 billion in 2011 made up of: Hospital: €1.2 billion Nursing and residential homes: €453 million Home care setting: €185 million

Table 1.18 Continued

Country	Author (year)	Patient group	Healthcare setting	Study design	Method used to calculate costs	Cost of DRM per patient	Total cost of DRM per annum
Hospital							
Australia	Rowell and Jackson (2011)[230]	Hospital patients >14 years (*n* = 256,865)	Hospital	Retrospective analysis	Costs were calculated using patient level costing data. Economic model used to estimate the cost of untreated malnutrition	Malnutrition increased costs by AU$1745	AU$10,7million in 2003-2004
Australia	Banks et al. (2010)[231]	Hospital patients ≥18years (*n* = 241,415 hospital discharges)	Hospital	Economic model	Costs based on hospital discharge data, incidence of pressure ulcers (PU), effect of malnutrition on the development of PU, effect of PU on LOS, cost of patient bed day.	NR	Cost of PU attributable to malnutrition in 2002/2003 AU$12,968,669 (SD$4,924,148)
Belgium	Ethgen et al. (2005)[232]	Hospital patients (age NR). Malnourished (*n* = 927) vs. well-nourished (matched controls *n* = 26067)	Hospital	Observational analysis	Compared overall hospital costs of malnourished vs. well-nourished	Mean cost difference per patient's hospital stay between malnourished and well-nourished €1,152 (95% CI €870; €1433)	NR
Canada	Curtis et al. (2016)	Adult patients ≥18 years admitted to surgical or medical wards (*n* = 958)	Hospital	Multi-center Prospective cohort study	LOS calculated for each participant by tracking admissions and transfers. Standardised data on hospital per diem expenses and direct expenses for functional units purchased from the Canadian Institute for Health Information	Severely malnourished: 38% higher total costs than well-nourished (p = 0.002) and 55% higher medical costs (p = 0.003). Moderately malnourished: 31% higher total costs than well-nourished (p = 0.003), 29% higher medical costs (p = 0.004) and 34% higher surgical costs (p = 0.022)	Total additional cost of malnutrition at hospital admission roughly estimated to be approx. $1.56 to $2.1 billion per year

Table 1.18 Continued

Country	Author (year)	Patient group	Healthcare setting	Study design	Method used to calculate costs	Cost of DRM per patient	Total cost of DRM per annum
Hospital							
France	Melchior et al. (2012)[204]	Colorectal cancer patients undergoing surgery	Hospital	Post-hoc analysis of prospective study	Individual costs were valued according to the French National Cost Construction Study (2008) and calculated by mean LOS x hospitalisation costs	Cost of hospitalisation increased by €3360 per patient for malnourished vs. non-malnourished	€10,159,436 per annum
Germany	Thomas et al. (2016)[207]	Surgical patients mean age 57.3 years	Hospital	Prospective observational study	Cost compensation calculated using the German Diagnosis-Related Group (G-DRG) system	Re-imbursement of €1979.67 per patient at risk for malnutrition and total re-imbursement for all malnourished patients €79,186.73	NR
Portugal	Guerra et al. (2016)[233]	Adults aged 18-91 years	Hospital	Prospective observational study	Hospitalisation cost was calculated for each inpatient based on the amounts defined by the discharge DRG codes	Cost of a nutritionally-at-risk or undernourished patient is between €416 (95% CI = €156–675) and €617 (95% CI = €293–855) higher than the average of the respective DRG	NR
Singapore	Lim et al. (2012)[51]	Adults aged 51.9 years ± 15.4 (n = 818)	Hospital	Prospective study (matched case-control)	Hospital costs calculated according to DRG codes	Mean difference between the actual cost and the average cost of hospitalisation for malnourished patients (SGA B+C) was greater than for well-nourished patients S$1392±6150 vs S$488±3494 p = 0.014	NR

Table 1.18 Continued

Country	Author (year)	Patient group	Healthcare setting	Study design	Method used to calculate costs	Cost of DRM per patient	Total cost of DRM per annum
Hospital							
Spain	Gastalver-Martín C et al. (2015)[209]	Adults	Hospital	Prospective observational study	Individual costs calculated per patient	Hospitalisation costs: 4158.90€ ± 4148.51 malnourished vs. cost of non-malnourished 2864.21€ ± 1747.95 (p = 0.015). Hospitalisation costs increased for patients that were malnourished on discharge (see Figure 1.33)	NR
Spain	Álvarez Hernández et al. (2015)[208]	Adults with dysphagia (mean age 69.15 years)	Hospital	Observational study	Costs based on average cost/day of admission provided by the Ministry of Health and Consumer Affairs (2009)	Increased costs for malnourished subjects €8004 ± 5854 vs. €6967 ± 5630, p = 0.11 Note result ns.	NR
Spain	Leon-Sanz et al. (2015)[199]	Adults mean age 73.7 years (malnourished) 60.48 years (controls)	Hospital	Case-control study	Costs calculated from direct costs of treatment and services and extrapolated to estimate national costs	Hospitalisation costs higher in malnourished €8590 ± €6127 vs. not malnourished €7085 ± €5625, (p = 0.015)	€1.143 billion per annum
Spain	Marco et al. (2011)[52]	Adults (mean age (sd) malnourished 72.37 years (17.89) vs. not malnourished 70.82 years (7.21)) (n = >1.5 million)	Hospital	Retrospective analysis	Malnourished patients identified from the Minimum Basic Data Set from Spanish hospitals, costing data also obtained from this	Cost per patient mean (sd): malnourished €5228.46 (€4593.04) vs. non-malnourished €3537.8 (€2858.07), p<0.001	NR

Table 1.18 Continued

Country	Author (year)	Patient group	Healthcare setting	Study design	Method used to calculate costs	Cost of DRM per patient	Total cost of DRM per annum
Hospital							
Switzerland	Khalatbari-Soltani and Marques-Vidal (2016)[53]	Adult patients (≥18 years)	Hospital	Retrospective study of electronic administrative data	Actual costs for each patient extracted from the hospital billing system	Hospital costs higher in at risk patients vs. not at risk patients (excess 5642.25±1479.80 CHF in 2013 and 5529.52±847.02 CHF in 2014)	NR
UK	Gomes et al. 2016[212]	Stroke patients (mean age 74.7 years)	Hospital	Prospective observational study	Costs based on hospital payment system in place in England (2012-2013)	Hospitalization costs increased with malnutrition risk category, from a median of less than £5000 (low risk) to more than £8000 (high risk) ($p<0.001$)	NR
US	Weiss et al. (2016)[72]	All non-maternal and non-neonatal hospital inpatient stays (n = 27.6 million)	Hospital	Descriptive summary report of Heath care Cost and Utilisation Project (HCUP)	Administrative health care data from the National (Nationwide) Inpatient Sample (NIS)	NR	In 2013, hospital stays involving malnutrition accounted for nearly $42 billion or 12.1% of aggregate non-maternal, non-neonatal hospital costs
Community							
Germany	Baumeister et al. (2011)[234]	Adults (55-74years)	Community	Economic study using population based cohort	Costs calculated by self-reported health-care resource use and standard costs based on official statistics	Predicted annual cost at 10 year follow-up €1383.16 (mean GNRI) vs. €2040.43 (low GNRI)	NR

Table 1.18 Continued

Country	Author (year)	Patient group	Healthcare setting	Study design	Method used to calculate costs	Cost of DRM per patient	Total cost of DRM per annum
Community							
Spain	Rodríguez-Mañas et al. (2014)[224]	Older adults (age NR)	Community (including those living in institutions)	Systematic review	Costs calculated from malnutrition prevalence, GP visits and hospitalizations. Unit costs were derived from health care cost databases available in Spain (Euros, 2014)	Annual cost of malnourished patient (€ 5,000.66) was 3.5 times higher than that of a well-nourished (€ 1,433.78).	NR
The Netherlands	Meijers et al. (2012)[235]	Nursing home residents (110 nursing homes, 9855 patients)	Nursing homes	Economic study based on data obtained by a survey of 30 dietitians	Costs calculated based on individual treatment and resources, malnutrition prevalence and extrapolated to entire nursing home population	Additional costs €8000/ patient/year for at risk patient €10000/patient/year for malnourished patient	Additional costs of malnutrition in nursing homes €279 million/year
UK	Collins et al. (2011)[236]	COPD patients (age NR)	Community	Prospective study	Costs calculated according to Department of Health NHS reference costs 2007	Highest costs associated with being underweight (BMI < 20 kg/m^2) (Actual costs NR)	NR
UK	Guest et al. (2011)[60]	Adults ≥18years (mean age 63 years)	Community	Economic study based on The Health Improvement Network (THIN) database	Costs calculated using a computer based model using the THIN dataset and costs based on 2007-08 prices	Cost per patient over 6 month period was £1753 (95% CI: £1628; £1878) per malnourished patient and £750 (95% CI: £684; £816) per non-malnourished patient	£3.7 billion for the first 6 months after diagnosis of malnutrition (based on incidence of malnutrition in community of 6%)

Table 1.18 Continued

Country	Author (year)	Patient group	Healthcare setting	Study design	Method used to calculate costs	Cost of DRM per patient	Total Cost of DRM per annum
Community							
USA	Snider et al. (2014)[223]	Covers all ages and genders	Community	Economic model based on population surveys, current literature and census information	Cost of community-based DRM was estimated using a burden of disease approach	$508 per U.S. resident	$156.7 billion ($51.3 billion associated with >65 years)
Children							
USA	Abdelhadi et al. (2016)[200]	Children (≤17 years)	Hospital	Retrospective analysis using patient-level data on hospital inpatient stays	Costs based on the 2010 Healthcare Cost and Utilization Project	Hospitalisation costs were US$ 55,255 for children with a malnutrition diagnosis vs. US$17,309 without	NR
Thailand	Kittisakmontri and Sukhosa (2016)[237]	Children >5 years (mean age 26.8 ± 1.8 months) (*n* = 105)	Hospital	Prospective cohort study	Direct costs were calculated individually	The cost (median (range)) of: Bed, 3500 Baht (400.0 -12,400) vs. 2275 Baht (400.0 - 36,400) $p = 0.01$), enteral formula 86 Baht (0 - 3300) vs. 312 Baht (0-16332); $p<0.01$ medical apparatus 2371.5 Baht (460 - 345,936) vs. 8074 Baht (240-125,667); $p=0.01$ and nursing care, 5920 Baht (582-119,520) vs. 11,235 Baht (1300 - 37,970); $p=0.02$ were significantly higher in the group of children classified as having stunting and wasting compared to those who were well nourished. Note difference in overall costs was ns	NR

DRM Disease related malnutrition; NR Not reported; DRG Diagnosis related group; THIN The Health Improvement Network; NHS National health service; GNRI Geriatric nutritional screening index ; LOS Length of stay; SGA Subjective Global Assessment.

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2

2.1 ABOUT MEDICAL NUTRITION

Summary

Good nutrition is an essential part of care, and it includes ensuring that the right people receive the right nutritional support at the right time during their care, regardless of whether that care is delivered in hospital, in an institution or in the person's own home. Good nutritional care also includes ensuring that people who are malnourished or at risk of malnutrition are identified through screening programmes, and that action is taken to ensure that they receive appropriate and timely nutritional support. Nutritional support may take many forms, e.g. dietary counselling, food fortification, oral nutritional supplements (ONS), enteral tube feeding (ETF) and parenteral nutrition (PN).

Medical nutrition products are specific nutritional compositions for disease intervention that effectively contribute to the therapeutic regimen by improving a patient's general condition. In circumstances where patients are unable to consume enough food to meet their nutritional needs to sustain life or optimize health, medical nutrition (ONS, ETF and/or PN) is used.

Medical nutrition helps to sustain life by providing either all or some of the patient's energy, protein, vitamin, mineral, trace element and fluid requirements depending on whether the patient is able or willing to consume some food. The aim may be to improve, maintain or minimise deterioration in nutritional status depending on the underlying health issue and prognosis. Medical nutrition may be required from birth or at any stage during infancy, childhood, adulthood or in old age. It may be required for a short period of time to support a patient through recovery from injury or through a course of medical or surgical treatment. In the case of chronic disease it may be needed for a prolonged period of time, for example weeks, months or years.

Medical nutrition products (ETF and ONS) are manufatured by specialist medical food companies. PN products are classed as prescription only medicines (POM) and are therefore only produced by companies with a pharmaceutical licence.

As progress in nutrition and medical research has advanced to meet the complex needs of patients, the manufacturers of medical nutrition products have responded to these needs by developing an increasingly diverse range of products specifically designed to meet the needs of different age groups and different medical condititons.

In subsequent sections of this document the evidence base for ONS, ETF and PN will be outlined to demonstrate the nutritional, functional, clinical and economic benefits of medical nutrition. As the needs of patients and healthcare providers have evolved over time, so too has the science behind medical nutrition. Research continues to drive innovation to achieve the optimal outcome for patients by identifying potential improvements in the formulation, timing, duration and route of nutrition support.

Conclusion

Medical nutrition products are specific nutritional compositions for disease intervention that effectively contribute to the therapeutic regimen by improving a patient's general condition. They are an essential part of the clinicans toolkit in delivering high quality, and in many cases, life-saving nutritional care.

Recommendations

Recommendations	Issues to consider
Continued efforts should be made to promote cross-sector (patient, clinical, academic, professional and commercial) partnerships and opportunities to continually drive innovation in, and the delivery of, medical nutrition to meet the needs of patients and healthcare providers Increased efforts are needed to integrate information on the prevalence, causes, consequences of DRM and how medical nutrition can be used to tackle malnutrition into education and training for healthcare professionals Resources should be allocated to deliver the improvements in policy and clinical practice needed to ensure access to appropriate nutritional care for all	• In addition to education for healthcare professionals (HCPs), public health campaigns could be employed to educate patients and carers about how to identify malnutrition, how to seek help and how to manage the condition. Patients and HCPs need to recognise that malnutrition is not an inevitable part of disease or ageing • To ensure equitable access to medical nutrition and to mitigate the high cost associated with DRM, healthcare providers and payors should take account of the evidence base for the cost effectiveness of medical nutrition to ensure that medical nutrition is funded with fair access to all those that need it

Before considering what constitutes medical nutrition it is important to explore the concept of 'good nutritional care' since medical nutrition is integral to patient care and forms an important part of a patient's healthcare journey.

2.1.1 What is good nutritional care?

Good nutrition is an essential part of care, and it includes ensuring that the right people receive the right nutritional support at the right time during their care, regardless of whether that care is delivered in hospital, in an institution or in the person's own home. Good nutritional care starts with ensuring that people have access to appetising and nutritious food that meets their preferences and nutritional, cultural and religious needs, and that they are supported to either provide this for themselves or to be able to avail themselves of it when it is provided by others, e.g. through assistance with shopping or cooking, lunch clubs, meals on wheels or assistance with eating and drinking.

Good nutritional care also includes ensuring that people who are malnourished or at risk of malnutrition are identified through screening programmes, and that action is taken to ensure that they receive appropriate and timely nutritional support. As outlined in Figure 2.1 nutritional support may take many forms, e.g. dietary counselling, food fortification, oral nutritional supplements (ONS), enteral tube feeding (ETF) and parenteral nutrition (PN).

The central factor in the development of malnutrition is that nutritional intake is insufficient to meet requirements. This can arise due to a number of different reasons related to disease and disability, impacting on food intake, losses of nutrients and/or increased requirements. Although in some cases improvement of the quality or quantity of food supplied can ameliorate the problem, in many cases, the person concerned is simply unable to consume sufficient normal food to meet his or her requirements and maintain a healthy nutritional status. In this case, it is vital to consider other options to improve nutritional intake i.e. nutritional support.

Principles underlying intervention with nutrition support (NICE 2006)[1]

'Good nutrition should benefit both those who are already overtly malnourished in terms of BMI or recent unintentional weight loss and those who are developing nutritional risks by having eaten little or nothing or be likely to eat little or nothing for over 5 days. In addition, nutrition support can often provide simple direct benefits by:

- Keeping patients who are eating inadequately, alive for long enough for specific medical or surgical interventions to take effect
- Making malnourished patients feel better, improving their ability to cope with ill-health
- Maintaining strength through patients' illnesses so that their recuperation is shortened and they are less susceptible to further problems
- Providing long-term support for those patients with chronic inability to eat, drink or absorb adequately'

2.1.2 What is nutritional support?

Oral strategies

Dietary counselling, modification of conventional food, and oral nutritional supplements (ONS) are all considered as strategies for improving nutritional intake and can be delivered by mouth.

Enteral strategies

When patients are unable to consume sufficient nutrition via the oral route, delivery of nutrients directly into the gut via enteral tube feeding (ETF) may be required.

Parenteral (intravenous) strategies

In cases when patients require complete bowel rest or have a non-functional, inaccessible or perforated gastrointestinal tract and can not be fed adequately and/or safely via the oral/enteral route, parenteral nutrition (PN), where nutrients are delivered intraveneously, will be needed.

Depending on a patient's nutritional status, underlying medical condition and the aim of nutritional support, a feeding method may be used alone or in combination with one or more other forms of nutritional support and this may differ at a specific point in time or during the course of a patient's healthcare journey.

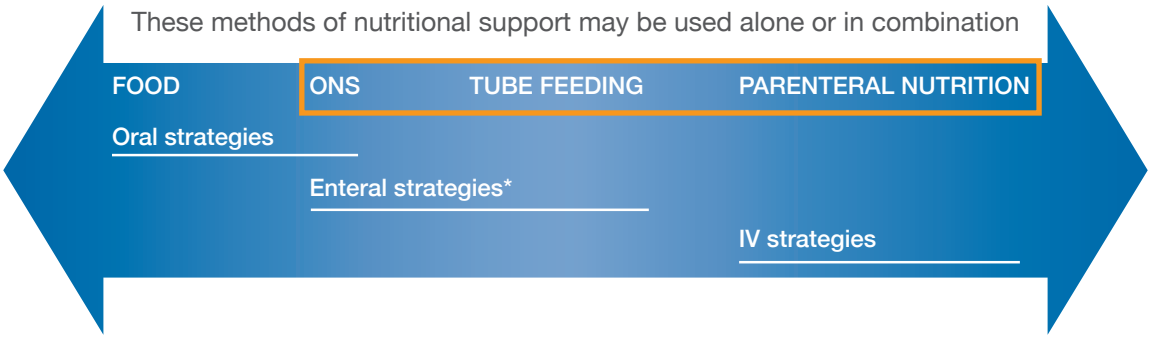

Figure 2.1 **The spectrum of nutritional support.** The strategies shown within the orange text box are included in the definition of 'medical nutrition' for the purposes of this dossier (*some definitions of enteral nutrition include ONS[i])

[i]The term enteral tube feeding (ETF) is used in this document (see Definition of terms). In instances where original sources have used enteral nutrition to include ONS this is clarified in the text.

2.1.3 What is Medical Nutrition?

What is medical nutrition?

Medical nutrition products are specific nutritional compositions for disease intervention that effectively contribute to the therapeutic regimen by improving a patient's general condition.[2] The products within the medical nutrition category are sometimes referred to collectively as medical foods, clinical nutrition, or individually as enteral tube feeds or ONS. In addition the term 'medical nutrition' is often used to refer to a particular category of foods defined within food law as Foods for Special Medical Purposes (FSMPs) (see also 'Who makes medical nutrition products?').

Parenteral nutrition is also a form of medical nutrition but it is regulated as a medicine it is not part of the FSMP category. For the purposes of this dossier the term 'medical nutrition' will be used to refer to the entire spectrum of nutrition support strategies that use commerically available products manufactured by medical nutrition companies. In essence it covers all nutrition support techniques except dietary counselling which involves modification of the normal diet and normal food (see Figure 2.1).

What are the different types of medical nutrition?

There are a variety of methods of nutrition support available which can be delivered via different routes i.e. oral, enteral and parenteral depending on the needs and clinical condition of the patient (see Figure 2.2).

Oral nutritional supplements (ONS) are liquid, semi-solid or powder products that provide macronutrients and micronutrients with the aim of increasing oral nutritional intake. ONS are typically used to supplement food intake which is insufficient to meet requirements. However, many ONS are nutritionally complete and in some situations can be used as a sole source of nutrition.

Enteral tube feeding (ETF) is nutrition support delivered directly into the gastrointestinal tract via a tube. A variety of enteral feeding tubes and routes are available and decisions about the most appropriate technique are influenced by a number of factors including underlying medical condition, likely duration of tube feeding, gastrointestinal access and function and patient preference. More detail about the different methods of ETF are covered in Section 3.2.

Parenteral nutrition (PN) is the intravenous administration of nutrients directly into the systemic circulation, bypassing the gastrointestinal tract. Depending on the accessibility of the venous system and the planned duration (short-term or long-term) of nutrition support, parenteral nutrition solutions are administered either via a central venous catheter or peripheral venous cannulas (see Figure 2.2). PN represents an alternative or additional approach for nutritional intervention when nutritional needs cannot be met from the oral or enteral routes alone, or are contraindicated.

Nutritional support is not restricted to the exclusive administration of ONS, EN or PN, but they may complement each other, e.g. enteral feeding with supplementary PN, overnight enteral tube feeding in addition to diet and/or ONS.

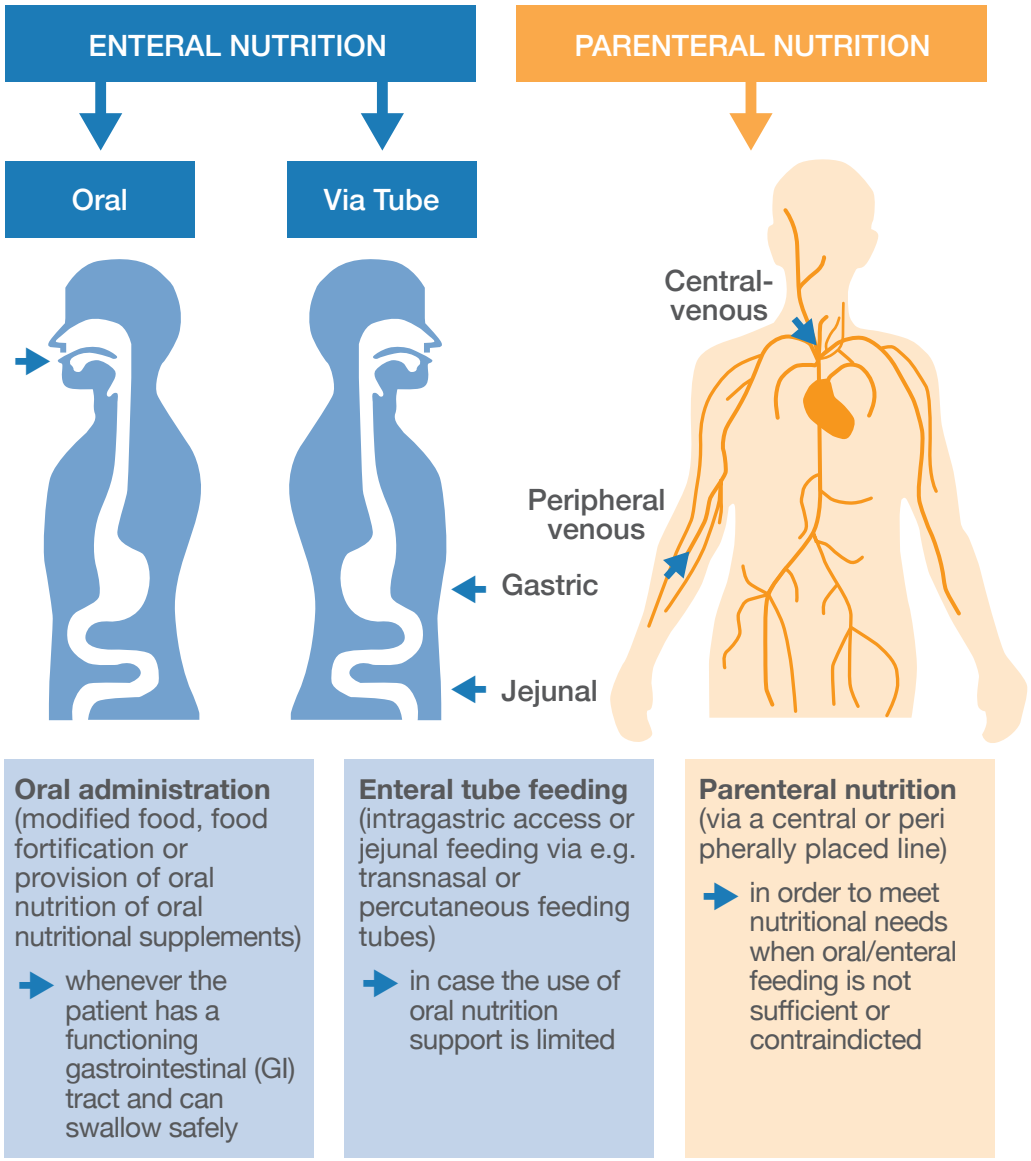

Figure 2.2 **Methods of nutrition support** (based on NICE (2006)[1] and reproduced by kind premission of Fresenius Kabi)

An extensive range of ONS, ETF and PN products is available, many of which can be used as a sole source of nutrition. In many patients medical nutrition is used to supplement oral intake, where food intake is insufficient to meet nutritional requirements.

Why is medical nutrition needed?

'Food and nutrition intake is fundamental to good health and resistance to disease. There is a positive duty at common law to care for and provide such treatment as is in the patient's best interests and to take such reasonable steps as are necessary to preserve life. Where nutrition as food and fluid (including nutrition support) is necessary to preserve life, the duty of care will normally require the supply of such nutrition or nutrition support.' (NICE, 2006)[1].

"How will history judge the early 21st century? If things go on as they are, the verdict will be dismay and condemnation, that wealthy societies and established social protection systems could allow the tragedy of malnutrition to occur in such a large segment of the population. This is just not tolerable, and the European Nutrition for Health Alliance, with growing support, is determined to tackle this issue." Mel Read, former Member of the European Parliament.

In circumstances where patients are unable to consume enough food to meet their nutritional needs to sustain life, medical nutrition (ONS, ETF and/or PN) is used. In all cases the potential benefits of nutrition support must be weighed against the potential risks or burden of providing it and this should be assessed on a case-by-case basis.

What decision process is used to decide if medical nutrition is needed?

Decisions regarding the need for medical nutrition are undertaken by healthcare professionals in collaboration with patients and/or care givers. To maximise postive outcomes and to ensure patient safety, decisions about intiating, monitoring and cessation of medical nutrition should be undertaken by healthcare professionals who are experts in the topic. A Nutrition Support Team (NST) is a multidisciplinary team consulted to manage patients with complex nutritional needs (enteral and parenteral) which serves the primary responsibility of assuring that patients receive optimal nutrition support. Core members can include doctors, dietitians, nurses and pharmacists.[3] Activities range from direct patient care to the development of guidelines and protocols for implementation by other healthcare workers (see Figure 2.3).

Healthcare professionals should look to evidence-based guidelines to assist them in selecting the most appropriate method of nutritional support for their patient, taking account of a wide variety of factors including:

- the goals of care
- patient's nutritional needs
- ability to take, digest, absorb, metabolise or excrete foods, nutrients or metabolites
- diagnosis and prognosis
- patient's ability to adhere to the intervention
- patient safety

Experts locally, such as a NST, or nationally and internationally can and have developed guidelines, protocols, pathways and decision trees that can be employed by other healthcare professionals in the management of patients who require medical nutrition. See section 4 for examples of international and internationally recognised guidelines that include ONS, EN and PN.

	Medical		Dietetics	Pharmacy	Nursing		Catering
Ward	Doctors		Dietitians	Pharmacists	Nurses		Ward Hostess
Supervisory	Patient's Consultant(s)	Team Consultant(s)	Specialist Dietitian	Specialist Pharmacist	Nutrition Nurse Specialist	Nurse Managers	Catering Managers
Organisational	Clinical Directorate		Lead Dietitian	Lead Pharmacist	Hospital Nursing Leads		Lead Caterer
Hospital Governance	Medical Director		Director of Operations	Director of Operations	Nursing Director		Director of Operations

Nutrition Support Team

- Training
- Advice
- Standards

Figure 2.3 **Nutrition Support Team members and range of activities** (adapted from BAPEN see http://www.bapen.org.uk/ofnsh/page7.html (accessed 06.05.17))

It is essential that healthcare professionals combine their clinical experience and practical common sense with a sound knowledge of the evidence base in the provision of nutritional support, e.g. a patient with a poor appetite may not be able or willing to consume extra food or may lack the energy or ability to prepare it, a patient who has lost the ability to swallow may need ETF or a patient with intestinal obstruction may need PN. Medical nutrition products were conceived specifically to meet these medical needs, providing energy and nutrient-dense solutions in easily delivered forms. Patient pathway algorithms are available to assist with decision making, an example is shown in Figure 2.4.

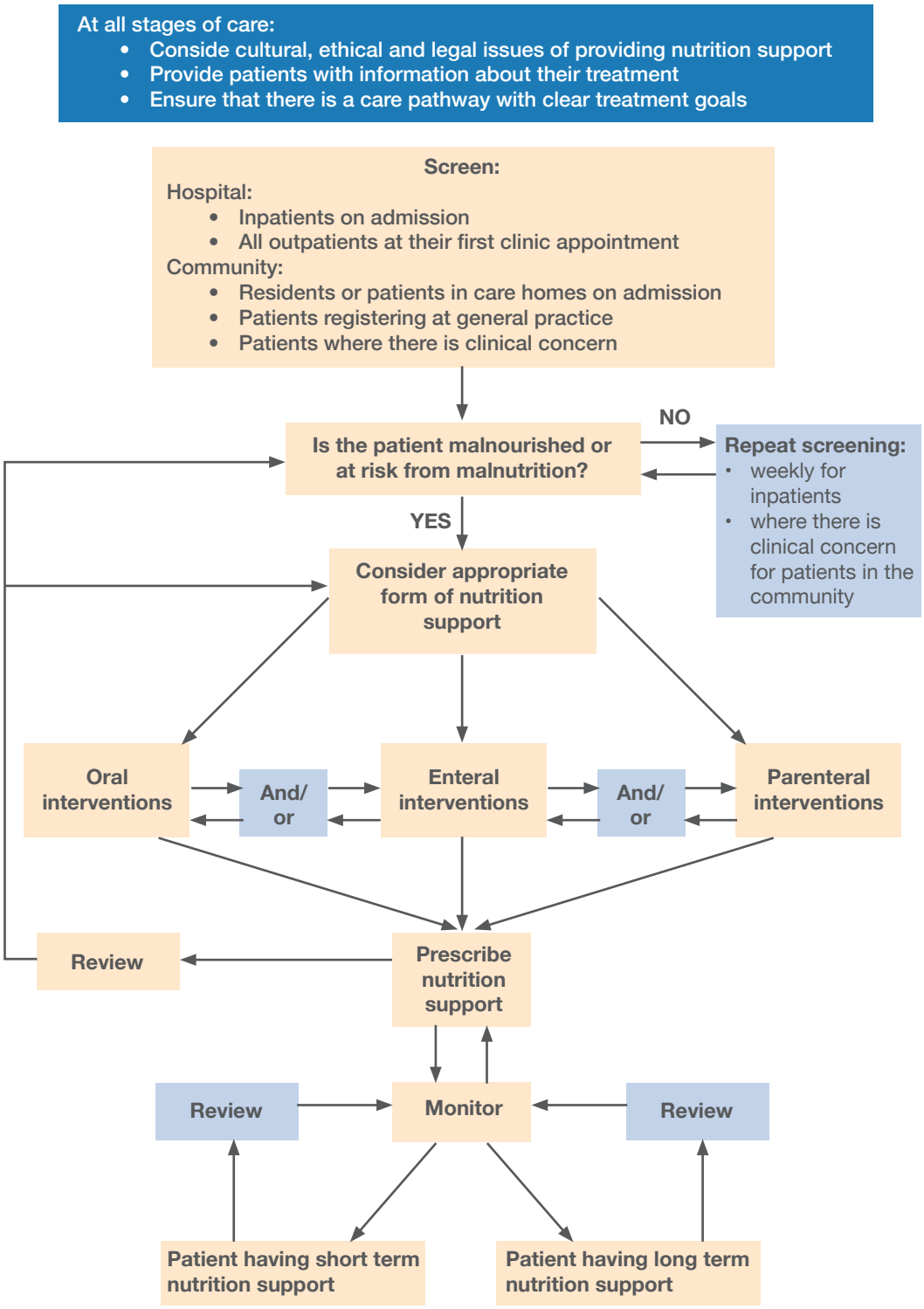

Figure 2.4 **Example of a patient pathway algorithm for medical nutrition/nutrition support** (NICE 2006)[1]

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What are the goals of nutrition support using medical nutrition?

The overall goal of nutrition support is to meet the total nutritional needs of the patient. Medical nutrition helps to sustain life by providing either all or some of the patient's energy, protein, vitamin, mineral, trace element and fluid requirements depending on whether the patient is able or willing to consume some food. The aim may be to improve, maintain or minimise deterioration in nutritional status depending on the underlying health issue and prognosis. A large body of evidence has accumulated over many years demonstrating the nutritional, functional, clinical and economic benefits of medical nutrition. This will be presented and discussed in subsequent sections of this document.

Who needs medical nutrition and when?

Medical nutrition may be required from birth or at any stage during infancy, childhood, adulthood or in old age. It may be required for a short period of time to support a patient through recovery from injury or through a course of medical or surgical treatment. In the case of chronic disease it may be needed for a prolonged period of time, for example weeks, months or years. It will be required for life in patients where the consumption of normal food is not possible e.g. paitients with rare metabolic disorders such as phenylketonuria (PKU), permament loss of swallowing following a stroke or for patients with short bowel syndrome where there is no longer sufficent functioning bowel available to adequately digest and absorb nutrients. Indications for nutrition support are outlined in Table 2.1 (adapted from Sobotka et al.)[4]

Table 2.1 **Typical general indications for oral nutrition supplements (ONS), enteral tube feeding (ETF) and parenteral nutrition (PN) in patients with malnutrition or risk of malnutrition in hospitals and the community** (adapted from Sobotka et al.)[4]

HOSPITAL	COMMUNITY
ONS Inadequate food intake in malnourished patients not requiring ETF or PN	**ONS** Inadequate food intake in malnourished patients not requiring ETF or PN
ETF Inadequate oral intake in patients with functional gut and/or swallowing problems (e.g. following stroke)	**ETF** Persistent swallowing problems (e.g. stroke, motor neurone disease, multiple sclerosis and cancer of the upper gastrointestinal tract)
PN Gut unavailable for adequate feeding (e.g. post operative ileus, gastrointestinal obstruction or mucositis)	**PN** Persistently or permanently unavailable gut (e.g. short bowel syndrome, gastrointestinal obstruction and pseudo-obstruction (propulsive disorder)) and/or inadequate feeding by ONS / ETF

Patients may require nutrition support using ONS, ETF or PN alone or in combination in hospital or in the community, either in institutions such as care homes or in their own home. The prevalence of HETF and HPN is covered in more detail in subsequent sections.

What would happen if patients could not access medical nutrition?

For many patients, either in hospital or living in institutions or in their own home in the community, medical nutrition is their sole source of nutrition. If medical nutrition products were unavailable these patients would be unable to meet their nutritional requirements resulting in deterioration in nutritional status and ultimately death through starvation and/or dehydration. Over the years there have been many innovations in the formulation of ONS and ETF products to meet the needs of specific patient groups. These products are design to deliver complete and balanced nutrition for patients of different age groups (infants, young children, adults and older people) with a wide range of conditions e.g. cancer, malabsorption, diabetes, liver or renal disease. Inability to access medical nutrition specifically designed for the correct age group or condition could lead to over- or under-delivery of essential nutrients.

Medical nutrition is also used to supplement inadequate food intake in patients who are unable to eat sufficent food to meet their needs or in a pre-thickened format for patients who have difficulty swallowing. Failure to meet nutritional needs over time leads to deterioration in nutritional status leading to loss of function, poorer clinical outcome and increased healthcare resource use and costs resulting from increased complication rates, longer hospital stay and more frequent readmission to hospital (See section 1.4 'Consequences of DRM' for further information).

Who makes medical nutrition products?

Medical nutrition products (ETF and ONS) are manufatured by specialist medical food companies. Medical Nutrition products are sometimes referred to as 'borderline substances' as they 'exist between conventional foods and pharmaceuticals at the so-called food-pharma interface'[2] (see Figure 2.5). PN products are classed as prescription only medicines (POM) and are therefore only produced by companies with a pharmaceutical licence.

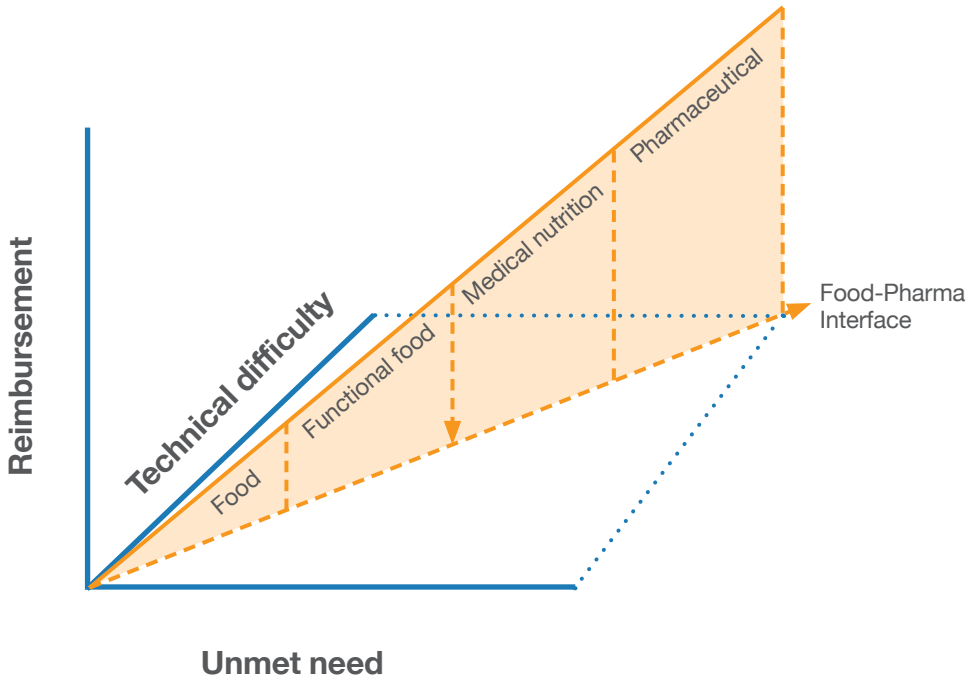

Table 2.5 **Industries situated at the food-pharma interface** (adapted from Weenan 2013).[2]

Medical nutrition that can be delivered via the oral or enteral route (see Figure 2.1) is classed as Foods for Special Medical Purposes (FSMPs) as defined in Regulation (EU) 609/2013 on food intended for infants and young children, food for special medical purposes and total diet replacement for weight control. The regulation defines FSMPs as "products specially processed or formulated and intended for the dietary management of patients, including infants, to be used under medical supervision; it is intended for the exclusive or partial feeding of patients with a limited, impaired or disturbed capacity to take, digest, absorb, metabolise or excrete ordinary food or certain nutrients contained therein, or metabolites, or with other medically-determined nutrient requirements, whose dietary management cannot be achieved by modification of the normal diet alone."

There are 6 important elements to the definition of an FSMP, all of which should be taken into account in determining whether a product falls within the scope of the category. A food product can only be categorised as an FSMP if all 6 elements of the definition are met, based on its intended use. When determining whether a product falls within the scope of the FSMP category, consideration must be given to each element.

Table 2.2 **The six elements of the Foods for Special Medical Purposes (FSMP) defintion.**

The six elements of the FSMP definition The product is:		
i	Specially processed or formulated for its intended use.	✓
ii	Intended for the dietary management of patients, including infants.	✓
iii	Intended to be used under medical supervision.	✓
iv	Intended for the exclusive or partial feeding of patients.	✓
v	Intended for patients who have a limited, impaired or disturbed capacity to take, digest, absorb, metabolise or excrete ordinary foodstuffs or certain nutrients contained therein or metabolites, or with other medically-determined nutrient requirements.	✓
vi	For patients whose dietary management cannot be achieved by modification of the normal diet alone.	✓

In Europe, the legal definition of FSMPs (e.g. ONS, ETF) highlights that medical nutrition products fall within the scope of the FSMP category of foods when the nutritional requirements associated with the disease or medical condition (for which the FSMP has been specially processed or formulated) cannot be achieved by the modification of the normal diet. There is no documented definition of modification of the normal diet but it can be considered to include the following:

- modification of balance of foods (i.e. eating more or less of certain foods)
- modification of nutrient density of foods, e.g. through adding cream, butter or sugar to increase the energy content of foods such as soups, vegetables and puddings,
- alteration of the consistency of foods, such as pureeing.

Medical nutrition is indicated when normal food items are not suitable, impractical or inadequate to meet the nutritional needs caused by the patient's disease or medical condition.

How has medical nutrition evolved?

Before the development of commercially available ETF formulas recipes of milk, eggs and additional nutrients or liquidised food made up in hospital kitchens were used to attempt to meet the nutritional needs of tube fed patients. These 'home-made' mixtures posed numerous problems including issues with food-borne microbial contamination, difficulties achieving reliable or consistent delivery of micronutrients, tube blockage due to difficulties in achieving a homogeneous consistency, the need to use very large bore tubes that were uncomfortable for patients, the time needed for preparation and administration, difficulties with storage and short-shelf life and in particular the problems associated with providing adequate nutrition and in a reasonable volume.

The first commercially available ETF formulas came on the market in the 1960s and were elemental i.e. consisted of amino acids and glucose. Later nutrient 'intact' formulas based on maltodextrin, protein and fats were introduced and were designed to be nutritionally complete. Many were flavoured and so could be used via a tube or taken orally.[5] Throughout the 1980s and beyond, many innovations in ETF and ONS took place including the addition of fibre and the modification of formulas to meet the nutritional needs of specific patient groups as mentioned earlier. A major development was the design of formulas to meet the needs of different age groups from infants and children to adults. More recently, developments such as the design of low volume, energy dense ONS, the addition of specific nutrients to help modulate the immune system (immuno-nutrition), addition of omega 3 fatty acids to target cancer cachexia or modifying the consistency of products to meet the needs of patients with swallowing problems have taken place.

In recent years there has been a trend amongst a minority of patients on HETF (and in some hospitals) choosing to use blenderized or liquidised home-made meals administered via enteral tubes. In the U.S. this appears to be driven in part by the lack of funding for commercially manufactured ETF products. In other areas it is more likely that this is due to the desire of patients and care givers to reconnect with caring by feeding home-made food. [6]

This practice carries risks of nutritional inadequacy, increased likihood of tube blockage, increase in infection risk and enteral feeding tubes/equipment have not designed for this purpose. In guidance relating to the prevention and control of healthcare-associated infections NICE recommend that 'wherever possible pre-packaged, ready-to-use feeds should be used in preference to feeds requiring decanting, reconstitution or dilution'.[7] There are particular risks of this mode of feeding to infants aged less than six months, patients fed via the jejunal route and patients who are immuno-compromised. Additional costs are likely both for the patient/care giver for additonal equipment and for the healthcare provided from increased dietetic resource required to support the patient and from increased complications as listed above. If patients or carers decide to administer liquidised food via an enteral feeding tube an individualised risk assessment should be carried out in line with local policy.[8]

Currently in Europe enteral tube feeds are integrated into reimbursement systems so funding issues are less of a concern. However, the issues associated with the use of 'home-made' feeds outlined above illustrate how important it is to maintain funding for ETF products to safeguard patients. For patients requiring PN, there is no alternative to medical nutrition and lack of it would quickly result in dehydration and death.

Parenteral nutrition entered clinical practice in the late 1960s and was one of the most important developments in medicine after antisepsis, anesthesia, and antibiotics.[9] PN is a highly complex, multi-component sterile drug with as many as fifty components making it probably the most complex therapy in modern medicine.[9] In the early days, PN was delivered with multi-bottle systems i.e. amino acids, glucose, electrolytes and fat administered in parallel from separate bottles by combining multiple connectors delivering into a common IV catheter. The single-bottle system is associated with various disadvantages rendering its use inconvenient in clinical practice, such as the need for a connector and multiple administration sets, frequent bottle changes, the necessity to set up

different, irregular flow rates and the need to make many additions which is time consuming and increases the probability of administration errors.[10; 11]

Innovations in formulation and presentation have enabled the provision of ready-to-use (RTU) bags. RTU systems comprise all components of PN (macronutrients, water, electrolytes, vitamins and trace elements) individually admixed in one container and administered via one single infusion line.[11] Clinical advantages of RTU admixtures include: simultaneous supply of all nutrients leading to improved utilization and nitrogen balance and less metabolic complications[12; 13; 14] and fewer manipulations leading to reduced risk of errors and infections.[14; 15]

Specialist medical nutrition manufacturers continue to invest in research programmes designed to identify and meet the existing and emerging health needs of patients of all ages from birth into older age and constantly strive to bring improvements and innovations that address patient safety issues.

What is the science behind medical nutrition and how has it evolved?

As progress in nutrition and medical research has advanced to meet the complex needs of patients, the manufacturers of medical nutrition products have responded to these needs by developing an increasingly diverse range of products specifically designed to meet the needs of different age groups and different medical conditions.

In addition to being based on sound medical and nutritional principles, medical nutrition products are often recommended and endorsed by expert groups and consensus panels from many European and national scientific medical and nutrition societies such as ESPEN (European Society for Clinical Nutrition and Metabolism), ESPGHAN (European Society of Paediatric Gastroenterology, Hepatology and Nutrition) and ECCO (European Crohn's and Colitis Organisation). In addition, they are also endorsed by national expert groups and reference groups and integrated in disease management protocols together with drug therapy and general medical support (for further information refer to Section 4 'Medical Nutrition in key guidelines'). Basics in nutrition and metabolism and basic principles for disease management together with the experience-based clinical practice supported by solid scientific data (epidemiological studies, observation studies, intervention studies and systematic reviews) lays the foundation for these state-of-the-art guidelines/recommendations. Medical nutrition products are designed accordingly. However, it should be noted that there are inherent difficulties in undertaking studies to demonstrate the clinical benefits of medical nutrition since it is undesirable and unethical to randomise patients who are malnourished or at risk of malnutrition to control groups that receive no nutrition support.

Medical nutrition is a new area that is rapidly evolving and brings a great deal of innovation to nutritional intervention. Since the 1960s many innovations in medical nutrition have supported better management of patients worldwide. Research undertaken by medical nutrition companies focuses on using medical nutrition to improve patients lives, target specific therapeutic areas at different stages in life and provide effective solutions for healthcare professionals to meet patients' needs.

In subsequent sections of this document the evidence base for ONS, ETF and PN will be outlined to demonstrate the nutritional, functional, clinical and economic benefits of medical nutrition. As the needs of patients and healthcare providers have evolved over time, so too has the science behind medical nutrition. Research continues to drive innovation to achieve the optimal outcome for patients by identifying potential improvements in the formulation, timing, duration and route of nutrition support. Increasingly healthcare providers and payors are interested in the cost-effectiveness of medical nutrition and so this has become a major focus in recent years.

Is medical nutrition part of recognised recommendations and standards in healthcare?

Section 4 of this document provides detailed lists of nationally and internationally recognized evidence-based standards and guidelines developed by learned societies or multi-professional groups that recommend ONS, ETF and PN as an integral part of patient care. The lists are organized by country, age and patient group and demonstrate the wide acceptance that medical nutrition is an essential part of good nutritional and overall patient care.

Is medical nutrition effective?

Section 3 of this document outlines the nutritional, functional and clinical benefits of ONS, ETF and PN. There is consistent, good quality evidence from multiple individual trials and meta-analyses demonstrating the beneficial nutritional, functional and clinical effects of ONS in malnourished patients. ETF is an important life-saving technique used widely across all healthcare settings in patients of all ages with a variety of medical conditions. The use of ETF is increasing in the community and many patients on home enteral tube feeding (HETF) live independently and achieve normal activity levels. ETF has nutritional, functional and clinical benefits but the evidence based from randomised controlled trials (RCTs) is more limited than for ONS. Because of the value of ETF in sustaining life it is often considered unethical to withhold treatment. This means undertaking RCTs, whereby one group of subjects is randomised to receive ETF whilst the other group don't, would be considered to be unethical. PN is also an important life-sustaining therapy for adults and children when oral and enteral nutrition is contraindicated, impossible or inadequate. PN can be used for patients of any age and across all healthcare settings. Use of PN has transformed the prognosis for many patients with formerly fatal conditions, and is considered one of the most important advances in paediatric therapeutics over the last four decades. Because PN is a life-saving therapy for patients with intestinal failure, evaluation of its efficacy compared with no nutrition support is not possible. RCT evidence for PN is more limited than for ONS or ETF. However, numerous prospective and retrospective observational studies (and some RCTs) have demonstrated nutritional, functional and clinical benefits of PN.

Is medical nutrition cost-effective?

Besides improving the well-being of patients, fighting malnutrition with ONS is an opportunity for healthcare providers to control costs. This is especially relevant in light of the ageing population and the high prevalence of chronic disease that adversely impacts nutritional status, which in turn contributes to increased cost burden. Comprehensive systematic reviews have shown that managing malnutrition with ONS can produce an average cost saving of around 10% compared to standard care across a broad range of patient groups. Meta-analyses in hospitalised patients show that ONS use is associated with 1 in 3 fewer deaths, 1 in 3 fewer complications and shorter length of hospital stays. Controlling and managing malnutrition with ONS is a clinically and cost-effective solution. There is limited data available in the literature about the potential cost savings and cost-effectiveness of ETF across healthcare settings, from different countries and in particular in children. However, in England an economic evaluation of the use of nutritional support including ONS, ETF and PN ultimately saves rather than costs money (£119,000 – £432,000 per 100,000 depending on the model used) (See Section 3, Figure 3.14). The report highlights that it is necessary to make a commitment to invest money before the financial benefits can be reaped.[16] Published data about the potential cost savings and cost-effectiveness of PN across healthcare settings and in different countries are limited. However, PN has been shown to compare favourably with other supportive treatments used in the ICU (e.g., dialysis). Furthermore, timely use of PN in the ICU has also been shown to significantly reduce the total cost of acute hospital care in the US. HPN is also likely to be cost-saving compared with hospital-based PN for many healthcare systems as it shortens length of hospital stay for patients who are ready to be discharged but who require intravenous nutrition.

Introduction of commercial, premixed multichamber bag PN also realises considerable cost savings for both adult and pediatric patients by reducing preparation costs and improving safety.

What are the current concerns/major obstacles to the use of medical nutrition?

Although in many countries advances have been made in recent years to implement screening programmes to ensure that patients who are malnourished or at risk of malnutrition are identified and managed appropriately, still malnutrition often goes unrecognised and untreated. Unless malnutrition is identified appropriate action cannot be taken.

A recent survey entitled 'experiences of patient malnutrition', carried out by Dods Research in association with AGE UK and the Malnutrition Task Force, examined the responses of 1,518 healthcare professionals in the UK. The research found that only half (51%) thought malnutrition was a priority in their organisations. Furthermore, just 47% felt confident that they had sufficient knowledge and skills to help people at most risk of malnutrition. This survey highlights the need for increased efforts to integrate information on the prevalence, causes, consequences of DRM and how medical nutrition can be used to tackle malnutrition, into the education and training of healthcare professionals. In addition, nutrition screening and management should be part of national healthcare policy and plans in all countries.

Many patients and carers see the development of malnutrition as an inevitable part of disease or ageing. Public health campaigns could be employed to educate patients and carers about how to identify malnutrition, how to seek help and how to manage the condition.

To ensure equitable access to medical nutrition and to mitigate the high cost associated with DRM healthcare providers and payors should take account of the evidence base for the cost effectiveness of medical nutrition to ensure that medical nutrition is funded and available to all those that need it.

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3 BENEFITS OF MEDICAL NUTRITION

3.1 Benefits of Oral Nutritional Supplements (ONS)

Summary and recommendations

ONS have proven nutritional, functional, clinical and economic benefits in both the hospital and community setting in a wide variety of patient groups. Studies show that ONS increase energy and protein intakes in both hospital and community patients without reducing spontaneous intake from food; indeed ONS may help to **stimulate appetite** e.g. in post-surgical patients and in older people. Improvements in clinical outcome and healthcare resource use have been consistently demonstrated in a number of trials and meta-analyses:

- Meta-analyses show that ONS lead to **weight gain** in patients in hospital and in those transferred to the community including older people e.g. average weight change between supplemented and control group +3%.
- Meta-analyses consistently show a **reduction in mortality** in patients given ONS compared with standard care (e.g. 24% reduction), particularly in undernourished older people.
- **Reductions in complication rates** of between 25% and over 50% are seen in meta-analyses of ONS compared with routine care.
- Meta-analysis shows that use of ONS significantly **reduces the proportion of patients (variety of conditions) admitted or readmitted to hospital** compared with routine care (24% vs 33%).
- Intervention with high-protein ONS has been shown to **reduce overall readmissions by 30%**.

Improvement in quality of life, activities of daily living, muscle strength, respiratory muscle function and sleep scores have been demonstrated in patients receiving ONS. ONS have been demonstrated to be more effective than dietary advice and snacks; **greater intakes of energy, protein and vitamins and fewer complications** have been shown in patients with fractured neck of femur when compared with snacks (with equal energy content). **Significantly greater energy and protein intakes** with ONS have been reported in a randomised controlled trial of ONS versus dietary advice in care home residents. Data on the benefits of dietary counselling and food fortification in the management of malnutrition are lacking or are of variable quality.

Potential cost savings as a result of reduced healthcare use have been demonstrated in patients supplemented with ONS and can be realised in both the hospital and the community setting. Economic modelling undertaken by NICE (2006 and 2012) showed ONS to be cost-effective as part of a screening programme.

Comprehensive systematic reviews have shown that managing malnutrition with ONS can produce **an average cost saving of around 10%** compared to standard care across a broad range of patient groups. Meta-analyses in hospitalised patients show that ONS use is associated with **1 in 3 fewer deaths, 1 in 3 fewer complications and shorter length of hospital stays**.

A holistic approach must be taken when considering the investment needed to manage malnutrition; the cost may be incurred in one setting whilst the benefit appears to occur in another. However, taken as a whole, effective prevention and management of malnutrition will realise cost savings across the social and healthcare system.

Conclusion

ONS are one of a spectrum of nutritional support strategies that can be used to tackle malnutrition. There is consistent, good quality evidence from multiple individual trials and meta-analyses demonstrating the beneficial nutritional, functional and clinical effects of ONS in malnourished patients. Besides improving the well-being of patients, fighting malnutrition with ONS is an opportunity for healthcare providers to control costs. This is especially relevant in light of the ageing population and the high prevalence of chronic disease that adversely impacts nutritional status, which in turn contributes to increased cost burden. Controlling and managing malnutrition is a clinically and cost-effective solution. This approach is summarised in the infographic presented in Figure 3.1.

Recommendations

On the **benefits of ONS** the MNI makes the following recommendation:

Action	Issues to consider
A wealth of evidence is available that demonstrates the benefits of ONS. This should be translated into practice to ensure that patients who need nutritional intervention receive it in a timely and appropriate manner	• Information about the benefits of ONS and how they should be used in practice should be included as part of education and training on the management of malnutrition • Patients' progress should be regularly monitored and their nutritional care plan, including all types of nutritional intervention, should be adjusted accordingly • Appropriate forms of nutritional intervention, including ONS, should be available to all patients when needed and access or ability to pay should not be a constraint

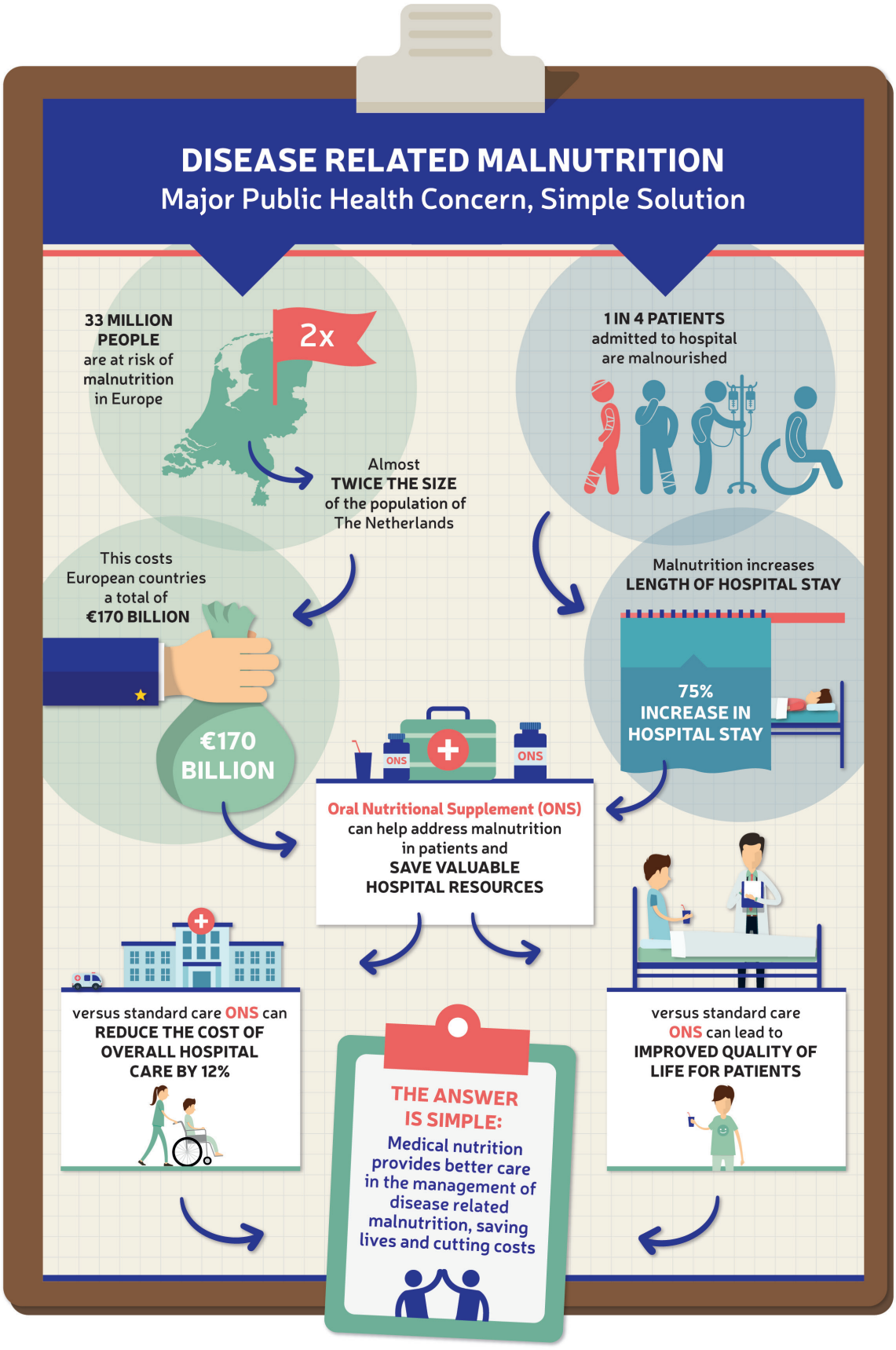

Figure 3.1 **Infographic depicting the scale of the problem of DRM in Europe and the beneficial role of ONS** (reproduced with kind permission of the Medical Nutrition International Industry (http://www.medicalnutritionindustry.com/evidence#infographic). Cost saving data from Elia et al. 2016.[1]

3.1.1 Nutritional benefits of ONS

3.1.1.1 NUTRITIONAL INTAKE

ONS increase total energy intake in adult hospital patients

- A comprehensive systematic review of trials in the hospital setting (58 trials, 34 RCTs, 25 [74% of the total RCTs] assessed intake with ONS) indicated the efficacy of ONS in increasing total energy intake in a variety of patient groups: patients with COPD, older people, post-surgical patients, orthopaedic patients, patients with liver disease, and patients with cancer.[2]
- The effect was observed regardless of whether the mean BMI of the group was < 20 kg/m^2 or > 20 kg/m^2.[2]
- Significantly increased energy intake (560 kcal vs 230 kcal; $p < 0.05$) was observed in moderately and severely malnourished patients randomized to receive ONS and dietary counselling ($n = 104$) compared with a control group who received the standard hospital diet and dietary counselling ($n = 103$) for 12 weeks.[3]
- In hospital patients, ONS have been shown not to substantially reduce food intake, and in some patient groups (e.g. post-surgical patients), ONS even appear to stimulate appetite and food intake (see Figure 3.2).[4] During acute illness, the effectiveness of ONS in increasing total energy intake may be limited.[2]

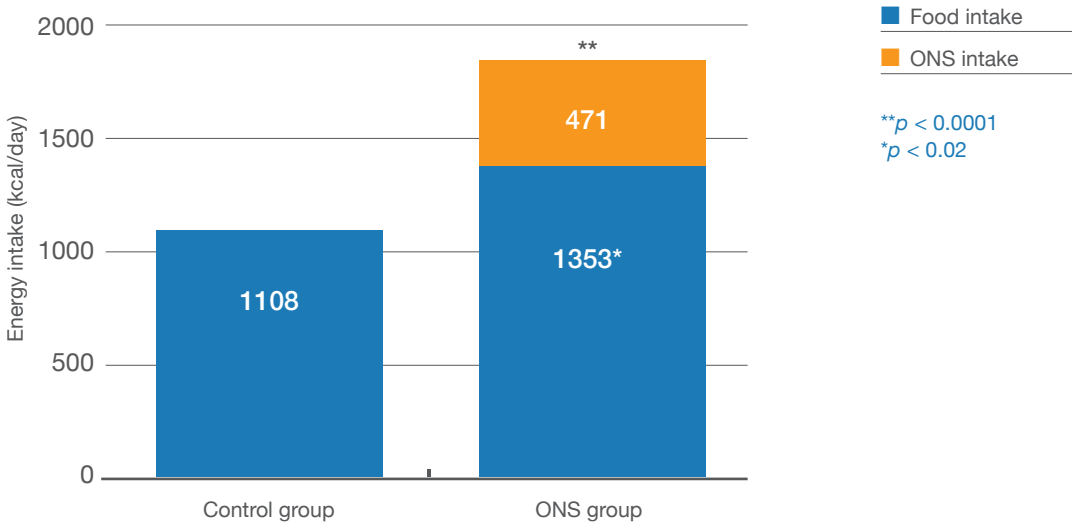

Figure 3.2 **Higher total food and energy intake in hospitalised post-surgical patients with ONS** (adapted from Rana et al. 1992)[4]

Significant increase in total energy intake, $p < 0.0001$; significant increase in intake from ward diet, $p < 0.02$.

ONS increase total energy intake in adult patients in the community

- In a systematic review of patients in the community setting (108 trials, 44 RCTs, $n = 3747$, the effect of ONS on energy intake was assessed in 32 RCTs), ONS increased total energy intake across a variety of patient groups: patients with COPD, older people, patients with cystic fibrosis, patients with Crohn's disease, patients with HIV, surgical patients and patients with liver disease.[2] In the RCTs assessing energy intake ($n = 29$), 91% showed improvements, of which > 70% were significant. The mean increase in total energy intake was equivalent to 69% of the ONS energy, although there was wide variation across the studies. The increase was greater in studies of patients with a mean BMI of < 20 kg/m^2 than > 20 kg/m^2.[2]

- A systematic review of the effects of oral nutritional intervention in care homes using ONS (3 RCTs [*n* = 196]) showed improvements in energy intake (mean difference 123 kcal [95% CI 92–154 kcal], $p < 0.0001$).[5]
- Cawood et al. undertook a subgroup analysis of 11 RCTs in community patients (*n* = 672) (in 2 RCTs, ONS commenced in hospital and continued after discharge), which showed significant improvements in total energy intake in patients who received oral nutritional intervention with high-protein ONS versus controls (349 kcal [95% CI 210–488], $p < 0.001$ random effects model).[6]

High-protein ONS increase total energy intake in adult patients across healthcare settings

- A systematic review and meta-analysis of 12 RCTs in patients across healthcare settings (*n* = 1242) (2 RCTs in hospitals, 10 RCTs in the community, and 3 RCTs across hospital and community) showed improvements in total energy intake in patients who received oral nutritional intervention with high-protein ONS versus controls in all but 1 trial (see Figure 3.3), and significantly so on meta-analysis (314 kcal [95% CI 146–482 kcal], $p < 0.001$ random effects model).[6]

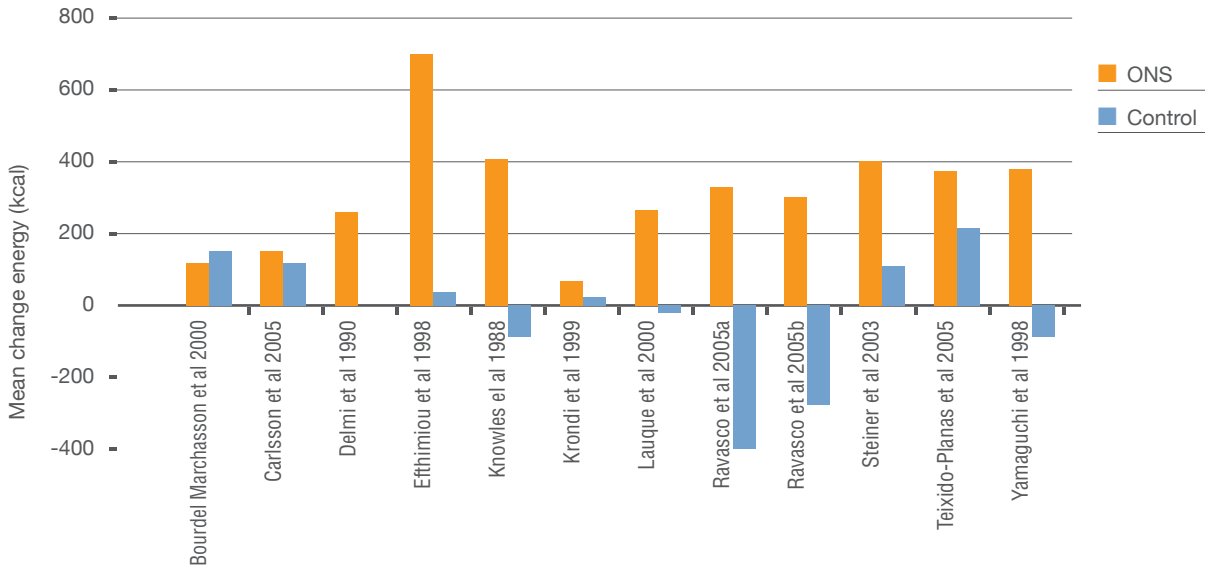

Figure 3.3 **Effect of high-protein ONS vs control on intake of energy** (adapted from Cawood et al. 2012).[6]

Mean change in intake during intervention period (baseline to end of intervention)

ONS are effective in increasing energy intake in older people in hospital

- Normally nourished or mildly undernourished older hip fracture patients (*n* = 60) supplemented with high-protein ONS during hospital admission had significantly higher total energy intake compared with controls (standard or texture modified diet) ($p < 0.05$).[7]
- Total daily energy intakes were significantly higher in acutely ill hospitalised older patients (aged >78 years) randomized to receive ONS plus an intense rehabilitation exercise programme (IG, *n* = 100) compared to a control group who received usual care (CG, *n* = 100) (1954.4 ±428.9 kcal and 1401 ±363.7 kcal respectively, $p < 0.001$). Spontaneous intake of hospital food was not reduced by the ONS (percentage of total food consumption during entire hospital stay was 72.8% in IG vs 71.3% in the CG, $p = 0.528$).[8]

- During the first 11 postoperative days, hospitalised older patients (>65 years) with hip fracture who received the normal hospital diet and ONS prescribed according to measured energy requirements/intake had a significantly higher mean daily energy intake vs. the control group who were offered the normal hospital diet and ONS if already prescribed prior to the study ($p = 0.001$). The calculated daily energy balance was significantly more positive in the intervention group ($p < 0.05$) from days 3 to 10 of the study.[9]
- An RCT of nutritional support in an acute hospital trauma ward found that patients supported by a dietetic assistant had a mean energy intake of 349 kcal/d greater than the 756 kcal/d achieved by patients receiving conventional nursing care. Of the additional 349 kcal/d, 286 kcal/d (82%) came from ONS.[10]

ONS are effective in increasing energy intake in older people across healthcare settings

- In a large systematic review of protein and energy supplementation (ONS) specifically in older people (62 trials, $n = 10187$ randomised participants), a significant increase in total daily energy intake was reported in the majority of studies (variety of inpatient and community settings).[11]
- A systematic review and meta-analysis looking at the effect of interventions to prevent and treat malnutrition in patients admitted for rehabilitation included 10 studies, 3 of which compared the provision of ONS plus usual meals with usual meals only as the control. These studies found that the consumption of ONS led to significantly greater energy ($p < 0.01$) and protein intakes ($p < 0.05$).[12]
- The effectiveness of interventions for the treatment of dysphagia and nutritional and fluid supplementation in stroke patients was evaluated in a systematic review including 33 studies, eight of which assessed the effect of nutritional supplementation. Nutritional supplementation (defined as protein and calorie supplements) increased energy ($t^{i} = 3$; n = 174; MD 430.18 kcal/day; 95% CI 141.61 to 718.75; $p = 0.003$; $I^2 = 91\%$) and protein intakes (t = 3; n = 174; MD 17.28 g/day; 95% CI 1.99to 32.56; $p = 0.03$; $I^2 = 92\%$) compared to no supplementation.[13]
- A systematic review and meta-analysis of twelve studies assessing the effect of nutritional supplementation in older adults with dementia at 6.5 ± 3.9 month follow-up when supplements were given compared to the control group (usual care - 8 studies, placebo drink/supplement - 4 studies). Meta-analysis of three studies showed that there were no significant differences in consumption at mealtimes between supplement and control groups (-0.024 ± 0.095kcal, $p = 0.8$), suggesting ONS did not have a negative effect on habitual food intake.[14]
- In a prospective RCT in older patients (> 75 years of age, at risk of malnutrition) investigating the effect of supplementation ($n = 35$) versus no supplementation ($n = 35$) throughout hospitalisation and convalescence, spontaneous intake was maintained despite supplementation, i.e. ONS may have stimulated appetite. The spontaneous energy intake (excluding supplements) was calculated for 10 control and 16 supplemented patients, and it was found to be significantly higher in the supplemented group ($p < 0.01$) (see Figure 3.4).[15]

[i] t = number of studies.

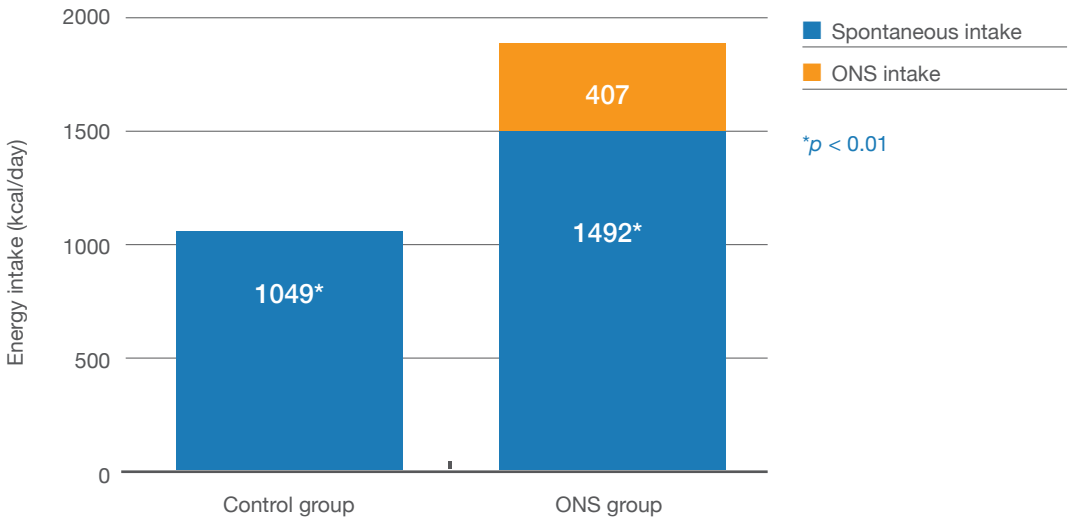

Figure 3.4 **Greater total energy intake with ONS in supplemented group vs control group** (adapted from Gazzotti et al. 2003).[15]

ONS started in hospital and continued in the community; spontaneous intake maintained despite supplementation with ONS (60 days after inclusion in the study; *$p < 0.01$)

- In an RCT of community free-living frail older people (aged ≥65 years) subjects randomized to receive ONS and dietary counselling ($n = 43$) for 12 weeks had significant improvements in energy intake compared to controls who were visited monthly ($n = 44$). The control group did not receive a placebo, ONS or dietary counselling.[16]
- In a prospective controlled crossover study undertaken in nursing homes in the UK in older patients (>65 years) with dementia ($n = 26$), Allen et al. found that significantly more energy was consumed on intervention days compared to control days ($p < 0.001$) (ONS was offered on alternate days for 1 week). No significant difference was found between energy consumed from food on intervention days compared to paired control days ($p = 0.641$). 55.8% of patients met their caloric goals on intervention days, compared to 17.3% on their adjacent control day ($p < 0.0001$).[17]
- Significant improvements in energy intake with ONS versus usual care have been observed in older patients with Alzheimer's disease at risk of malnutrition in hospital and day care centres (total energy intake at 3 months was 291 kcal/d greater than at baseline) and in older malnourished patients (≥ 75 years of age) discharged from hospital into the community (significantly greater energy intake in ONS group vs control group, $p = 0.022$).[18;19]
- A 12 week randomised, parallel, open-label trial comparing the effectiveness of ONS with dietary advice in care home residents ($n = 104$) at risk of malnutrition (using 'MUST' [medium and high risk]) showed that energy intakes were significantly higher in residents randomised to receive ONS than in residents who received dietary advice (on average by 351 kcal/d). Figure 3.5 shows that consumption of the ONS accounted for the main difference in energy intake.[20]

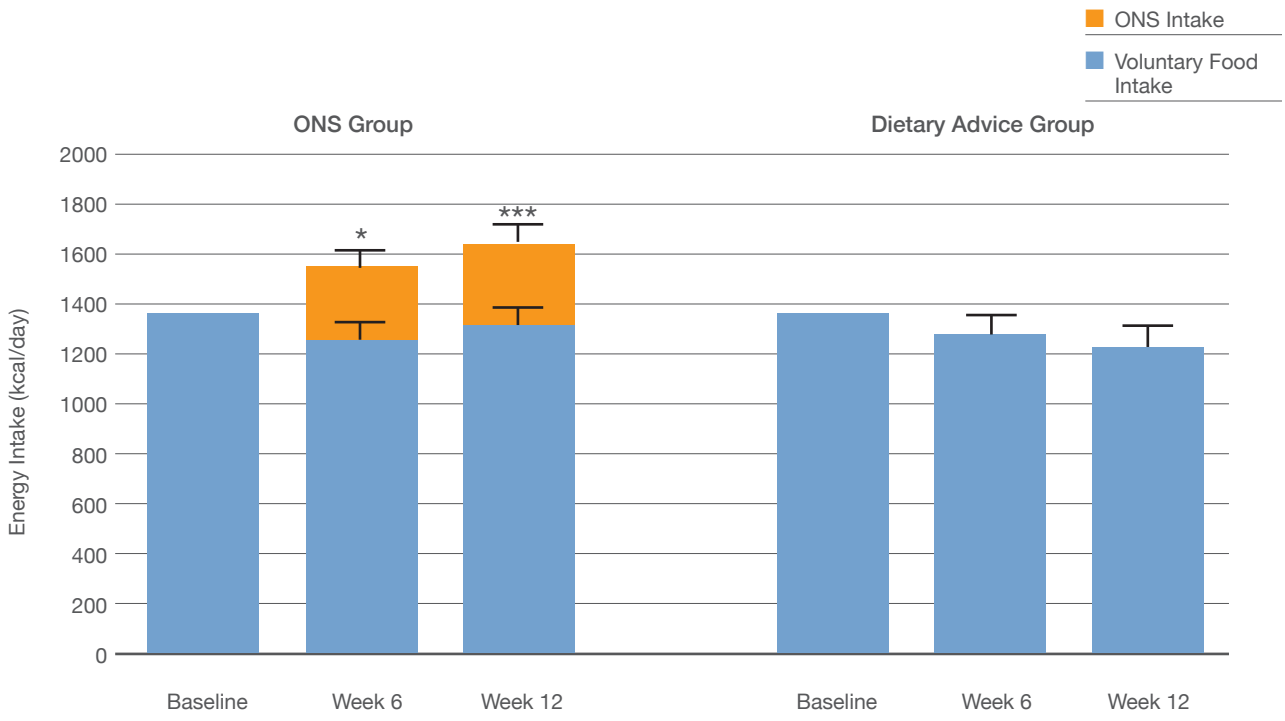

Figure 3.5 **Daily intake (mean ± SE) of energy (kcal/day) in the ONS and Dietary advice groups at week 12, using a per protocol analysis.** (Adapted from Parsons et al. 2016)[20]

The blue bars indicate voluntary food intake and the orange bars intake from ONS. The error bars at the top of the highest point of the 6 and 12 week shaded bars relate to total intake of energy. The 6 and 12 week results are adjusted for baseline intake values, 'MUST' category and type of care.*p <0.05 and ***p < 0.001 for the differences between groups.

ONS increase energy intake in a variety of diseases in adults and children

- A systematic review of the effect of ONS in community patients including children by Stratton et al. (2003) concluded that:[2]
  - ~ nutritionally complete ONS can be used as a sole source of nutrition in both adults and children with acute exacerbations of Crohn's disease. The review also suggested that ONS may increase total energy intake without substantially reducing food intake;
  - ~ in undernourished cystic fibrosis patients (adults and children), ONS can increase total energy intake without substantially reducing food intake. The increase in total intake may be equivalent to more than 80% of ONS energy, although large volumes of unpalatable formulations may reduce appetite.
- A systematic review of 4 studies including children with cystic fibrosis and malignant disease looked at the effect of protein-calorie supplements (administered orally, in any amount and given for a period of at least one month), compared with no intervention, routine nutritional advice or placebo. A significant difference in mean total energy intake at six months (mean difference 304.86 kcal/day [95% CI 5.62 to 604.10], p = 0.046) and at 12 months, (mean difference 265.70 kcal/day [95%CI 42.94 to 485.46], p = 0.019) was found to favour the treatment group. No significant differences were found for protein or fat intakes between the treatment and control arms.[21]

ONS are effective in increasing protein intake in adult patients across healthcare settings

- In a review of trials of ONS versus standard care (hospital and community, malnourished or at risk of malnutrition), NICE (National Institute for Health and Care Excellence) (2006) reported higher protein intakes in the supplemented groups, and that ONS may be more effective in increasing intake than dietary advice.[22] Stratton et al. (2003) also reported significant increases in protein intake in patients receiving ONS.[2]

- A systematic review and meta-analysis of 10 RCTs in patients across healthcare settings (n = 1152) showed improvements in total protein intake in patients who received oral nutritional intervention with high-protein ONS versus controls in all but 1 trial (see Figure 3.6), and significantly so on meta-analysis (22 g [95% CI 10–34 g], $p < 0.001$ random effects model).[6]

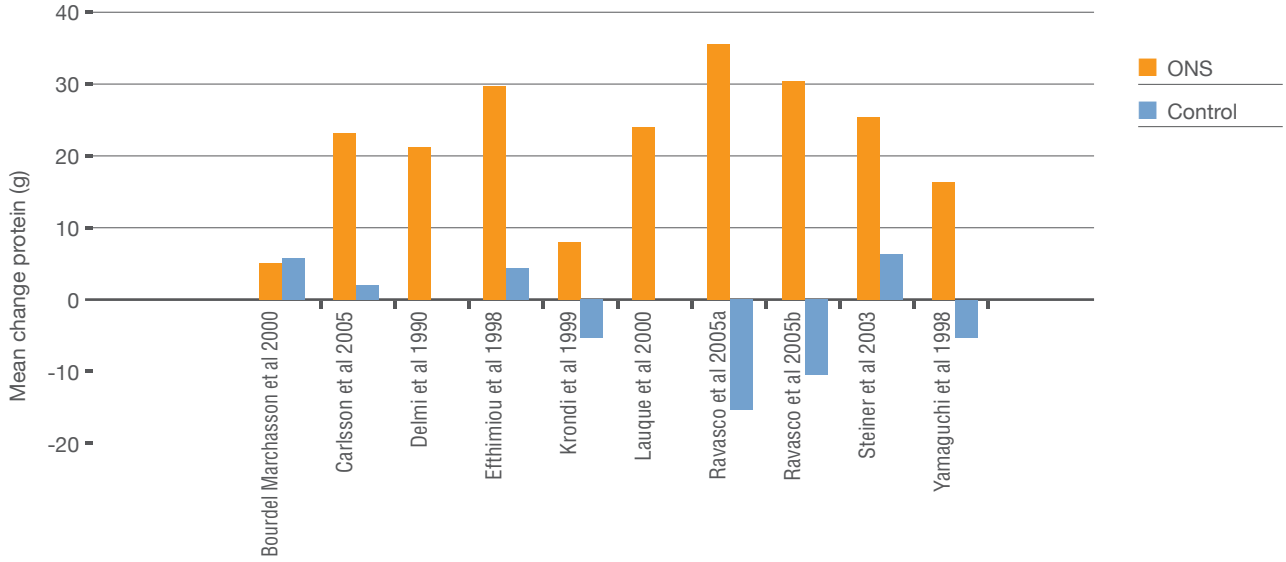

Figure 3.6 **Effect of high-protein ONS vs control on intake of energy** (adapted from Cawood et al.)[6]
Mean change in intake during intervention period (baseline to end of intervention).

- Malnourished adult community patients with benign GI disease randomised to receive high-protein ONS plus dietary counselling for 3 months achieved a significantly higher daily total protein intake (57% higher) than patients randomised to receive dietary counselling alone (117.1±34.7 g protein/day vs 74.6±44.6 g protein/day, $p < 0.0001$).[23]

ONS are effective in increasing protein intake in older people across healthcare settings

- In a large systematic review of protein and energy supplementation specifically in older people (62 trials, n = 10187 randomised participants), a significant increase in total daily protein intake was reported in the majority of studies (variety of inpatient and community settings).[11]
- Normally nourished or mildly undernourished older hip fracture patients (n = 60) supplemented with high-protein ONS during hospital admission had significantly higher total protein intake compared with controls (standard or texture modified diet) ($p < 0.05$).[7]
- Use of ONS has been demonstrated in clinical trials to significantly increase protein intake in:
  - ~ older patients recently discharged home (achieved >80% increase in mean daily protein intake 2 months after hospital admission), (see Figure 3.7);[15]
  - ~ malnourished older patients in hospital (n = 17) compared with controls (n = 6) who received no ONS but careful attention from nursing staff to finish meals (+65% protein intake vs +32%, $p < 0.0001$);[24]

- acutely ill hospitalised older patients (>78 years). Total daily protein intakes were significantly higher in the ONS plus intense rehabilitation exercise programme group vs controls who received routine care ($p < 0.001$);[8]
- hospitalised older hip fracture patients (>65 years). The intervention group had a significantly higher mean daily intake of protein vs. control group during the first 11 postoperative days ($p = 0.001$);[9]
- older patients recovering from hip fracture in a rehabilitation hospital given high-protein supplements (vs standard supplements [63 g vs 50 g protein/d, $p < 0.048$]);[25]
- older adults with dementia (aged > 65years). Significantly more total protein was consumed on intervention days vs. control days ($p < 0.0001$). No difference in protein intake from food was observed on intervention vs. control days ($p = 0.576$). On intervention days RDA for protein was more frequently met compared to on control days ($p < 0.0001$);[17]
- older patients with Alzheimer's disease at risk of malnutrition in hospital and day care centres (total protein intake at 3 months was 16 g/d greater than at baseline $p < 0.001$).[18]

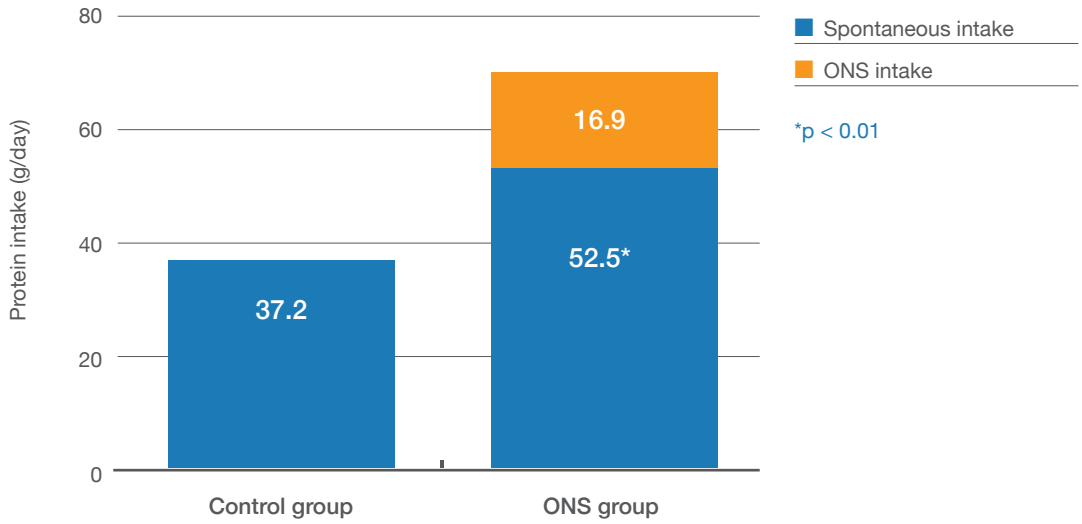

Figure 3.7 **Greater total protein intake with ONS** (adapted from Gazzotti et al. 2003).[15]

ONS started in hospital and continued in the community in the supplemented group vs the control group (60 days after inclusion in the study; *$p < 0.01$). Note spontaneous food intake assessment based on $n = 10$ in control group and $n = 16$ in ONS group.

- A randomized, parallel, open-label trial comparing the effectiveness of ONS with dietary advice in care home residents ($n = 104$) at risk of malnutrition (using 'MUST' [medium and high risk]) showed that protein intakes were significantly higher in residents randomised to receive ONS than in residents who received dietary advice (on average by 12.2g protein/day) (see Figure 3.8).[20]

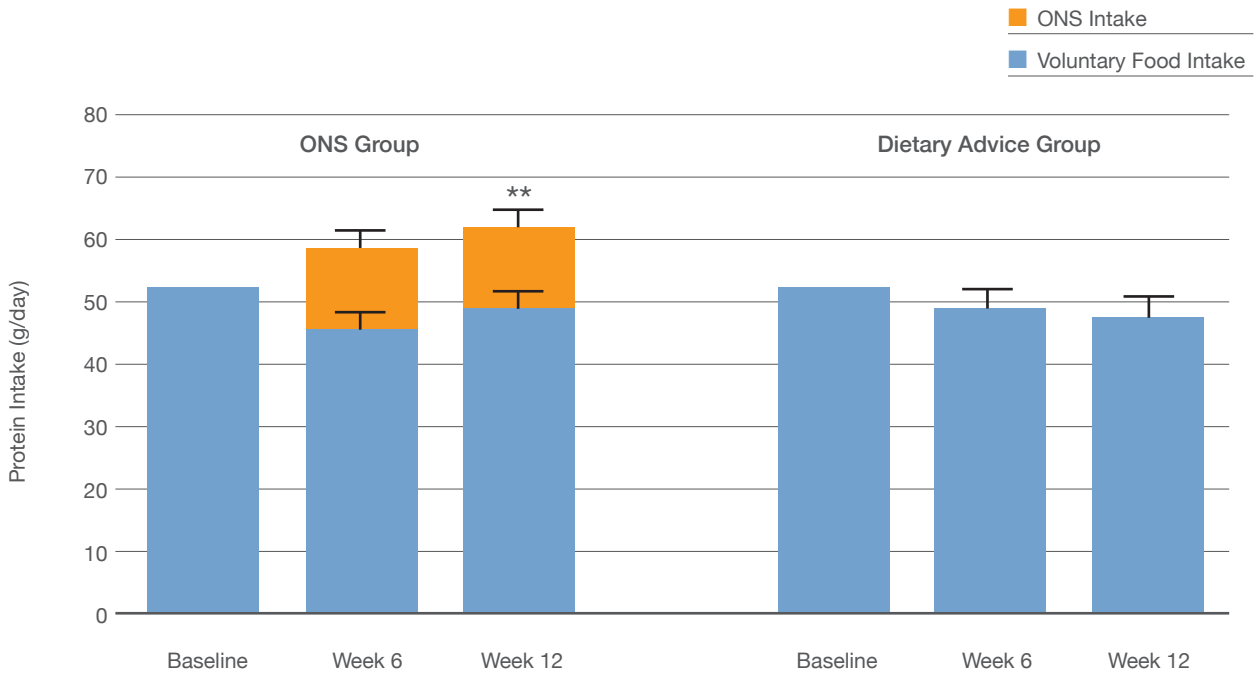

Figure 3.8 **Daily intake (mean ± SE) of protein (g/day) in the ONS and Dietary advice groups at week 12, using a per protocol analysis.** (Adapted from Parsons et al. 2016).[20]

The blue bars indicate voluntary food intake and the orange bars intake from ONS. The error bars at the top of the highest point of the 6 and 12 week shaded bars relate to total intake of protein. The 6 and 12 week results are adjusted for baseline intake values, 'MUST' category and type of care. $^{**}p < 0.01$ for the differences between groups.

ONS increase micronutrient intakes and can be more effective than food snacks or dietary advice

- In a study of older people resident in nursing homes, a non-randomised subgroup analysis (n = 66) showed an increased intake of a wide range of vitamins and minerals in patients who received nutrient-enriched ONS compared with placebos ($p < 0.001$).[26]
- A randomized, parallel, open-label trial comparing the effectiveness of ONS with dietary advice in care home residents (n = 104) at risk of malnutrition (using 'MUST' [medium and high risk]) found significantly higher intake of a range of vitamins and minerals in residents randomised to receive ONS compared with residents who received dietary advice.[20]
- Food snacks are often used with the aim of increasing nutrient intake. However, in a trial of hospital patients with fractured neck of femur at risk of malnutrition (screened using 'MUST') (n = 50, median age 82 [range 46–97], median BMI 19 [range 12.5–26 kg/m^2]) randomised to receive either ONS (300 kcal per serving) or isoenergetic readily available snacks (typical snacks used in UK hospitals include full-fat yogurt, cheese and crackers, cake, and chocolate) ad libitum postoperatively, the ONS group had significantly greater intakes of protein, energy and water-soluble vitamins than the snack group (see Figure 3.9, and Table 3.1).[27; 28] Although intakes of some vitamins were above the RNI, they fell within safe intakes.

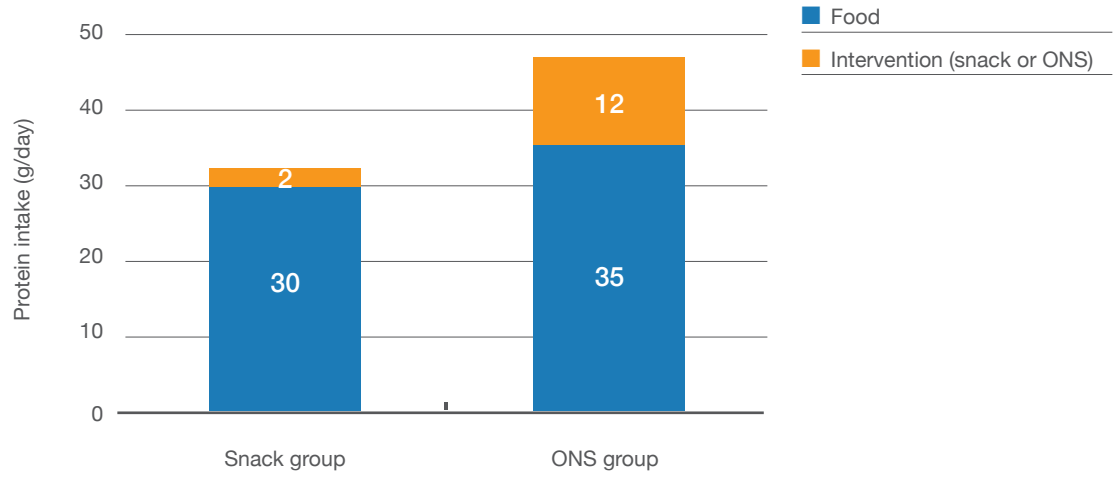

Figure 3.9 **Greater total protein intakes with ONS vs isoenergetic food snacks** (adapted from Stratton et al. 2006)[26]

Table 3.1 **Greater total mean intakes of water-soluble vitamins with ONS vs isoenergetic food snacks** (adapted from Stratton et al. 2006)[27]

VITAMIN	SNACK GROUP (*n* = 24) MEAN	SD	ONS GROUP (*n* = 26) MEAN	SD
Thiamin (mg/d)	0.73	0.38	1.59*	1.36
Riboflavin (mg/d)	0.98	0.49	1.80*	1.24
Vitamin B_6 (mg/d)	0.84	0.41	1.60**	0.75
Folate (µg/d)	108.00	49.60	221.00**	110.00
Niacin (mg/d)	7.98	4.73	15.80**	7.72
Vitamin C (mg/d)	37.40	20.10	77.00**	41.10

Mean total intakes for the ONS group were significantly higher than those for the food snack group (unpaired t test): *$p < 0.004$, **$p < 0.0005$. Intakes of biotin and pantothenate for the ONS group were significantly higher than those for the food snack group ($p < 0.0005$) (data not listed in Stratton et al. 2006).[27]

3.1.1.2 NUTRITIONAL STATUS

ONS lead to weight gain and prevention of weight loss in adult hospital patients

- In a systematic review by Stratton et al. (58 trials, 34 RCT, *n* = 3883) in the hospital setting, ONS were found to improve body weight in 81% of trials (35 assessed weight), of which 46% were significant. Average weight change between supplemented and control patients was +3% (17 RCTs) across a variety of patient groups: surgical patients, older people, patients with COPD. A similar effect was seen in trials in which mean BMI was < 20 kg/m^2 or > 20 kg/m^2.[2]
- In a meta-analysis by NICE of ONS versus standard care in hospital patients who were malnourished or at risk of malnutrition, it was demonstrated that the use of ONS led to significant increases in weight (weighted mean difference 1.13 [95% CI 0.51–1.75, p = 0.0003]) (see Figure 3.10).[22]

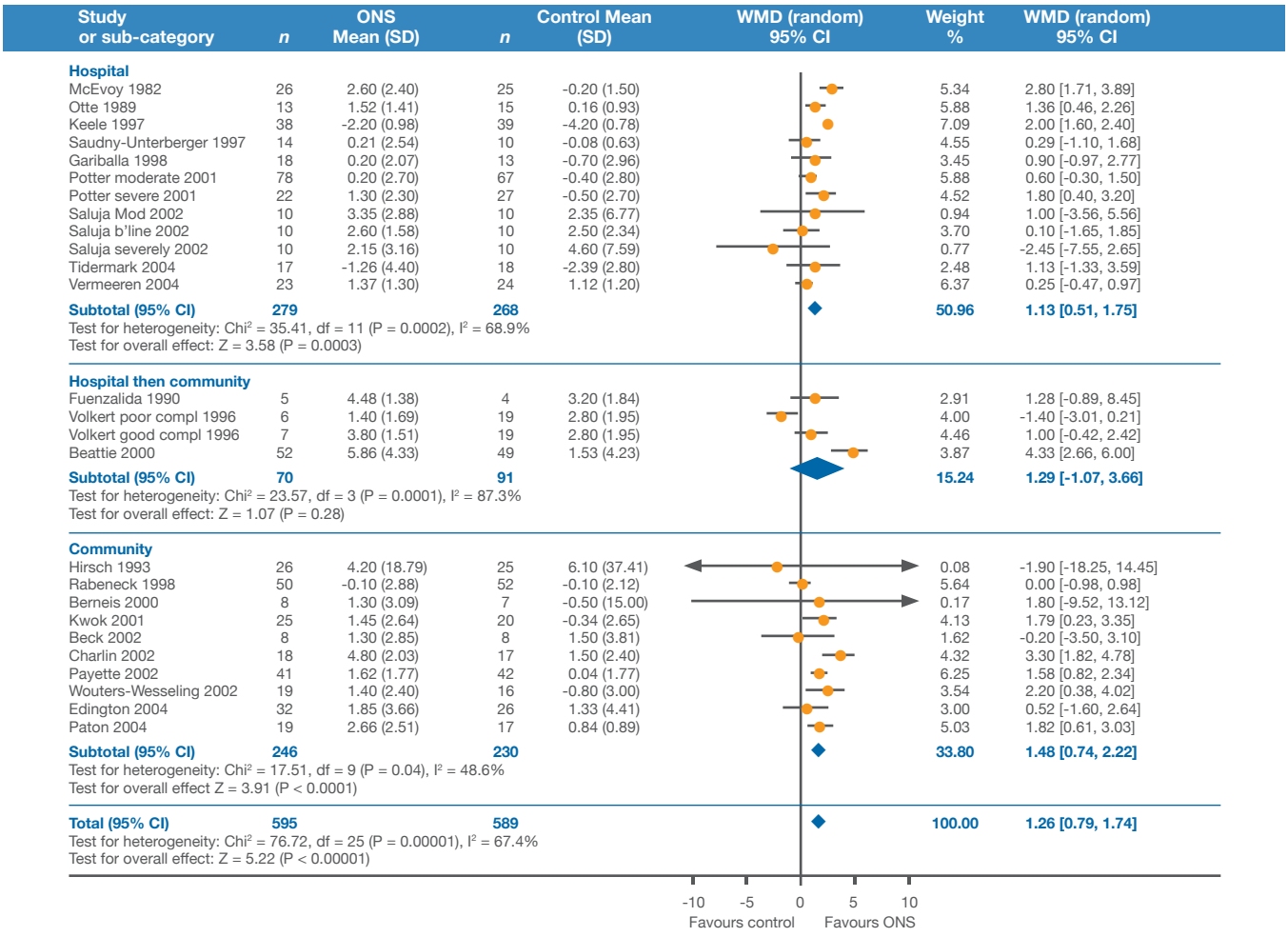

Figure 3.10 ONS versus standard care (all patients): weight change by setting (adapted from NICE 2006)[22]

ONS lead to weight gain and prevention of weight loss in adult patients in community settings

- Meta-analysis of percentage weight change in 13 RCTs (COPD, older people, HIV, liver disease, cancer, post-surgical patients) showed a mean significant effect size with ONS of 0.61 (95% CI 0.50–0.71), though with considerable heterogeneity between the trials.[2]

- In the meta-analysis conducted by NICE of ONS versus standard care in patients who were malnourished or at risk of malnutrition, it was demonstrated that the use of ONS led to increases in weight in patients in the community (weighted mean difference 1.48 [95% CI 0.74–2.22, $p < 0.0001$]) (see Figure 3.10).[22]
- A systematic review and meta-analysis of the effects of oral nutritional intervention in care homes using ONS (3 RCTs [$n = 195$]) found a significant difference in body weight (1.7 [95% CI 0.8–2.6] kg, $p < 0.001$ random effects model).[5]

High-protein ONS lead to weight gain in adult patients across healthcare settings

- Meta-analysis of 12 RCTs in patients across healthcare settings ($n = 1244$) (2 RCTs in hospital, 7 RCTs in the community and 3 RCTs across hospital and community) showed significantly increased weight in patients who received oral nutritional intervention with high-protein ONS versus controls (1.7 kg [95% CI 0.8–2.7], $p < 0.001$ random effects model) (see Figure 3.11).[6]

STUDY	SETTING	STATISTICS FOR EACH STUDY				DIFFERENCE IN MEANS AND 95% CI
		Difference in means	Lower limit	Upper limit	p-Value	
Bruce et al. 2003	Hospital-Community	0.400	-0.651	1.451	0.456	
Efthimiou et al. 1988	Community	4.900	-1.491	11.291	0.133	
Gariballa et al. 2006	Hospital-Community	1.000	-0.134	2.134	0.084	
Lauque et al. 2000	Community	2.700	-1.482	6.882	0.206	
McEvoy et al. 1982	Hospital	2.800	1.696	3.904	0.000	
Norman et al. 2006	Community	0.900	-1.708	3.508	0.499	
Olofsson et al. 2007	Hospital	-0.400	-2.096	1.296	0.644	
Otte et al. 1989	Community	1.360	0.486	2.234	0.002	
Steiner et al. 2003	Community	1.210	-1.384	3.804	0.361	
Teixido-Planas et al. 2005	Community	8.280	5.305	11.255	0.000	
Tidermark et al. 2004	Community	1.130	-1.156	3.416	0.333	
Volkert et al. 1996	Hospital-Community	2.400	-0.419	5.219	0.095	
		1.743	**0.785**	**2.702**	**0.000**	

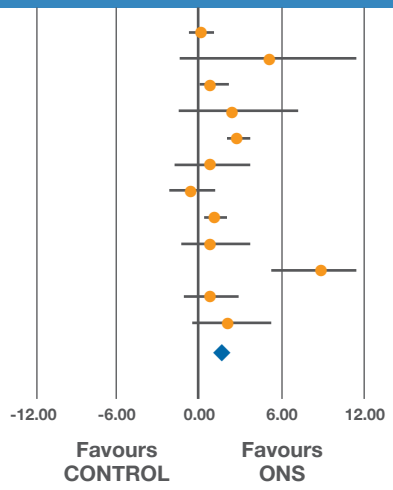

Figure 3.11 **Meta-analysis showing significant improvement in weight with oral nutritional intervention with high-protein ONS** (adapted from Cawood et al. 2012)[6]

ONS lead to weight gain in older people across healthcare settings

- In a large meta-analysis of studies in older people, greater weight gain was seen with supplementation compared with routine care (pooled weighted mean difference for percentage weight change was 2.15%; 95% CI 1.8–2.49) (variety of in-patient and community settings) (see Figure 3.12).[11] Analyses for weight change carried out in subgroups based on diagnosis showed a significant increase in weight with supplementation for:
  - ~ a mixed group of patients with geriatric conditions (weighted mean difference 2.65%; 95% CI 2.19–3.10);
  - ~ patients with chest conditions (weighted mean difference 1.58%; 95% CI 0.99–2.17).
- Dietary advice and ONS given for 4 months to older people at risk of malnutrition on discharge from a geriatric service resulted in prevention of weight loss, whereas controls lost 3.1 kg during the study.[29]

- A systematic review and meta-analysis of 12 studies assessing the effect of ONS in older adults with dementia showed a significant improvement in weight ($p < 0.0001$) and Body Mass Index (BMI) ($p < 0.0001$) at 6.5 ± 3.9 month follow-up when supplements were given compared to the control group (usual care in 8 studies, placebo drink/supplement in 4 studies).[14]
- ONS have been shown to increase body weight in community-dwelling undernourished older people compared with controls (weight gain mean difference of 1.17 kg [95% CI 0.07–2.27, $p = 0.04$] following adjustment for adherence).[30]
- A randomised double-blind placebo controlled trial (RDBPCT) in older care home residents has shown that oral nutrition intervention with ONS led to weight gain (1.6 kg difference in change, $p = 0.035$).[31]

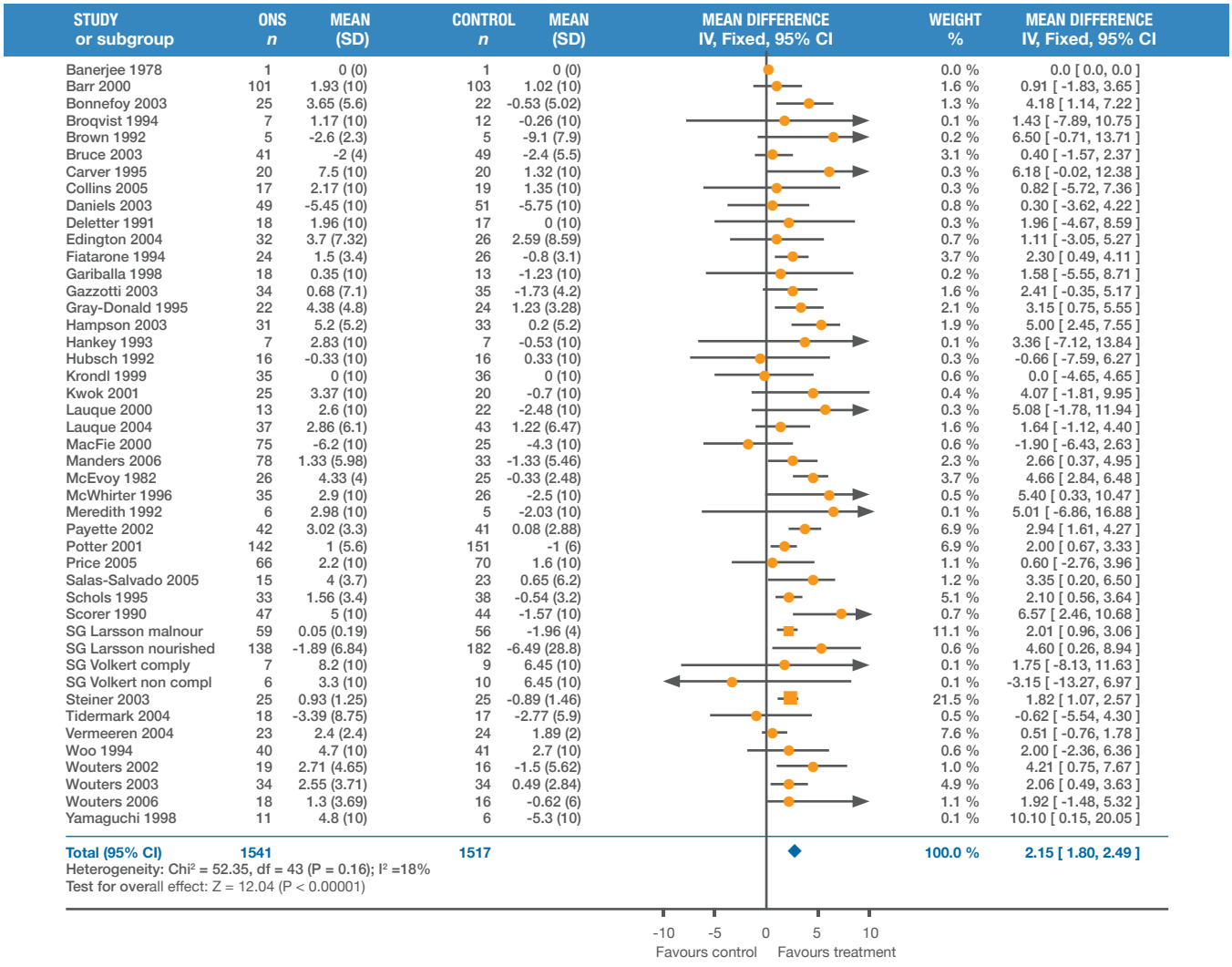

Figure 3.12 **Weight change in older people with protein and energy supplementation vs routine care** (adapted from Milne et al. 2009)[11]

ONS improve micronutrient status

- NICE (2006) highlighted that care should be taken when using food fortification strategies as a means of increasing oral nutrient intake, as food fortification tends to increase energy and/or protein intake without increasing micronutrient intake. Oral nutritional support should contain a balanced mixture of protein, energy, fibre and micronutrients.[22] Under European law, Foods for Special Medical Purposes (FSMPs), which include ONS, must comply with compositional standards which specify required levels of vitamins and minerals.[32] Deviations are permitted but they must be based on a sound scientific rationale.
- In an RDBPCT of high-protein ONS during acute illness in older people (ONS continued after discharge), significant improvements were seen in markers of micronutrient status, e.g. red cell folate and plasma vitamin B12 levels, compared with the decrease seen in the placebo group. This effect was sustained at 6 months (see Figure 3.13).[33]

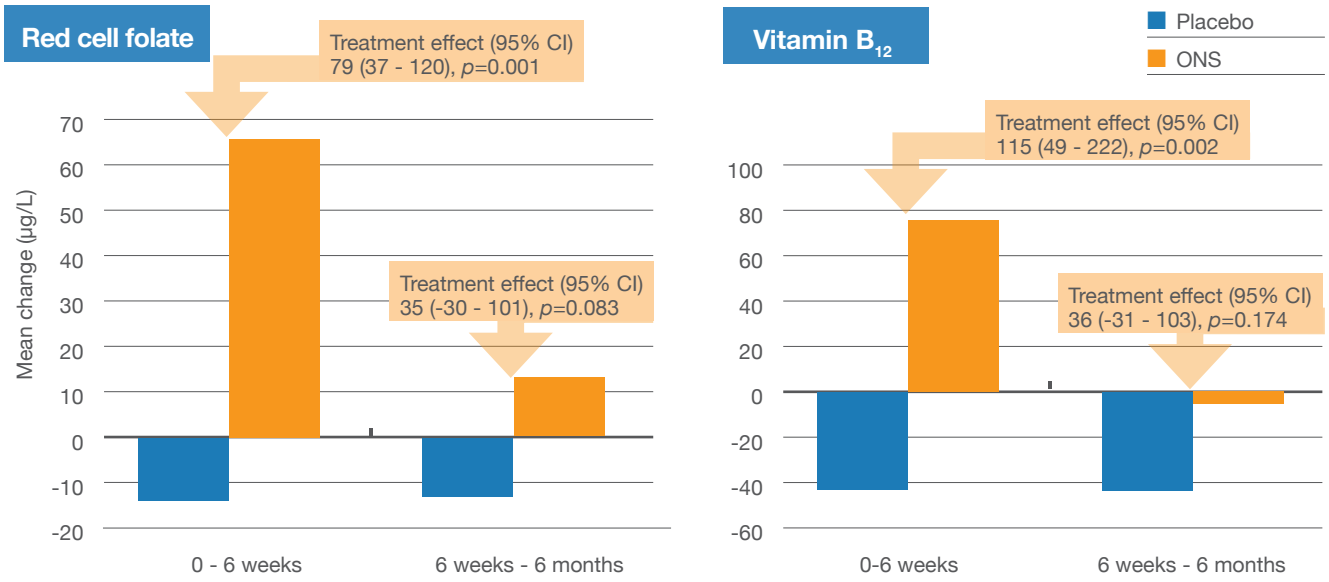

Figure 3.13 **Improved red cell folate and plasma vitamin B_{12} concentrations in patients supplemented with ONS compared with placebo group** (adapted from Gariballa et al. 2006)[33]

- An improvement in micronutrient status (vitamin B_1, thiamine diphosphate, vitamin B_6, vitamin B_{12}, folate and vitamin D) has also been observed following supplementation with ONS compared with placebos in a group of psycho-geriatric nursing home patients.[34]
- Improved plasma vitamin D, vitamin B_{12}, vitamin B_6, homocysteine and folate levels have been observed in older residents of care homes given ONS versus placebos.[31] Most vitamin deficiencies normalised, most notably vitamin D (10% vs 75% remained deficient in the ONS vs the placebo groups).[26]

ONS improve lean body mass in older people

Loss of lean body mass (LBM) (muscle) can lead to reduced muscle function and fatigue, and in turn reduced function, e.g. ability to self-care, ability to undertake normal daily activities, risk of falls (see also Section 3.1.2, Functional Benefits of ONS).

- Use of ONS has been demonstrated in clinical trials to improve LBM among:
  - ~ older people with Alzheimer's disease in hospitals and day care centres who are nutritionally at risk (significant increase in fat-free mass [FFM] 0.78±1.4 kg, $p < 0.001$);[18]
  - ~ older hospital patients who are malnourished (significant increase in FFM + 1.3 kg, $p < 0.001$);[24]
  - ~ older patients in a meta-analysis of 15 trials, $n = 1382$ (pooled weighted mean difference for percent arm muscle circumference change 1.20%; 95% CI 0.45–1.96%).[11]

High-protein ONS lead to improvements in body mass in adult patients across healthcare settings

- Meta-analysis of 4 RCTs ($n = 118$) (1 RCT in hospital and 3 RCTs in community patients) showed significant improvements in MAMC (an indicator of nutritional depletion) in patients who received oral nutritional intervention with high-protein ONS versus controls (mean difference 0.47 cm [95% CI 0.30–0.64], $p < 0.05$).[6]

ONS may improve body weight and growth in children with a variety of diseases

- A systematic review of the effect of ONS in children by Stratton et al. (2003) concluded that:[2]
  - ~ a rather limited evidence base suggests that ONS may increase body weight, muscle mass and growth in growth-retarded children with CD;
  - ~ non-randomised trials consistently show that use of ONS is associated with increased growth in growth-retarded children with cystic fibrosis.
- A multi-centre randomised parallel open study of nutritional counselling with or without ONS in children with growth faltering (mean age 48.5 months, range 36.0–61.0 months; $n = 92$) and picky eating behaviour not related to an underlying medical condition showed significantly greater increases in weight and height in the study group versus controls.[35]
- In an uncontrolled study of children with spastic quadriplegia ($n = 35$), ONS significantly improved anthropometric parameters (baseline vs 6-month follow-up), including height, weight, MAC, TSFT, weight z-score, WFA (%), WFH (%) and BMI.[36]
- In 2014 Smyth et al. undertook a systematic review of 3 randomised or quasi-randomised controlled trials ($n = 131$) investigating the effect of ONS in children with cystic fibrosis vs. nutritional advice or no intervention and found a trend in the ONS group for greater improvement in weight at 3 months, (2 trials, $n = 112$, mean difference 0.32 kg; 95% CI -0.09 to 0.72, $p = 0.12$) and 6 months (2 trials, $n = 117$, mean difference 0.47 kg; 95% CI -0.07 to 1.02, $p = 0.087$) but not at 12 months (1 trial, $n = 102$, mean difference 0.16 kg; 95%CI -0.68 to 1.00).[37] This review was updated in 2015 by Francis et al. who also found no statistically significant effect of ONS for the outcome 'change in weight (kg)'.[21] No significant change in any other measure of height, weight, BMI or MAMC was observed in either review.[21; 37] In the 2014 review data on change in weight and height from 13 subjects (at 3 months) from the Kalnins trial were included, however in the 2015 update data from only 8 subjects (3 & 6 months) were included as a result of personal correspondence between the review authors and Dr Kalnin.[21] Care should be taken when interpreting the results on parameters of nutritional status from both the 2014[37] and 2015[21] reviews since they include only 3 trials, 2 of which had a very small number of

participants (Hanning et al. 1993 *n* = 16[38] & Kalnins et al. 2005 *n* = 13[39]). In addition, the trial by Hanning et al. 1993 was an explanatory trial designed to investigate the relationship between nutritional status and skeletal muscle i.e. it sought to explain the biological mechanism rather than to provide treatment recommendations.[37] Finally, the trial by Poustie et al. 2006[40] which contributed the majority of the subjects to the reviews (*n* = 102, and the only one to follow up at 12 months) may have had poor compliance coupled with an overly ambitious end-point in cystic fibrosis patients of a 10-point difference in centile for BMI within one year, which may explain the lack of effect of the intervention.[41]

- In a prospective randomised study in children with malignant disease undergoing intensive chemotherapy (*n* = 52, mean age 7.5 ±3.0 years), significantly fewer patients in the intervention group (EPA-enriched ONS) showed a loss in body weight (6.1% vs 47.4%; *p* = 0.001) and BMI (12.1% vs 52.6%; *p* = 0.002), and a negative deviation in weight percentile (6.1% vs 31.6%; *p* = 0.021) compared to the control group at 3 months. After 6 months (*n* = 23), the percentage of patients with weight loss was significantly lower in the treatment group versus the controls (6.7% vs 50%; *p* = 0.03).[42]

3.1.2 Functional benefits of ONS

ONS lead to functional benefits in adult hospital patients

- In a review by Stratton et al. (2003), a number of individual RCTs in hospital patients showed significant improvements in functional measures with ONS compared with a control group, such as:[2]
  - ~ improved ventilatory capacity in patients with COPD;
  - ~ improved functional benefits, including increased activity (assessed using Norton scores) and activities of daily living (ADL) levels in older people;
  - ~ retention of skeletal (hand-grip) muscle strength and improved physical and mental health/QOL in surgical patients.
- In post-stroke patients admitted to a stroke service in a rehabilitation hospital and allocated to receive intensive ONS (higher energy, protein and vitamin C content) compared with standard ONS, significant improvements in functional and mobility measures were observed in the intensive ONS group (Functional Independence Measure [FIM] total score [31.49 intensive vs 22.94 standard, $p < 0.001$], FIM motor sub-score [24.25 vs 16.71, $p < 0.001$], 2-minute walk [101.60 vs 43.98, $p < 0.001$], and 6-minute walk [299.28 vs 170.59, $p < 0.001$]).[43]

ONS lead to functional benefits in adult patients in the community

- The comprehensive review undertaken by Stratton et al. (2003) showed that in individual randomised controlled studies, ONS led to significant improvements in functional parameters compared with controls in patients in the community, such as:[2]
  - ~ improved respiratory muscle function, hand-grip strength and walking distances in patients with COPD;
  - ~ increased ADL levels and reduced number of falls in older people.

ONS lead to significant functional benefits, particularly in older people in the community

- Significant functional improvements have been reported in patients receiving ONS in a number of trials, particularly in older people in the community (see Table A2.1, Appendix 2).
- In studies where older patients were given high-protein ONS, improvements in hand-grip strength, objective measures of physical activity, depressive symptoms and QOL, particularly in physical scales, have been reported compared with controls.[30;44;45]
- Supplementation with ONS for between 6 and 16 weeks has shown positive effects on functional outcomes (patients receiving supplements for 6 weeks commenced ONS in hospital and continued after discharge).[44; 45]
- Improvement in Katz ADL levels was observed in older patients at risk of malnutrition randomised to receive ONS and dietary counselling on discharge from hospital for 4 months in treated-as-protocol analysis ($p < 0.001$; $p < 0.05$ between groups) (see Figure 3.14).[29]
- Milne et al. (2009) reported that meta-analysis of measures of functional status was not possible as the measures reported in trials were often disease-specific and too diverse to integrate for analysis.[11] Some studies were not included in the review by Milne et al. (2009) as they appear to have been published after the point at which searches were completed, e.g. Norman et al. (2008) and Gariballa et al. (2007) (functional outcomes of these studies are therefore summarised above or in Table A2.1, Appendix 2).[23;44;45]

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- A systematic review and meta-analysis of 12 studies assessing the effect of ONS in older adults with dementia showed a significant improvement in cognition (measured by mini mental state examination, (p= 0.002)) at 6.5 ± 3.9 month follow-up when ONS were given compared to the control group (usual care in 8 studies, placebo drink/supplement in 4 studies).[14] There was no statistically significant difference between the control groups and the intervention (ONS) groups for functional ability (ADL) in the 3 studies that measured this outcome for 3[18; 34] or 6 months.[46] It is possible that follow up of a much larger group for a longer period of time would be necessary to see any significant reductions in the deterioration rates for performance of ADL especially as subjects only received ONS for 3 months in 2 studies and 5 months in another and only followed up for up to 6 months.[14]
- Edington et al. (2004) reported a significant improvement in hand-grip strength during supplementation of older malnourished patients in the community, but this was not sustained after supplementation was stopped. Furthermore, positive effects on QOL were not seen, although mobility scores were better in the ONS group than in the controls. The authors concluded that in a group of already malnourished subjects, who have many serious underlying disorders, it may be too late to expect to see improvements in functional or QOL parameters simply by providing a short course (8 weeks) of ONS, and that supplementation for a longer period may possibly have a more profound effect.[47]

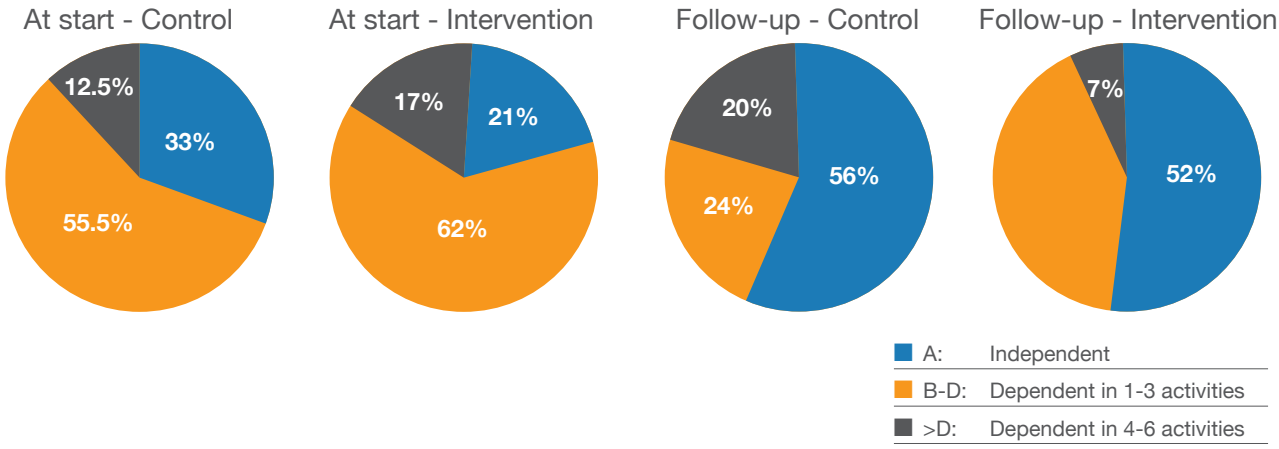

Figure 3.14 **Activities of daily life (ADL) registered by the Katz Index at the start and after 4 months of intervention** (adapted from Persson et al. 2007)[29]

Activities included: bathing, dressing, toilet, transfer, continence and feeding

- Malnourished older people with a variety of conditions randomised to receive ONS post hospital discharge had a significant decrease in functional limitations (mean difference -0.72, 95% CI -1.15 to -0.28) with no difference in costs compared with patients who received usual care.[48]

Emerging data demonstrates that ONS can improve QOL in care home residents

- QOL (adjusted for baseline QOL, malnutrition risk, type of care received [nursing or residential]) was found to be significantly higher in care home patients managed with ONS rather than dietary advice (intention to treat analysis at week 12 weeks; n = 104). EQ-5D TTO scores (mean ± SE) were 0.50 ± 0.04 vs 0.36 ± 0.05 (p < 0.005), representing a 39% improvement in HRQOL (UK).[20]

- Intervention with low-volume, energy and nutrient-dense ONS in malnourished or at risk of malnutrition nursing home residents (n = 77; 87±6 years, 91% female) increased positive self-perception (1 of 10 QOL categories) (Germany).[49]

High-protein ONS can improve hand-grip strength in older community patients

- A systematic review and meta-analysis of 4 RCTs in community patients with COPD, GI disease and hip fracture found that multi-nutrient, high-protein ONS can significantly improve hand-grip strength compared with the controls (1.76kg [95% CI 0.36–3.17], n = 219, p = 0.014 random effects model).[6]

ONS in combination with exercise training can improve muscle strength in older people

- Improvements in muscle strength and muscle power have been observed among frail older people in the community and in long-term care settings who received resistance training/ physical exercise in conjunction with ONS.[50;51]

3.1.3 Clinical benefits of ONS

3.1.3.1 MORTALITY

Meta-analyses consistently show a reduction in mortality in patients given ONS versus standard care

- Stratton et al. (2003) found that in hospital patients, mortality rates were significantly lower in supplemented (19%) than control (25%) patients (see Figure 3.15) (older people, liver disease, surgery and orthopaedics, $p < 0.001$; OR 0.61 [95% CI 0.48–0.78], meta-analysis of 11 trials, $n = 1965$; no significant heterogeneity between individual studies).[2] This represented a 24% reduction in mortality.

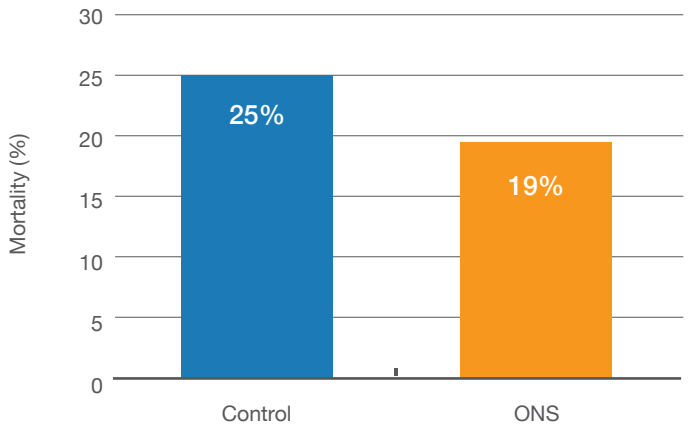

Figure 3.15 **Lower mortality in supplemented versus control patients** (adapted from Stratton et al. 2003)[2]

- The reduction in mortality with ONS tended to be greater in patient groups in which the average BMI was < 20 kg/m^2 than in those with a BMI > 20 kg/m^2.[2]
- Meta-analysis as part of a comprehensive systematic review of the cost and cost-effectiveness of using standard ONS in the hospital setting showed a 1 in 3 reduction in deaths in patients given ONS versus controls (35% reduction in mortality). (see Figure 3.16)[1]
- Meta-analysis by NICE (2006) of RCTs of ONS versus standard care in malnourished patients across healthcare settings and diagnoses demonstrated a statistically significant reduction in mortality (25 studies, relative risk [RR] 0.82; 95% CI 0.69–0.98) (see Figure 3.17)[22]

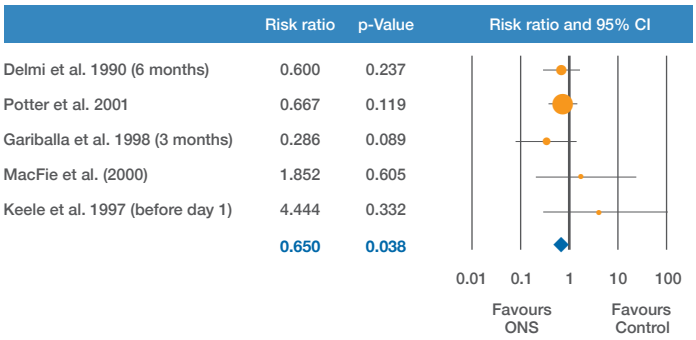

Figure 3.16 **Random effects meta-analysis of mortality reported in hospital studies with economic outcomes.** (Adapted from Elia et al. 2016)[1]

(Risk ratio 0.650 [95% CI 0.432, 0.976], $p = 0.038$; $I^2 = 0\%$, $p = 0.459$). The studies that reported mortality at 3 months and 6 months are indicated according to originally designated group

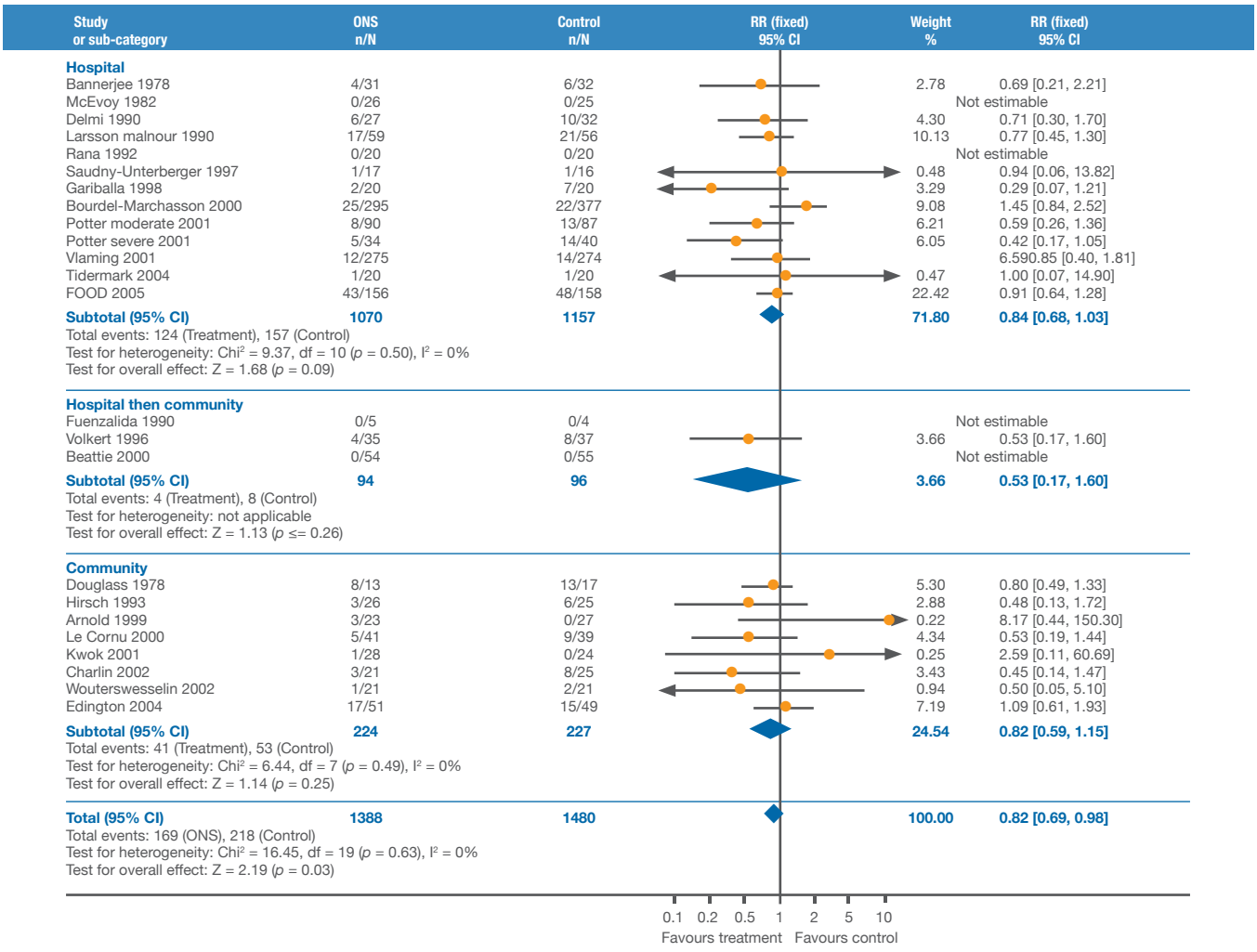

Figure 3.17 **ONS vs standard care (all patients): mortality by setting** (adapted from NICE 2006)[22]

High protein ONS can lead to a reduction in mortality in hospital patients

- A high-protein oral nutritional supplement containing beta-hydroxy-beta-methylbutyrate (HP-HMB) was shown to reduce 90 day mortality by 50% compared to placebo in a multi-centre RCT (4.8% vs. 9.7%; relative risk 0.49, [95% CI 0.27 to 0.90]; $p = 0.018$) in older, malnourished adults (≥ 65years, $n = 652$) hospitalised for congestive heart failure, acute myocardial infarction, pneumonia, or chronic obstructive pulmonary disease. Supplementation was started in hospital and continued in the community.[52]

Meta-analyses show a reduction in mortality in undernourished older patients given ONS

- A Cochrane systematic review (Avenell et al. 2006) of intervention with ONS among older hip fracture patients showed that significantly fewer patients had unfavourable outcomes (combined outcome of mortality and survivors with medical complications) with ONS versus routine care (RR 0.52; 95% CI 0.32–0.84).[53] A recent update of this review no longer shows a significant effect (original review intervention group $n = 66$ and control group $n = 73$, updated review intervention group $n = 126$ and control group $n = 103$).[54] The update includes 1 new study, i.e. a study of ONS in normally nourished or mildly malnourished older patients where malnourished individuals were excluded.[55]
- A Cochrane systematic review completed by Milne et al. in 2005 of protein and energy supplementation in older people reported that nutritional supplementation was associated with a statistically significant reduction in mortality (32 trials, $n = 3021$; RR 0.74; 95% CI 0.59–0.92). In subgroup analysis in this report, improved survival with ONS was observed in undernourished patients (21 trials, $n = 1825$; RR 0.72; 95% CI 0.55–0.94), when people were aged ≥ 75 years of age (24 trials, $n = 2033$; RR 0.69; 95% CI 0.54–0.87), when participants were not well (28 trials, $n = 2628$; RR 0.73; 95% CI 0.59–0.92), and when they were offered ≥ 400 kcal/d as ONS (19 trials, $n = 2177$; RR 0.71; 95% CI 0.56–0.90).[56]
- The reduction in mortality with ONS was borderline statistically significant in an update of this meta-analysis in 2006 (25 trials, $n = 6852$, OR 0.86; CI 0.74–1.00)[57] and not significant in a further update in 2009 (42 trials, $n = 8031$, RR 0.92; 95% CI 0.81–1.04).[11] The updates included the Feed Or Ordinary Diet (FOOD) trial, which contributed 4,023 patients of whom only 8% were classified as malnourished at baseline. As most patients were well-nourished, it has been suggested that the wrong patient group was selected for nutritional support.[58] The results of the FOOD trial suggested that routine use of ONS in well-nourished stroke patients is unlikely to be useful; however, the potential benefit of ONS in malnourished patients was not investigated in this trial.[59] The patients most likely to benefit from nutritional support, i.e. severely malnourished patients, are often excluded from trials in nutritional support, as withholding treatment may be unethical.[60]
- The 2009 updated Cochrane review by Milne et al.[11] also included Gariballa et al. (2006), where the number of deaths reported at 6 months was higher in the supplemented group (32/223; 14%) compared with the placebo group (19/222; 9%), but this was not significant ($p = 0.6$).[33] Twelve of the deaths in the supplemented group and 7 in the placebo group occurred within the first 6 weeks of randomisation, and 15 of the patients who died in the supplemented group consumed 3 or less of the total number of ONS prescribed.[33] This may reflect the nature of the study group, i.e. acutely ill older patients.
- However, subgroup analyses in all 3 meta-analyses by Milne et al. (2005, 2006 & 2009) have consistently shown a statistically significant reduction in mortality in undernourished patients receiving ONS compared to routine care (21 trials, $n = 1825$, RR 0.72; 95% CI 0.55–0.94;[56; 61] 17 trials, $n = 2093$, OR 0.73; CI 0.56–0.94;[57] 25 trials, $n = 2466$, RR 0.79; 95% CI 0.64–0.97[11]). Furthermore, an improvement in survival was also consistently shown in all three meta-analyses when patients were offered ≥ 400 kcal/d as ONS (19 trials, $n = 2177$, RR 0.71; 95% CI 0.56–0.90;[56] 15 trials, $n = 6157$, OR 0.85; CI 0.73–0.99;[57] 24 trials, $n = 7307$, RR 0.89; 95% CI 0.78–1.00[11]).

- Significantly lower mortality was found in older undernourished medical patients who were randomised to receive individualised treatment in hospital and the community, which included ONS (Group 1) (3.8%), than in patients who received individualised treatment (including ONS) in hospital only (Group 2) or standard hospital care (Group 3) (11.8%, $p = 0.046$).[62]

3.1.3.2 COMPLICATIONS (INCLUDING DEVELOPMENT OF PRESSURE ULCERS)

Meta-analyses show a reduction in a variety of complications in patients given ONS compared with standard care

- Stratton et al. (2003) showed that complication rates (infective and others such as GI perforation, pressure ulcers, anaemia, cardiac complications) were significantly lower in supplemented (18%) than in unsupplemented (41%) **hospital patients** (see Figure 3.18) (surgical, orthopaedic, older people, neurology, $p < 0.001$; OR 0.31; 95% CI 0.17–0.56, meta-analysis of 7 trials, $n = 384$; no significant heterogeneity between studies).[2] This represented a 56% reduction.

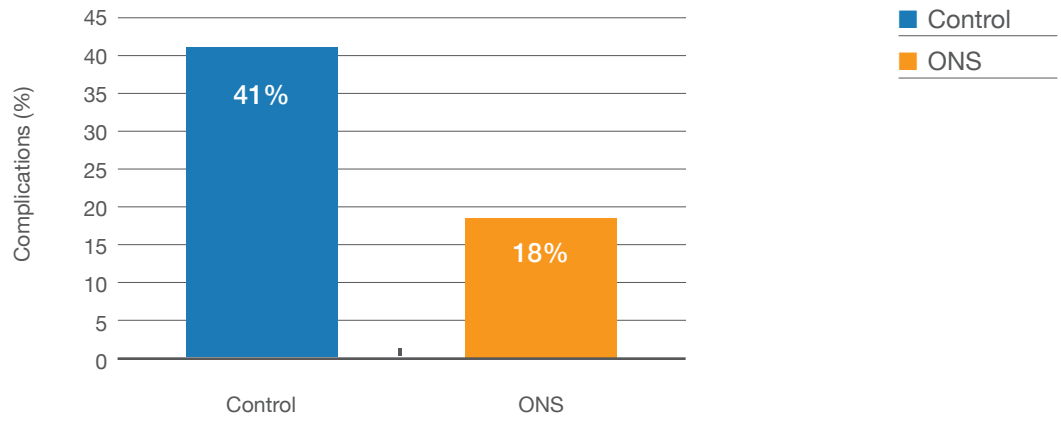

Figure 3.18 **Lower complication rates in supplemented vs control patients in hospital** (adapted from Stratton et al. 2003)[2]

- Complication rates were reduced by >50% in patients managed with ONS independent of BMI (with a BMI < 20 kg/m^2 [3 trials, 12% vs 27%; OR 0.38; 95% CI 0.07–1.97] and > 20 kg/m^2 [1 trial, 12% vs 27%]) or when BMI was unknown (3 trials, 38% vs 75%, OR 0.21; 95% CI 0.04–1.18).[2]
- NICE (2006) similarly found a significant reduction in complications in **hospital patients** given ONS versus standard care (9 trials, RR 0.75; CI 0.64–0.88) (see Figure 3.19).[22]
- Meta-analysis by Milne et al. (2009) showed a reduction in complications in **older people** treated with ONS compared to routine care (24 trials, $n = 6225$, RR 0.86; 95% CI 0.75–0.99) and in a subgroup analysis of patients with **hip fracture** (6 trials, $n = 298$, RR 0.60; 95% CI 0.40–0.91) but not in other patient subgroups (variety of hospital and community settings) (see Figure 3.20).[11]

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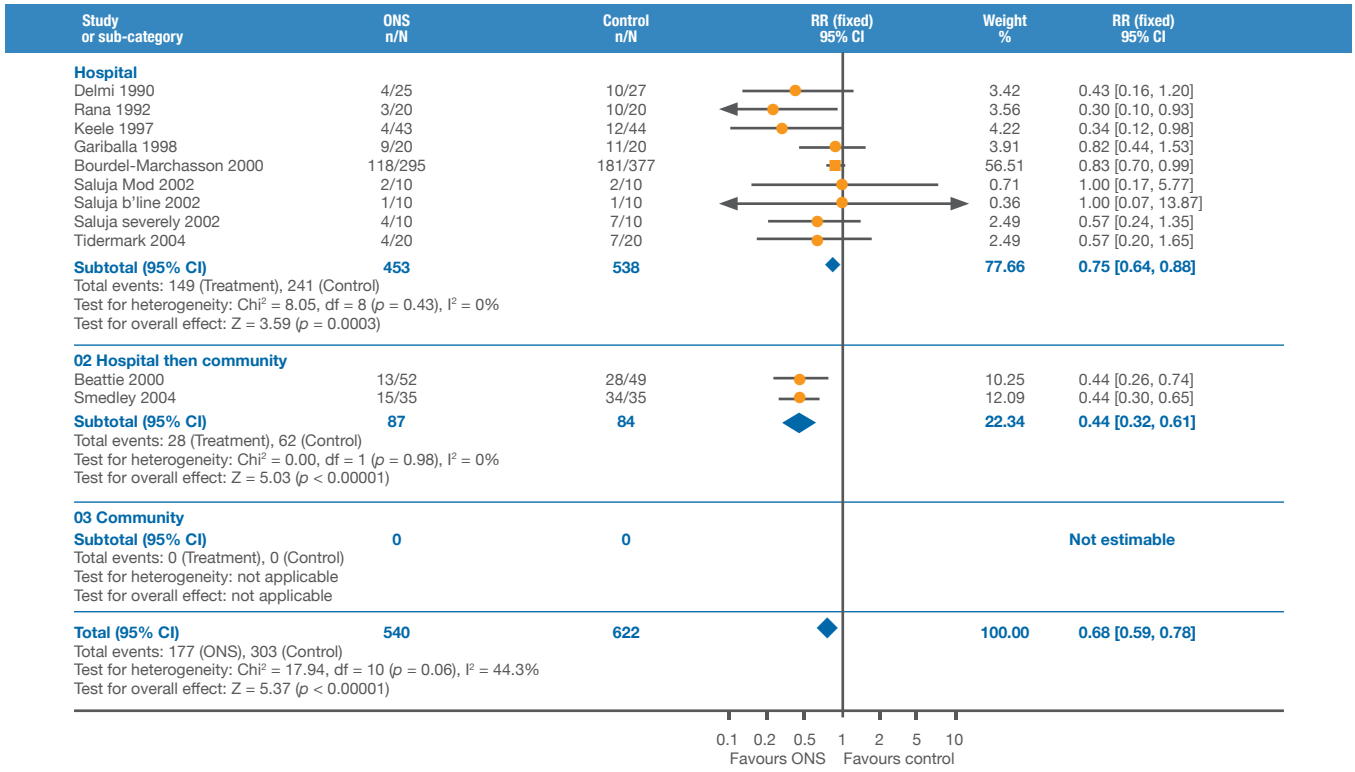

Figure 3.19 **ONS versus standard care (all patients): complications by setting** (adapted from NICE 2006)[22]

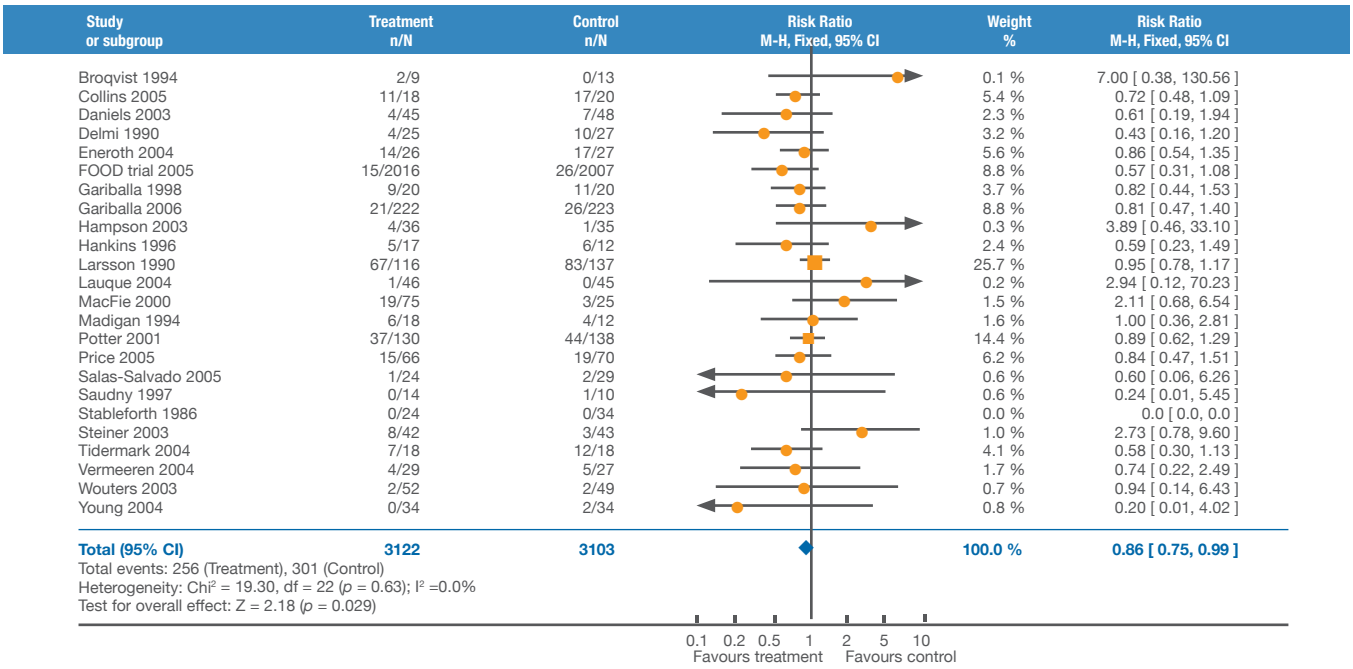

Figure 3.20 **ONS vs routine care in older patients (variety of settings): complications** (adapted from Milne et al. 2009)[11]

- The effectiveness of interventions for the treatment of dysphagia and nutritional and fluid supplementation in **stroke patients** was evaluated in a systematic review including 33 studies, eight of which assessed the effect of nutritional supplementation. ONS was associated with reduced pressure sores (2 trials; n = 4125; OR 0.56; 95% CI 0.32 to 0.96; p = 0.03; I^2 = 0%) compared to no supplementation.[13] Note that the majority of patients in the review were from the FOOD trial, only 8% of whom were malnourished.

- A systematic review evaluating the effect of pre-operative nutritional support in elective **GI surgical patients** reviewed 13 studies of which 3 evaluated standard ONS. The results from these 3 studies combined showed no difference in the clinical outcomes (total complications [n = 263], infectious complications [n = 250]) or length of stay between standard ONS vs. no nutrition[63] even though one of the studies did find significantly less post-operative weight loss in the ONS vs. no nutrition group ($p < 0.05$) and fewer minor complications ($p < 0.05$)[64].The review did not appear to take into account the variation in duration of supplementation prior to surgery (5-59 days in Macfie et al. 2000;[65] 10-252 days in Burden et al. 2011[66] and 7-61 days in Smedley et al. 2004[64])or analyse the effect of patients' nutritional status. The review authors note that the majority of participants included in the trials reviewed were well nourished and highlight that "..participants who would be most likely to benefit from nutritional support were not included..".[63]
- A subgroup analysis in Burden et al. 2011 (unblinded RCT) showed a significant reduction in surgical site infections (Buzby criteria) in weight-losing patients admitted to hospital for elective curative **surgery for colorectal cancer** who received high-protein ONS preoperatively (p = 0.034) compared with patients who received dietary advice.[66]
- Meta-analysis as part of a large comprehensive systematic review of the cost and cost-effectiveness of using standard ONS in the hospital setting showed a 1 in 3 reduction in complications in **surgical patients** given ONS versus controls (35% reduction in complications) (see Figure 3.21).[1]

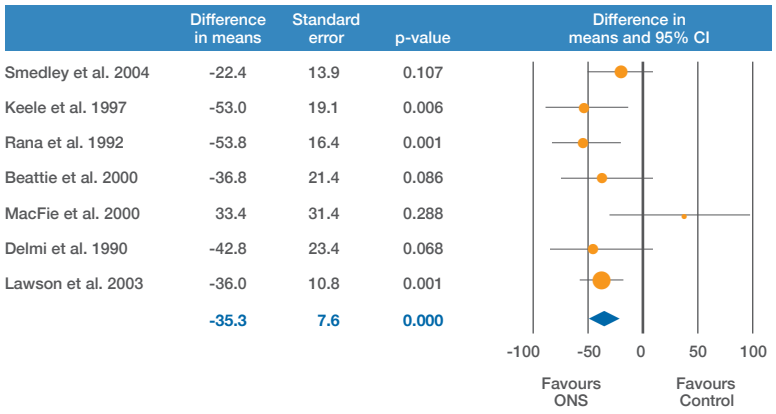

Figure 3.21 **Random effects meta-analysis of complications in surgical patients expressed as percentage of total complications.** (Adapted from Elia et al. 2016)[1]

A negative sign indicates fewer complications in the ONS group (difference -35.3 [se 7.6]%, $p < 0.001$; I^2 = 23.9%, p = 0.247).

- The total complication rate was found to be significantly lower in hospitalised **hip fracture patients** (aged >65 years) supplemented with ONS according to measured energy requirements/intake vs. a control group who received a normal diet and ONS if already prescribed (27.3% vs. 64.3%, p = 0.012). This was mainly due to a 73% reduction in the number of infectious complications in the intervention group (13.6% vs. 50%, p = 0.008).[9]

ONS reduce complications in patients who start ONS in hospital and continue in the community

- The meta-analysis undertaken by NICE (2006) showed fewer complications in patients who started on ONS in the hospital setting and then continued in the community (2 trials, RR 0.44, CI 0.32–0.61).[22]
- In **GI surgical patients** undergoing a variety of procedures, a significant reduction in complication rates was seen in patients receiving ONS (250–600 kcal/d for 7 days to 10 weeks, 6 trials, OR 0.37, CI 0.23–0.60).[67]
- A systematic review of post-discharge supplementation with ONS in patients undergoing **GI surgery** highlighted the lack of available data specifically on the post-discharge period; nevertheless, it concluded that it would be sensible to offer nutritional support to malnourished patients at high risk of poor nutritional intake post discharge.[68]

High protein supplements may be of special interest in reducing clinical complications

- A Cochrane systematic review (Avenell and Handoll 2010) of intervention with ONS among **older hip fracture patients** concluded that protein-enriched ONS (> 20% total energy from protein) reduce the number of long-term medical complications (RR 0.78; 95% CI 0.65–0.95).[70]
- Specifically, high protein ONS have been shown to significantly reduce the incidence of complications in hospital and community settings in patients with **hip fracture, leg and pressure ulcers and acutely ill patients** compared with controls (10 RCTs, $n = 1830$; OR 0.68, 95% CI 0.55–0.83, $p < 0.001$), corresponding to an average of 19% absolute reduction in complications (see Figure 3.22). The effect remained significant in subgroup analyses by setting (hospital: 3 RCTs, $n = 932$; OR 0.69, 95% CI 0.53–0.89, $p = 0.005$; community: 7 RCTs [4 starting in hospital], $n = 846$; OR 0.66, 95% CI 0.47–0.93, $p = 0.017$).[6]

Study	Setting	Odds ratio	Lower limit	Upper limit	z-Value	p-Value	Comp/Total ONS	Comp/Total Control
Botella-Carretero et al. 2008	Hospital-Community	1.308	0.473	3.615	0.517	0.605	17/30	15/30
Bourdel-Marchasson et al. 2000	Hospital	0.722	0.530	0.983	-2.071	0.038	119/295	181/377
Delmi et al. 1990	Hospital-Community	0.383	0.104	1.402	-1.450	0.147	4/27	10/32
Eneroth et al. 2004	Community	0.686	0.229	2.057	-0.672	0.501	14/26	17/27
Espaulella et al. 2000	Hospital-Community	0.515	0.269	0.985	-2.006	0.045	44/80	57/81
Gariballa et al. 2006	Hospital-Community	0.792	0.431	1.454	-0.754	0.451	21/222	26/223
Houwing et al. 2003	Hospital	0.825	0.379	1.796	-0.485	0.628	27/51	30/52
Olofsson et al. 2007	Hospital	0.482	0.252	0.921	-2.210	0.027	27/83	37/74
Otte et al. 1989	Community	0.825	0.147	4.628	-0.219	0.827	3/13	4/15
Tidermark et al. 2004	Community	0.359	0.100	1.294	-1.566	0.117	7/20	12/20
		0.676	**0.548**	**0.832**	**-3.683**	**0.000**	**282/847**	**389/931**

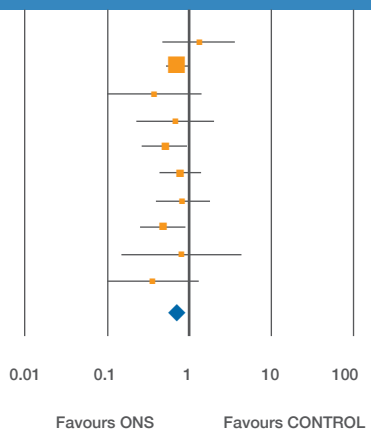

Figure 3.22 **Significantly lower rate of complications with high-protein ONS compared with controls** (adapted from Cawood et al. 2012)[6]

High protein ONS are of particular interest in the prevention of development of pressure ulcers

- Pressure ulcers affect 10% of people in hospitals, and older malnourished people are at highest risk. Older people recovering from illness appear to develop fewer pressure ulcers when given 2 high-protein ONS daily.[70]
- Meta-analysis of studies using high-protein ONS showed a significant reduction in the risk of developing pressure ulcers in high-risk patient groups (by 25%) (4 trials, *n* = 1224, OR 0.75; 95% CI 0.62–0.89) (see Figure 3.23).[71]

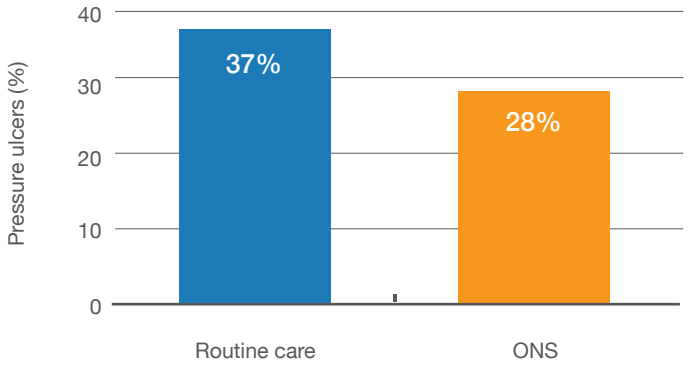

Figure 3.23 **Prevention of pressure ulcers in at risk patients with ONS (hospital and long-term care): summary of results from a meta-analysis** (adapted from Stratton et al. 2005)[71]

Clinical benefits of ONS in children

Complications

- A multi-centre randomised parallel open study of nutritional counselling with or without ONS in children with growth faltering (mean age 48.5 months, range 36.0–61.0 months; *n* = 92) and picky eating behaviour not related to an underlying medical condition showed a significantly lower percentage of upper respiratory tract infections in the study group versus the controls (28% vs 51%, *p* = 0.027).[35]

Other

- In a prospective randomised study in children with malignant disease undergoing intensive chemotherapy (*n* = 52, mean age 7.5±3.0 years), the remission rate was significantly higher in the group supplemented with protein- and energy-dense ONS (enriched with EPA) compared with the group who received usual care (87.9% vs 63.2%; *p* = 0.036).[42]

Nutritional intervention with ONS can improve energy intake and reduce weight loss in cancer patients

- Stratton et al. (2003) reviewed the effect of ONS in patients with cancer and found that ONS may improve total energy intake and food intake but that these improvements may not be sustained over time. Significant improvements in total energy intake were seen in 2 out of 3 RCTs.[2]
- Regular nutrition intervention (dietary counselling with ONS) has been demonstrated to improve nutrient intake and nutritional status during radiotherapy in patients with oesophageal and head and neck cancers in various stages.[72]
- A systematic review with meta-analysis of patients with cancers in various locations and of various grades undergoing radiotherapy demonstrated that that ONS significantly increased dietary intake by an average of 381 kcal/d (95% CI 193–569 kcal in 3 RCTs).[73]
- Patients admitted to hospital for elective curative surgery for colorectal cancer who received high-protein ONS had significantly higher total energy intake preoperatively compared with controls (who received dietary advice) (1722 [489] kcal/d vs 745 [366], $p = 0.001$).[66]
- A study investigating weight loss in patients with oropharyngeal cancers undergoing radiotherapy +/- chemotherapy demonstrated that **all groups receiving ONS alongside dietary counselling showed significantly less weight loss than those not receiving ONS**. In the radiotherapy group, a relative reduction in weight loss of 40% was seen versus routine care ($p = 0.008$), and in those undergoing radiotherapy, a 37% relative reduction was seen ($p = 0.007$).[74]

Nutritional intervention with ONS can improve QOL outcomes in malnourished patients with cancer

- Patients with GI or head and neck malignancies undergoing radiotherapy who received nutritional intervention comprising intensive counselling plus ONS versus usual care showed a significantly smaller decrease and faster recovery in global QOL ($p = 0.009$) and physical function ($p = 0.012$) over a 12-week period.[75]

Nutritional intervention with ONS may result in cost savings in patients with cancer

- Use of ONS alongside nutritional counselling in oropharyngeal patients undergoing radiotherapy was associated with decreased need for Percutaneous Endoscopic Gastrostomy (PEG) tube placement (reduced from 31% to 6%), demonstrating potential cost savings from reduction in tubes, placement costs and complications.[74]
- The majority of studies published include patients with cancers of the head and neck or GI tract. A systematic review of patients with head and neck squamous cell carcinoma receiving radiotherapy with or without chemotherapy was published in 2010. Within this review, 80% of the studies demonstrated reduced weight loss in those patients receiving nutritional counselling and ONS and support the use of ONS as an adjunct to counselling by a professional dietitian.[76]

Benefits of EPA-enriched ONS in cancer patients

- The role of EPA, a long-chain polyunsaturated fatty acid derived from fish oil, has been of increasing interest in the management of patients with cancer. EPA may modulate many aspects of the systemic inflammatory response associated with cancer cachexia.[73;77] It has also been associated with reducing and reversing weight loss in cancer patients and improvements in QOL.[78]
- In clinical practice, EPA has been supplemented as capsules and also in the form of EPA-enriched energy- and protein-dense ONS, which may work together to manage a reduced nutritional intake alongside the metabolic changes.[77]

Nutritional intervention with EPA-enriched ONS lead to improved nutritional intake and reduced weight change in cancer patients

- Supplementation with EPA-enriched ONS (versus isocaloric, isonitrogenous standard ONS) in non-surgical malnourished lung cancer patients resulted in significant improvements in energy and protein intakes after 4 weeks: 2456 kJ ($p = 0.03$) and 25.0 g ($p = 0.01$) respectively. Intervention resulted in better weight maintenance (by 1.7 kg, $p = 0.04$) after 4 weeks and a smaller reduction in LBM (1.9 kg, $p < 0.05$) after 5 weeks.[79]
- A post-hoc dose response analysis of intake of EPA-enriched ONS versus standard ONS in patients with advanced pancreatic cancer showed significant correlations between supplement intake and weight gain in the EPA group ($r = 0.5$, $p < 0.001$) and increase in LBM ($r = 0.33$, $p = 0.036$) that were not seen in the control group.[80]
- A prospective observational study supplementing patients undergoing surgical treatment for squamous cell cancers of the head and neck with EPA-enriched ONS perioperatively showed that 70% maintained or gained weight prior to surgery, with 57% continuing to maintain or gain weight during hospital admission. There was a statistically significant increase in LBM (+3.21 kg over course of the study ($p < 0.01$) in the study group.[81]
- In a small study of colorectal cancer patients receiving EPA-enriched ONS prior to and during chemotherapy, a significant weight increase in the 3 weeks prior to the start of chemotherapy (mean 2.5 kg, $p = 0.03$) was maintained during the subsequent 6 weeks of treatment.[82]

Where weight gain occurs, this is associated with better QOL outcomes

- Functional status and symptom scale domains of the European Organisation for Research and Treatment of Cancer Quality of life Questionnaire (EORTC QLQ-C30) were significantly improved after 30 days and 60 days in patients with lung cancer undergoing chemotherapy, who gained weight when receiving EPA-enriched ONS ($p = 0.05$).[83]
- Intake of EPA-enriched ONS and weight gain correlate positively with QOL measured by the EQ-5D index in pancreatic cancer patients ($r = 0.37$, $p = 0.01$ and $r = 0.46$, $p < 0.001$).[80]

3.1.4 Economic benefits of ONS

3.1.4.1 HEALTHCARE RESOURCES

ONS reduce length of hospital stay

- Meta-analysis by Stratton et al. (2003) showed that length of hospital stay in supplemented compared with control patients was reduced significantly in all 9 RCTs that presented results, either as means or medians (9/9 trials; two-tailed binomial test, $p < 0.004$). The average reductions ranged from 2 days (in surgical patients) to 33 days (in orthopaedic patients). Meta-analysis of 4 trials that recorded the mean of LOS in surgical and orthopaedic patients indicated that ONS were associated with reduced LOS relative to control patients (effect size -0.80 days [95% CI -1.24–0.36]).[2]
- The reduction in LOS appeared to be greater in patient groups with a BMI < 20 kg/m^2 than when BMI was > 20 kg/m^2.[2]
- Meta-analysis of 9 RCTs in hip fracture and acutely ill patients ($n = 1227$) (ONS given in hospital [1 RCT], in the community [1 RCT] and across hospital and community [7 RCTs]) showed a significant reduction in length of stay in patients who received oral nutritional intervention with high-protein ONS versus controls (-3.77 [95% CI -7.37–0.17] days, $p = 0.040$ random effects model).[6]
- In a comprehensive systematic review that aimed to examine the cost and cost-effectiveness of use of standard ONS in hospital patients, meta-analysis of five UK studies in surgical patients showed a reduction in length of hospital stay in studies where patients were given ONS vs. controls. Length of stay was reduced by 2 days corresponding to ~13% reduction. Of the 12 studies included in the review, 10 (83%) had a mean or median length of stay shorter in the ONS group compared to controls (p =0.039, binomial test).[1]

Meta-analyses consistently show that ONS reduce hospitalization

- A series of meta-analyses (using 10 datasets from 8 publications) in a comprehensive systematic review of the cost and cost-effectiveness of using standard ONS in community and care home settings demonstrated that standard ONS significantly reduce hospitalization:[84]
  - ~ by 16.5% in meta-analysis of 9 datasets from full text papers only ([se 4.0], $p = 0.001$; $n = 1051$ subjects; $I^2 = 16\%$, $p = 0.307$) (see Figure 3.24);
  - ~ by 20% in meta-analysis of longer term studies of ≥ 3 months of ONS supplementation (point estimate 20.3% [se 6.4%], $p = 0.001$; 6 datasets, $n = 747$ subjects; $I^2 = 26\%$, $p = 0.239$);
  - ~ by 12.9% in meta-analysis of only short-term (<3 months of ONS supplementation) surgical studies ([se 4.9%], $p = 0.008$; 4 datasets, $n = 383$; $I^2 = 0\%$, $p = 0.716$);
  - ~ by 14.9% when only the surgical studies involving pre-operative ONS administration in the community component were considered ([se 5.4%], $p = 0.007$; 5 datasets, $n = 304$); $I^2 = 0\%$, $p = 0.694$).

- In an earlier systematic review and meta-analysis of the impact of oral nutritional supplements on hospital readmissions by Stratton et al. 2013, a meta-analysis of 6 RCT that reported the number of patients (re)admitted to hospital (n = 857) showed that the proportion of patients readmitted to hospital was significantly less in the ONS group than in the control group (23.9% vs. 33.8% respectively (OR 0.591, 95% CI 0.434-0.804, p = 0.001)[85] (see Figure 3.25).
- In the same report a meta-analysis of all the RCT reporting (re)admissions to hospital (8 RCT, n = 999) also showed that the proportion of patients (re)admitted to hospital was significantly less (23% less) in the ONS group than in the control group (standardized difference -0.230, 95% CI -0.363 to -0.097, p = 0.001)[85] (see Figure 3.26).

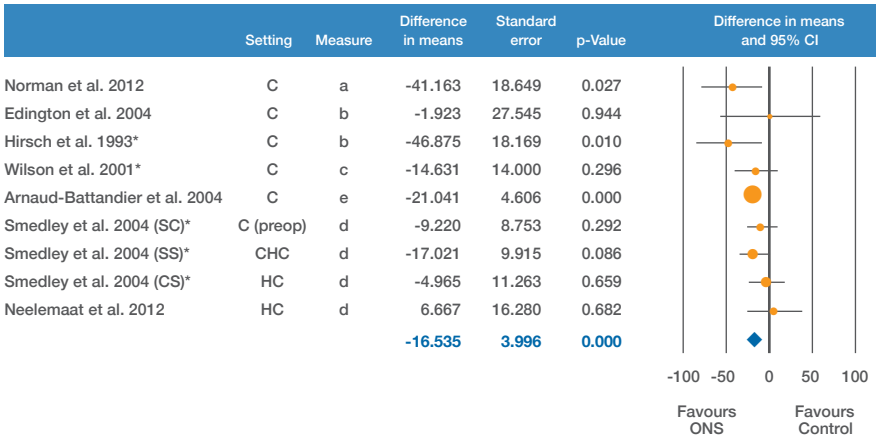

Figure 3.24 **Meta-analysis of hospitalisation in the ONS and comparison (control) groups based on RCTs.** (Adapted from Elia et al. 2016)[84]

The results expressed as a percentage of control group (negative values indicate a cost saving in favour of the ONS group); C = community; CHC = community followed by hospital and in the community again after discharge from hospital; HC = hospital followed by the community; C (pre-op) = preoperatively although it may have been continued for a short period in hospital before surgery). a = proportion of patients admitted; b = n admission/patient; c = proportion of study period spent in hospital; d = bed-days/patient. *Calculated using data presented in the BAPEN report.

Figure 3.25 **Random effects meta-analysis of RCT reporting number of patients (re)admitted to hospital with ONS.** (6 RCT, n = 852) (Adapted from Stratton et al 2013)[85]

Figure 3.26 **Random effects meta-analysis of all RCT reporting (re)admissions to hospital with ONS.** (8 RCT, *n* = 999) (adapted from Stratton et al. 2013)[85]

- Meta-analysis of 2 RCTs in acutely ill patients with a wide variety of conditions and in GI disease patients (*n* = 546) (ONS given in hospital and community in 1 trial and in the community in the other trial) showed that oral nutritional intervention with high-protein ONS had a significant effect on reduction of hospital readmissions compared with controls (OR 0.59 [95% CI 0.41–0.84] days, *p* = 0.004 random effects model) (see Figure 3.27).[6] High-protein ONS reduced overall readmissions by 30% (number of readmissions in the control group used as a reference).[6]

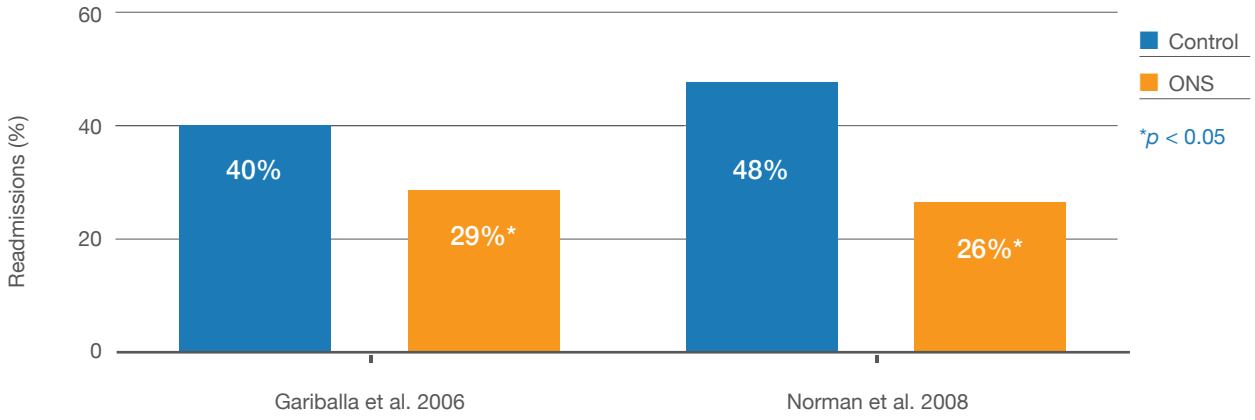

Figure 3.27 **Significant reductions in readmissions with high protein ONS** (adapted from Cawood et al. 2012)[6]

ONS can improve rehabilitation outcome

- In undernourished patients admitted to a stroke service, those randomised to receive an intensive (higher energy, protein and vitamin C content) supplement (*n* = 51) were more likely to be discharged home (63%) compared with those (*n* = 51) given standard ONS (43%) (*p* < 0.05) (34% reduction in discharges to institutional settings).[43]
- A study in older patients with hip fracture investigating the effects of hospital meals plus ONS vs hospital meals (both groups also received usual rehabilitation therapy, oral calcium and vitamin D supplements) for 4 weeks found that patients in the intervention group had a significantly lower length of stay in rehabilitation (mean [SD] 26.2 days [8.2] vs. 29.9 days [11.2]; *p* = 0.04) than the control group.[86]

3.1.4.2 COST SAVINGS AND COST EFFECTIVENESS

ONS can reduce the cost of overall hospital care by 12% (vs routine care)

- In a comprehensive systematic review of the cost and cost-effectiveness of using ONS in the hospital setting twelve studies were found to produce a net cost saving favouring the ONS group by an average (mean) of 12.2% (calculation of costs were based on bed-day costs). Twelve out of fourteen (86%) studies favoured the ONS group (see Table 3.2). Results of subgroup analyses according to age, nutritional status, type of intervention and type of analysis universally favoured the ONS group, although the numbers of studies was small.[1]

Table 3.2 **Post hoc analyses of hospital studies comparing ONS with no ONS or routine care.** (Adapted from Elia et al. 2016)[1]

Study	Country	N	Nutritional Status	Age group (years)	Type of study	Comparison	Cost saving per subject in favour of ONS group	Cost saving (% of control)
BAPEN report 2005								
i Rana et al. 1992	UK	40	M + NM	<65	I	ONS v no ONS	£1249.4	20.71
ii Keele et al. 1997	UK	86	M + NM	<65	I	ONS v no ONS	£896.7	18.1
iii Smedley et al. 2004	UK	89	M + NM	<65	I	ONS v no ONS	£260.7	4.93
iv MacFie et al. 2000	UK	62	M + NM	<65	I	ONS v no ONS	£1125.8	23.04
v Beattie et al. 2000	UK	101	M	<65	I	ONS v routine care	£830.6	10.59
vi Delmi et al. 1990	CH	59	M	≥65	I	ONS v no ONS	£4491.2	39.94
vii Lawson et al. 2003	UK	181	M + NM	≥65	I	ONS v no ONS	£444.9	9.92
viii Potter et al. 2001	UK	381	M + NM	≥65	I	ONS v routine care	£330.4	10.8
ix Gazzotti et al. 2003	BE	60	M	≥65	I	ONS v no ONS	-£246.4	-7.32
x Gariballa et al. 1998	UK	40	M	≥65	I	ONS v no ONS	£2090.8	42.73
xi Vlaming et al. 2001	UK	281	M	≥65	I	ONS v no ONS	-£1306.3	-49.29
Banks et al. 2013	AU	1356	M	≥65	I + O	ONS v no ONS	€143.6 (£93.25)	
Philipson et al. 2013	US	1160088		≥65	O	ONS v no ONS	$4734.0 (£3148)	21.6
NICE 2012	UK	1410440	M	≥65	I + O	ONS v no ONS		

86% of the cost analyses favoured the ONS group*

12.2%†

*12 of 14 cost analyses comparing ONS with no ONS or routine care. †Based on twelve studies with quantitative data.
UK = United Kingdom; CH = Switzerland; BE = Belgium; AU = Australia; US = United States; M = malnourished; NM = non-malnourished; I = interventional study; O = observational study.

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- A meta-analysis of 5 studies in abdominal surgical patients (n = 368) showed a mean cost saving of £746 or 13.5% with ONS versus standard care. This is based on 2003 prices. Following adjustment for inflation, using specific healthcare inflation rates, the savings in 2015 could be as high as £1,014 (or €1,415) (see Figure 3.28).[1] [ii]

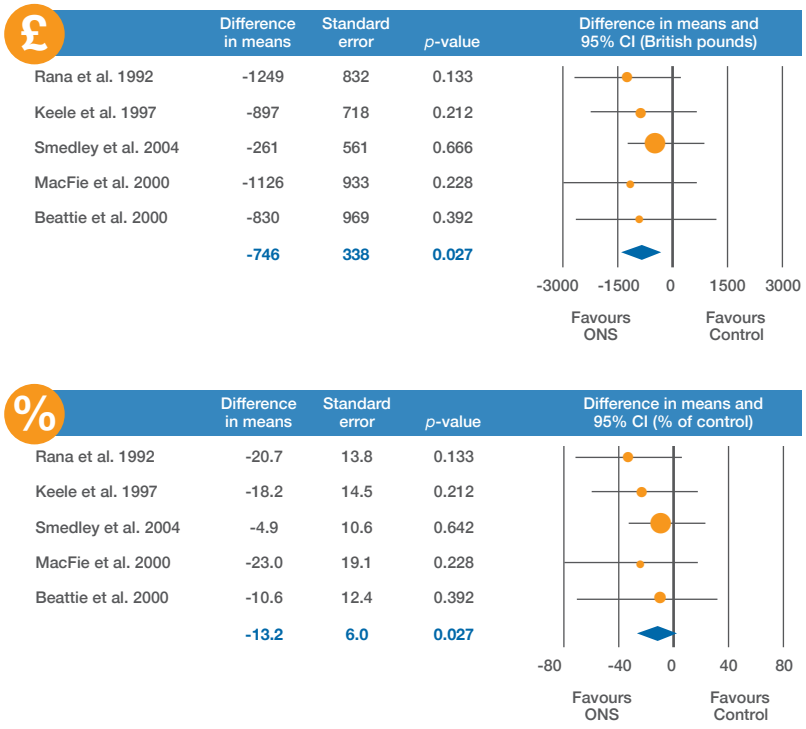

Figure 3.28 **Meta-analysis (with inverse variance weighting) of net cost saving of five randomised controlled trials of abdominal surgery in the UK (n = 358).** (Adapted from Elia et al. 2016)[1]

Upper graph results are presented in GBP (£) (2003 prices) (mean cost saving £746/patient [se £338], p = 0.027; I^2 = 0%) Lower graph results presented as percent reduction of control group (mean cost saving 13.2% [se 6.0%], p = 0.027; I^2 = 0%). Negative signs indicate cost saving * based on retrospective data analysis as provided in the BAPEN report.

- Lassen et al. (2006) performed a cost analysis that estimated the potential savings achieved by reducing the number of medical inpatient days through appropriate use of ONS. The analysis considered an average €197[iii] (USD 226 per day [1997 values]) cost reduction for each day less spent in hospital. The results of the analysis indicated that with appropriate use of ONS, there is a potential for hospitals in Denmark to realise cost savings of approximately €19.2 million[iii] (USD 22 million) in the period of a year.[87]
- A retrospective cost analysis was undertaken by Stratton et al. (2003) of 9 RCTs (with and without use of ONS). This simple analysis demonstrated mean cost savings of between €396[iv] (£352) and €9,197[iv] (£8,179) per patient in surgical, orthopaedic, elderly and cerebrovascular accident patients.[2]

[ii]GBP (£) (2003 prices) se £346, p = 0.026; I^2 = 0%. **se 6.1%, p = 0.026; I^2 = 0%. Calculated based on Hospital and Community Health Services (HCHS) pay and prices inflation figures 2013-2014. Calculation for 2015 based on 2013-2014 figures. [iii]Calculated based on an exchange rate of 1 USD = 0.8712 EUR (Source: Interbank 12/07/2017). [iv]Calculated based on an exchange rate of 1 GBP = 1.1245 EUR (Source: Interbank 12/07/2017)

Use of ONS for <3 months in patients in the community leads to cost saving of 9.2%

- Elia et al. undertook a comprehensive review of the cost and cost-effectiveness of using standard ONS in community and care homes. To provide an overview of studies undertaken in different countries at different times using different currencies, the results were presented as percentage cost savings. Overall there was a significant cost saving (median 8.1%) in favour of the ONS group. When used for <3months the mean cost saving was 9.2% and when used for ≥3months there was a median cost saving of 5%. Abstracts were not included in the analysis above, but all favoured the ONS group (see Table 3.3).[84]

Table 3.3 **Retrospective cost-analyses of community studies comparing ONS with control groups[a]** (adapted from Elia et al.)[84]

Study[b]	N	Setting	Cost saving per subject in favour of ONS group[c]	Cost saving (% of control)[c]	Nutritional Status	Age group (years)	Type of study	Single-or multi-centre	Comparison	ONS use (months)
Smedley et al. 2004	85	C(pre-op)	£440.6[b]	9.2	M+NM	<65	I	Multi	ONS v no ONS	<3
MacFie et al. 2000	49	C(pre-op)	£330.1[b]	7.3	M+NM	≥65[d]	I	Single	ONS v no ONS	<3
Flynn et al. 1987	36	C(pre-op)	£1113.1[b]	13.7	M	<65	I	Single	ONS v no ONS	<3
Smedley et al. 2004	76	C(pre-op)H	£853.2[b]	16.2	M+NM	<65	I	Multi	ONS v no ONS	<3
MacFie et al. 2000	49	C(pre-op)H	£704.8[b]	14.4	M+NM	<65[d]	I	Single	ONS v no ONS	<3
Freijer & Nuijten 2010	Model	C(pre-op)H	€252.0[b]	7.6	M	<65	IO	Multi	ONS v no ONS	<3
Smedley et al. 2004	76	C(pre-op)HC (post op)	£788.5[b]	14.9	M+NM	<65	I	Multi	ONS v no ONS	<3
Beattie et al. 2000	101	HC(post-op)	£668.2[b]	8.5	M	<65	I	Single	Other[f]	<3
Smedley et al. 2000	79	HC(post-op)	£260.7[b]	4.9	M+NM	<65	I	Multi	ONS v no ONS	<3
Neelemaat et al. 2012	184	HC(post-discharge)	-€403.0	-4.9	M	≥65	I	Single	Other	≥3
Edington et al. 2004	100	C	-£1159.34[b]	-54.0	M	≥65	I	Multi	Other	≥3
Arnaud-Battandier et al. 1999	378	C	€195.0	7.2	M	≥65	O	Multi	Other	≥3
Nuijten & Mittendorf 2012	Model	C	€245.5	14.1	M	<65[e]	I	Multi	ONS v no ONS	≥3
Freijer et al. 2012	Model	C	€90.1	4.7	M	≥65	I	Multi	ONS v no ONS	≥3
Hirsch et al. 1993	51	C	-(loss)[b]	loss	M+NM	<65	I	Single	ONS v no ONS	≥3
Wilson et al. 2001	32	C	+(saving)[b]	saving	M	<65	I	Multi	Other	≥3

H = Hospital; C = Community; pre-op = pre-operative; post-op = post-operative. The sequence indicates the order in which ONS was administered (e.g. HC = hospital first and then community); M = malnourished; NM = non-malnourished; I = interventional; O = observational. [a]Only full text papers and analyses of full text papers in reports are included. [b]Details of the retrospective economic analyses can be found in the BAPEN report. [c]Positive values indicate that the net balance favours the ONS group (lower cost in the ONS group than the comparison group) and the negative sign, the comparison group (higher cost in the ONS group than the comparison group). [d]Based on average of the mean age of the groups involved. [e]Largely based on Norman et al. 2008[23]. [f]ONS v routine care (which may include use of some ONS).

- In the same review by Elia et al. (2016) examination of the RCTs that pre-planned to undertake cost analysis showed that ONS administration for between about 2 weeks and 3 months contributed to only 1-11% of the total treatment cost (mean of less than 5%) while hospitalisation contributed to 69 to >90% of costs.[84]
- A budget impact model was used to investigate the impact of using ONS to manage older people in the community in England at high risk of malnutrition ('MUST'). Pooled analysis of data showed reductions in pressure ulcers, infections, antibiotic prescriptions and hospital admissions (by 88%, 32%, 56% and 33% respectively) with oral nutritional intervention using ready-made ONS versus controls.The resulting reduction in costs (-€99 million[v] [-£88 million]) more than offset the total costs of using ONS in conjunction with monitoring by healthcare professionals (€94[v] [£84 million]). Overall the budget impact showed annual cost savings of €18 million[v] (£16 million) when using ONS to manage DRM in eligible older people in England.[88]

[v]Calculated based on an exchange rate of 1 GBP = 1.1245 EUR (Source: Interbank 12/07/2017)

- A systematic review and meta-analysis of RCTs investigated the effect of high-protein ONS versus control (routine care, placebo) on length of stay, readmissions and costs (hospital and community). Meta-analysis of 9 RCTs showed an associated reduction in bed-day costs corresponding to €1,580[v] (£1,405) per patient enrolled in the study resulting from significantly reduced length of stay compared to controls. Meta-analysis of 2 RCTs showed significant cost savings of €363[v] (£323) (95%; CI €124–€599[v] [£110–£533], $p = 0.003$) per patient enrolled associated with significant reductions in readmissions in favour of ONS.[89]
- Nutritional support in adults is listed in the top 6 of the NICE cost-saving guidance, with estimates suggesting that improving screening, assessment and treatment of malnourished patients could lead to cost savings of €80,740[v] (£71,800) per 100,000 population). Among NICE clinical guidelines/quality standards, it ranks third highest in terms of cost savings.[vi]
- The economic budget impact analyses from a report from the Malnutrition Action Group of BAPEN and the National Institute for Health Research Southampton Biomedical Research Centre indicate that the use of nutritional support including ONS, EFT and PN ultimately save rather than cost money (€134,000 - €486,000[v] [£119,000 – £432,000] per 100,000) depending on the model used. It is necessary to make a commitment to invest money before the financial benefits can be reaped (see Figure 3.29).[90]

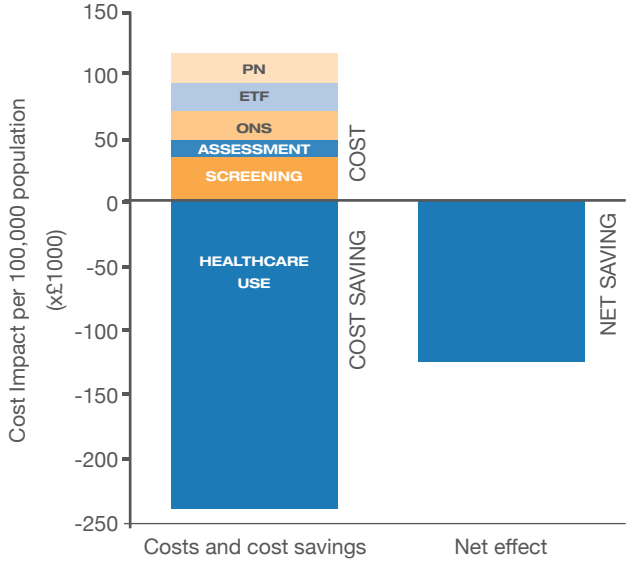

Figure 3.29 **The costs, cost savings and budget impact (net effect) of providing nutritional support to -85% of subjects with high risk of nutrition (model 5).** (Adapted from Elia, M. 2015)[90]
PN = parenteral nutrtion, ETF = enteral tube feeding, ONS = oral nutritional supplements.

- Treatment group patients gained 0.011 more QALYs[vii] than control group subjects in an economic evaluation carried out alongside a multi-centre, randomized, controlled clinical trial comparing a high-protein ONS (containing beta-hydroxy-beta-methylbutyrate) with placebo in a cohort of malnourished older adults ($n = 652$).[91]
- An economic evaluation carried out alongside a multi-centre, randomized, controlled clinical trial comparing a high-protein ONS (containing beta-hydroxy-beta-methylbutyrate) with placebo in a cohort of malnourished older adults ($n = 652$) showed that the cost effectiveness of the intervention based on the first 90 days' post-discharge was €22,413[viii] US$25,727 per QALY (€25,682[viii] US$29,479 per life-year). The incremental cost-effectiveness ratio (ICER) over the 90-day follow-up period was €29,462[viii] US$33,818/QALY and when the time horizon was extended to patients' entire lifetime, the intervention cost was €457[viii] US$524 per life-year saved.[91]

[v]Calculated based on an exchange rate of 1 GBP = 1.1245 EUR (Source: Interbank 12/07/2017) [vi]Source: http://www.bapen.org.uk/resources-and-education/publications-and-reports/malnutrition/cost-of-malnutrition-in-england (Accessed 13.07.17) [vii]QALY is an index of survival that is adjusted to account for the patient's quality of life. QALYs have the advantage of incorporating changes in both quantity (longevity/mortality) and quality (morbidity, psychological, functional, social and other factors) of life. QALYs are used to measure benefits in cost-utility analysis [viii]Calculated based on an exchange rate of 1 USD = 0.8712 EUR (Source: Interbank 12/07/2017).

The cost-effectiveness plane

Figure 3.30 depicts a cost-effectiveness plane. The origin is the standard of care, the y-axis represents the costs, and the x-axis represents the effects.

- All values in the north-west quadrant depict more costly but also less effective interventions. These interventions are not considered cost-effective, and based on these grounds they will be rejected by decision-makers.
- All interventions in the south-east quadrant depict less costly but also more effective interventions. These will therefore be considered cost-effective and should be adopted by decision-makers.
- The results in the north-east quadrant are more costly but also more effective. The decision made about results in this section is related to the amount of money decision-makers are willing to pay for the added benefit.
- The results in the south-west quadrant represent less costly and also less effective choices. Most authorities do not consider interventions that are less effective than the standard of care. However, if the standard of care weighs very heavily on healthcare budgets, interventions in the south-west quadrant will be considered for subgroups with mild disease severity.

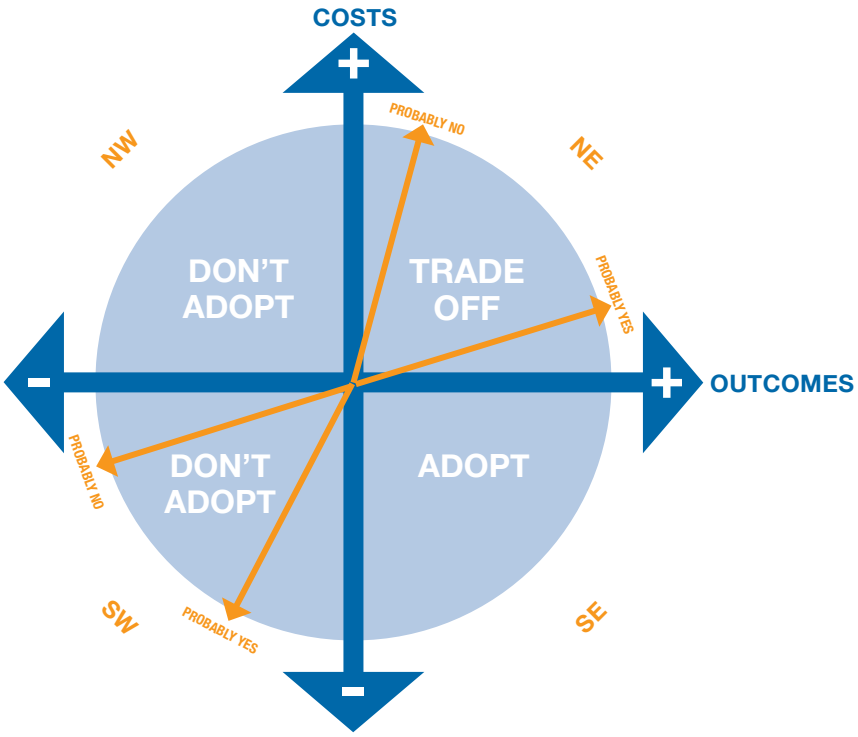

Figure 3.30 The cost-effectiveness plane

- Many of the studies discussed earlier in this section show that oral nutritional intervention with ONS leads to cost savings. Therefore, these results always depict the south quadrants. The studies discussed in Section 3.1.3 Clinical Benefits of ONS show that most studies place the use of ONS in the east quadrants. As explained above, interventions in the south-east quadrant should be adopted because they are more effective and less costly. Those in the north-east quadrant may be cost-effective depending on the ceiling ratios or thresholds considered by decision-makers (willingness to pay for added value to the healthcare system) (see Figure 3.31).

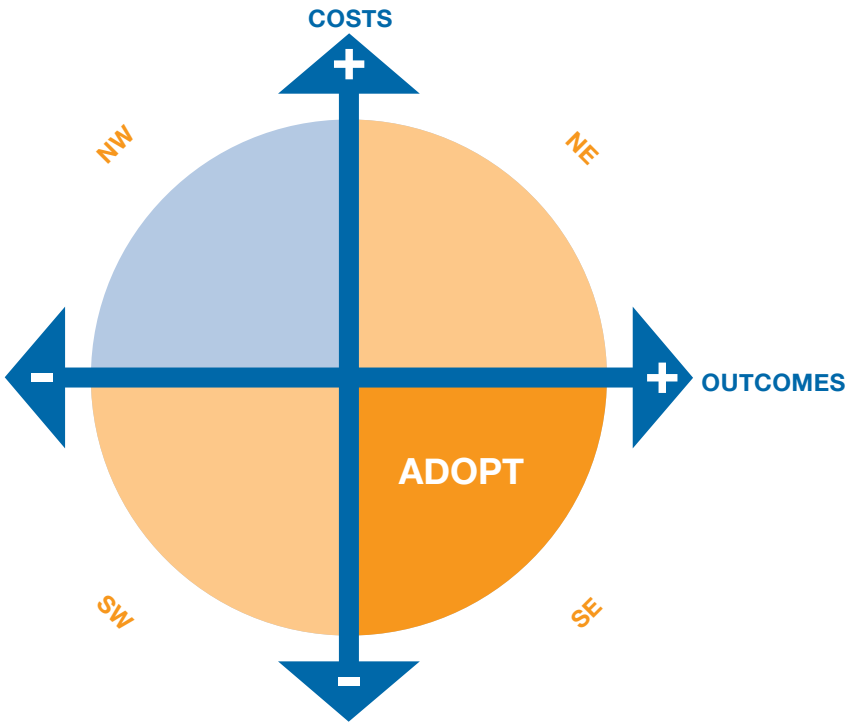

Figure 3.31 **Based on clinical trials, oral nutritional intervention with ONS has clinical benefits, placing the use of ONS in the east quadrants. Studies which have demonstrated cost savings place the use of ONS in the south quadrants.**

Cost savings and cost-effectiveness of ONS in children

- To date, there have been few health economic analyses of the economic benefit of oral nutritional intervention with ONS in children. In the absence of this data, it is worth keeping in mind that ONS has been shown to generate significant cost savings on a per patient and per population basis in adults and that ONS have been shown to be cost-effective.
- Retrospective analysis of 557,348 hospitalizations of children aged 2–8 years in the Premier Research Database examined the use of ONS on LOS and episode cost in a propensity score-matched sample (analyses with and without the use of instrumental variables (IVs) to reduce confounding from unobserved variables). ONS were prescribed in 6066 of 557,348 inpatient episodes (1.09%). In IV analysis, using a matched sample of 11,031 episodes, hospitalizations with ONS use had 14.8% shorter LOS (6.4 vs 7.5 days; 1.1 days [95% CI, 0.2–2.4]) and 9.7% lower cost (€14,420 vs €15,960; €1540 {95% CI, €1676 - €1404])[ix] ($16,552 vs $18,320; $1768 [95% CI, $1924 – $1612]).[92]

[ix]Calculated based on an exchange rate of 1 USD = 0.8712 EUR (Source: Interbank 12/07/2017)

3.1.5 Other forms of oral nutritional intervention

- A variety of oral nutritional intervention strategies other than ONS are used in clinical practice for the management of malnutrition, including dietary advice, food snacks, and food fortification, although evidence of their effectiveness and cost-effectiveness is lacking.

Evidence for the benefits of dietary advice and food fortification in managing disease-related malnutrition is lacking or is of variable quality

- NICE (2006) was unable to demonstrate any evidence of the effect of dietary advice; studies were too small and heterogeneous to allow any conclusions to be drawn, and many failed to report outcomes of interest.[22]
- A review designed to assess the specific impact of the provision of adequate nutritional care (including the routine provision of food and drink) rather than proprietary nutritional support (e.g. ONS) concluded that there is a serious lack of evidence to support non-ONS interventions designed to improve nutritional care, meaning that firm conclusions for practice could not be made.[93]
- A systematic review of the effects of oral nutritional interventions in care homes (searches up to December 2009) did not identify any trials comparing dietary advice and routine care in this healthcare setting.[5]
- In a systematic review and meta-analysis of 45 RCTs in adults with DRM in a variety of healthcare settings (*n* = 3186), Baldwin and Weekes (2011) compared dietary advice (DA) with a) no DA, b) ONS, and c) DA + ONS. In addition, they compared DA + ONS if required with no DA or ONS. Table 3.4 summarises the main results and shows that DA alone may improve body weight and MAMC, but the studies are of variable quality. DA combined with ONS improves nutritional status.[94]
- No significant differences were seen in any comparison between groups for mortality or morbidity. This is in contrast to previous systematic reviews (see Section 3.1.3.1 and 3.1.3.2). Almost half of the studies included in this review that reported on mortality (14 of 31 trials across groups) reported no deaths at all. Very few trials reported morbidity data (5 studies in total across all groups).[94]
- There was appreciable clinical (and statistical) heterogeneity between patient groups in these trials, and it is acknowledged that in most of the studies there was minimal information provided on the nature and intensity and duration of dietary advice provided. Within the groups using ONS, the amount, composition and duration of use varied considerably.[94]

Table 3.4 **Summary of the main results for primary outcomes from a systematic review and meta-analysis of dietary advice (with or without ONS) for DRM in adults**[94]

Primary Outcomes	Measures	Comparison	Mean difference (95% CI)	Notes
Clinical	Mortality	No comparison showed a significant difference between groups		
	Morbidity*			
Nutritional status	Body weight	DA vs no DA	3.75 kg (0.97–6.53) 1.47 kg (0.32–2.61)	For interventions lasting > 12 months All studies combined (significant heterogeneity)
		DA + ONS if required vs no DA	2.20 kg (1.16–3.25)	
	MAMC	DA vs no DA	0.81 mm (0.31–1.31)	All studies combined (moderate heterogeneity)
		DA + ONS vs no DA	-0.89 mm (-1.35–0.43)	
	TSFT	DA + ONS vs no DA	-1.22 mm (-2.34–0.09)	Studies on TSFT heterogeneous

*Measured as risk of hospital admission, readmission and length of hospital stay.

- A systematic review of the effects of oral nutritional intervention in care homes (searches up to December 2009) found that 1 fortification trial reported small non-significant changes in energy intake. No significant differences were reported in the few food fortification trials that reported functional outcomes, and no food fortification trials reported clinical outcomes.[5] Trials of ONS in this review did not report functional outcomes; however, significant clinical outcomes such as reductions in infections and bed-days, improved pressure ulcer healing, and increases in energy intake and body weight were reported.[5]
- Food fortification is employed widely with the aim of increasing the energy and nutrient density of food; however, care should be taken with this approach since high levels of fortification have been shown to have detrimental effects on the aesthetic ratings of commonly fortified foods, such as soup and milk puddings, potentially making them unappealing and less likely to be consumed.[95]

ONS have been shown to be more effective than dietary advice or snacks

- In a trial of hospital patients with fractured neck of femur at risk of malnutrition (screened using 'MUST') (n = 50, median age 82 [range 46–97], median BMI 19 kg/m^2 [range 12.5–26 kg/m^2]) randomised to receive either ONS (300 kcal per serving) or isoenergetic readily available snacks ad libitum post-operatively, significantly fewer patients in the ONS group had complications than in the snack group (27% vs 58%, p = 0.04). Although not significant, a reduction in the incidence of specific complications was also observed, i.e. infections, 17% vs 33%, and wound-related complications (poor wound healing, pressure ulcers), 17% vs 38%.[96]
- See Table A4.1, Appendix IV for a comparison of the average nutrient content of ONS with typical food snacks.

- An RCT comparing the effectiveness of ONS with DA in care home residents (n = 104) at risk of malnutrition (using 'MUST' [medium and high risk]) showed that energy and protein intakes were significantly higher in residents randomised to receive ONS than in residents who received dietary advice. Appetite sensations were not significantly different between the 2 groups.[97]

3.1.6 Compliance

Compliance to ONS is good. Compliance to other methods of oral nutritional intervention need investigation

- A systematic review investigating whether patients' compliance to ONS (amount consumed relative to amount prescribed) varied according to healthcare setting, ONS type, volume or duration and patient characteristics such as age or condition found that:[98]
  - ~ Overall pooled mean compliance to ONS was 78.2% (SD 15, range 37-100%; n = 52 studies) and in 62% of studies compliance was ≥ 75%;
  - ~ Mean percentage compliance to ONS was 80.9% in studies in the **community** (included patients attending hospital outpatients, residents in care homes and free-living individuals) (SD 13, n = 33 studies), 67.2% in studies in **hospitals** (SD 12, n = 10) and 80.7% (SD 8, n = 3) in studies in **multiple settings** (included patients in both hospital and community);
  - ~ Energy density was the main ONS-related factor positively associated with compliance (r^2 = 0.093) with significantly higher mean percentage compliance to ONS containing ≥ 2 kcal/ml than ONS with 1-1.3 kcal/ml or 1.5 kcal/ml (91% vs 77% vs 78% respectively, $p < 0.05$);
  - ~ Duration of ONS intervention or volume of ONS prescription did not appear to be correlated with compliance (duration: r^2 = 0.055, p = 0.124, n = 44 studies; volume: r^2 = 0.0002, p = 0.774, n = 39 studies);
  - ~ Compliance was negatively associated with age (r^2 = 0.148, p = 0.01, n = 44 studies), but no significant difference in compliance to ONS was found in different patient groups (p = 0.130);
  - ~ Compliance to ONS was positively associated with greater ONS energy intake (r^2 = 0.106, p = 0.024, n = 48 studies) and total energy intakes (energy from food plus ONS) (r^2 = 0.307, p = 0.002, n = 29 studies).

Other reviews: Mixed patient groups and combination of different forms of nutrition support

- A review published in 2016 by Bally et al. appears to conflict with the results of the two reviews by Elia et al. described above. However, the inclusion and exclusion criteria for reviews can differ substantially and should be carefully examined before making comparisons and drawing overall conclusions. Bally et al. aimed to assess the effects of nutritional support on outcomes of medical inpatients with malnutrition or at risk for malnutrition in a systematic review of randomized clinical trials (RCTs). In contrast to the reviews by Elia et al. they did not show a significant reduction in mortality, hospital-acquired infections, functional outcomes or length of hospital stay.[99]

- However, Bally et al. included studies of any type of nutritional support except parenteral nutrition. They included studies that examined interventions as diverse as dietary advice, food fortification, oral supplementation and enteral feeding. In addition, they excluded studies of surgical patients except where there was a mixed cohort of medical and surgical patients where the results for the medical patients were not reported separately. The study populations and type of intervention differed from the reviews by Elia et al. Therefore, it is unsurprising that the findings were different. Similar to the Elia et al. review Bally et al. did show a significant reduction in non-elective readmissions in the intervention group compared with controls (20.5% vs. 20.9%; risk ratio, 0.71; 95% CI, 0.57-0.87.[99]
- A Cochrane review on the effectiveness and efficacy of nutritional therapy reviewed nine randomized controlled trials and two meta-analyses but gave non-conclusive results whether re-admissions within 30 days from hospital discharge could be reduced by nutritional therapy.[100] Nutritional therapy included oral/enteral/ and parenteral nutrition therapy but excluded dietary advice/counselling as the sole intervention. It also included immuno-nutrition which is outside the scope of this document and therefore has not been discussed. Interestingly the review considered 16 studies to specifically determine the economic benefits of nutrition support in hospitalised patients and concluded that all the studies analyzed consistently found that nutritional interventions provide economic benefits in terms of savings and cost-effectiveness. The authors stated that this conclusion should be interpreted in light of the limited strength of the evidence available. The review also included two community studies and concluded that nutritional intervention may be cost-effective in selected sub-groups of outpatients; however the evidence-base is limited.[100]

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3

BENEFITS OF MEDICAL NUTRITION

3.2 Use and Benefits Of Enteral Tube Feeding (ETF)

Summary

Enteral tube feeding (ETF) is a life-saving technique without which patients with a functioning gut, who are unable to consume sufficient food and drink via the oral route to meet their nutritional needs, would die due to dehydration and starvation. Enteral tube feeding is indicated if a patient has a functioning gut but is unable or unwilling to consume sufficient food or fluid orally to meet their nutritional requirements.

ETF is frequently used in patients of all age groups across all healthcare settings e.g. hospitals, nursing homes and in patients living in their own homes. The use of ETF in the community or home enteral tube feeding (HETF) has become more common globally as a result of developments in technology, the development of the percutaneous endoscopic gastrostomy (PEG) and as a result of the need for more community care as governments' attempt to refocus the delivery of healthcare away from the costly acute healthcare setting and closer to patients at home. The prevalence of HETF is steadily growing year on year.

ETF is used to support adult patients with a wide variety of conditions. In national surveys of HETF the main disease areas in which patients receive tube feeding are cancers, neurological disorders and non-malignant GI diseases.

Many patients receiving HETF live in their own homes. Data from national registers and retrospective studies shows that many people receiving HETF live independently and self-manage their daily care whilst also achieving normal activity levels. In the UK there is an increasing trend towards HETF patients living independently which may reflect the younger age groups in which HETF is initiated. Unsurprisingly, those HETF patients that live in nursing homes tend to require total care and are generally immobile.

HETF is used to support children of all ages in the community but particularly children under the age of 5 years. Most children on HETF live at home with their family.

From a clinical perspective it is clear that ETF is indicated for particular clinical conditions. Its value is generally undisputed in patients who are likely to recover from a period of unconsciousness or in those who have swallowing difficulties but otherwise are in good health or have a good quality of life. Because of the value of ETF in sustaining life it is often considered unethical to withhold treatment. This also means that undertaking randomised controlled trials, whereby one group of subjects are randomised to receive ETF whilst the other group don't, would also be considered to be unethical.

Systematic reviews have shown a number of benefits of ETF such as improving nutritional intake in patients across healthcare settings; attenuating loss of body weight and lean tissue mass in hospital patients; improving body weight and lean tissue mass in patients in the community and improving growth in children in the community. ETF is associated with functional improvements (depending on patient group) such as improved wound healing and well-being in hospital patients; improved pulmonary function and well-being in community patients and improvements in some aspects of quality of life e.g. in patients with head and neck cancer who undergo prophylactic gastrostomy feeding (6 month data).

ETF is associated with reductions in mortality and complications in hospital patients, including patients who are critically ill. In one systematic review mortality rates were significantly reduced by ETF compared with routine care in some patient groups (11% vs. 23%). There is limited data available in the literature about the potential cost savings and cost-effectiveness of ETF across healthcare settings, from different countries and in particular in children. However, a small number of studies have been undertaken. In England, the potential savings from reduced length of hospital stay associated with use of ETF and PN

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combined have been estimated to be approximately £11 million. In Poland a study showed that after introduction of reimbursement for commercial ETF there was a reduction in the number of hospital admissions and length of stay with savings in annual hospitalization costs.

Conclusion

ETF is an important life-saving technique used widely across all healthcare settings in patients of all ages with a variety of medical conditions. The use of ETF is increasing in the community and many patients live independently and achieve normal activity levels. ETF has nutritional, functional and clinical benefits and data is emerging showing that it is cost-effective in adults and children.

Recommendations

On the issue of the **benefits of ETF** the MNI makes the following recommendation:

Action	Issues to consider
Evidence is available that demonstrates benefits of ETF in a range of patient groups. This information should be translated into practice to ensure that patients who need nutritional intervention, in particular ETF, receive it in a timely and appropriate manner	• Information about the benefits of ETF and how it should be used in practice should be included as part of education and training for healthcare professionals on the management of patients with, or at risk of, malnutrition • Patients' progress should be regularly monitored and their nutritional care plans, including all types of nutrition intervention, should be adjusted accordingly. Particular attention should be paid to how and when to initiate ETF • ETF is a potentially life-saving technique and should be available to all patients when needed. Access or ability to pay should not be a constraint

3.2.1 Prevalence and use of ETF

Enteral tube feeding (ETF) is a life-saving technique

Enteral tube feeding (ETF) is a life-saving technique without which patients with a functioning gut, who are unable to consume sufficient food and drink via the oral route to meet their nutritional needs, would die due to dehydration and starvation.

It is commonly accepted that ETF is the preferred method of artificial nutrition support and for this reason is widely used in hospitals across many specialities and ages. The majority of ETF in this setting is relatively short-term, generally in response to an immediate need to meet nutritional requirements due to acute illness, surgery and/or medical treatment. However, many patients require longer term ETF due to the nature of their clinical condition. This, together with an emphasis on community care, means these patients are increasingly receiving ETF in different care settings e.g. at home or within a care home. ETF administered in the community is often referred to as home enteral tube feeding (HETF) or home enteral nutrition (HEN).

Enteral tube feeding is indicated if a patient has a functioning gut but is unable or unwilling to consume sufficient food or fluid orally to meet their nutritional requirements.[1] Depending on the patient's individual needs it may be used as a supplemental or sole source of nutrition. In some cases ETF may be contraindicated e.g. intestinal failure; bowel ischaemia; post-operative stasis; complete intestinal obstruction; inability to access the gut; high loss intestinal fistulae or where the burden from ETF to the patient would outweigh the potential benefits e.g. terminal care.[1] In these cases parenteral nutrition may be indicated, except for the latter example.

The Medical Nutrition provided through a tube should be introduced to the gastrointestinal tract at the point where it is possible to absorb it. Figure 3.1 shows the gut can be accessed in many different places. The choice of feeding route should be based on the underlying pathology, the likely duration of tube feeding and individual patient preference.[1]

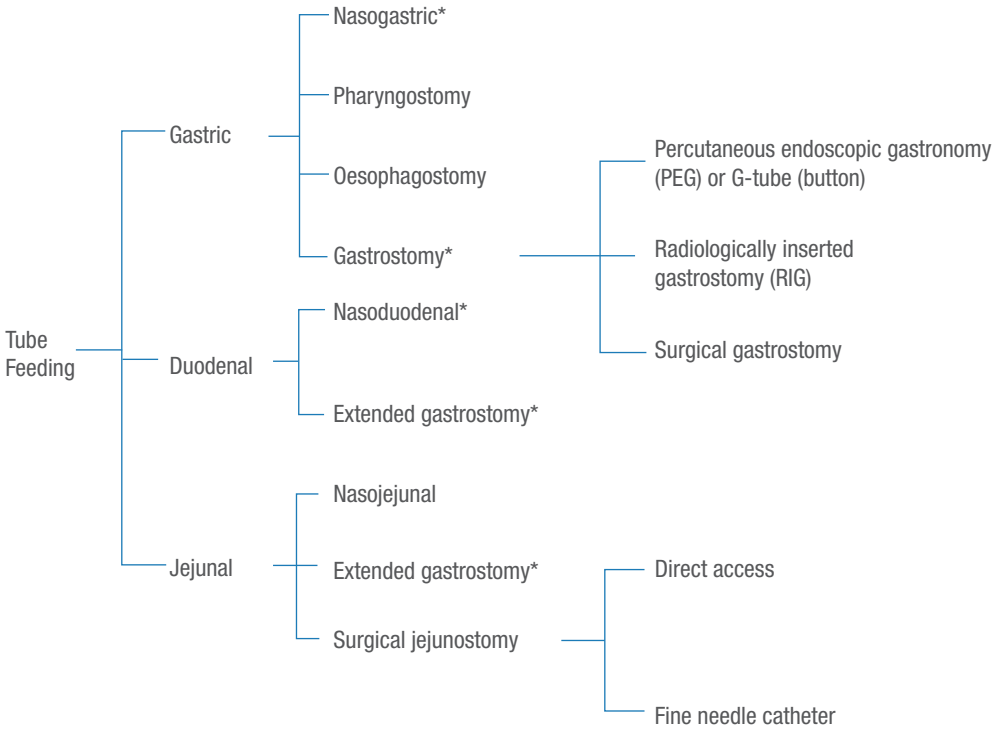


Figure 3.1 **Routes for Enteral Tube Feeding (ETF).** *Preferred routes. (adapted from Sobotka 2011)[1]

ETF is frequently used in patients in hospitals

There are little data available in the published scientific literature about the prevalence of ETF in hospital patients. However, some data are available from the national reports from the nutritionDay surveys. NutritionDay is a worldwide annual initiative which aims to benchmark, monitor and improve nutritional care across Europe and beyond. Data are collected during a one-day cross-sectional audit on individual nutritional care and the nutritional status of patients aged >7 years of age.

- Data from the hospital surveys conducted between 2011 and 2015 show that about 6 to 8% of the cross-section of hospitalised patients captured in the survey are receiving ETF[i]. A small number of patients receive both enteral and parenteral nutrition concurrently. However, it is important to note that not all patients who are malnourished or at risk of malnutrition are identified and receive nutritional intervention (See Section 1 for more information on this topic) so these figures do not necessarily represent the number of patients who may need ETF, simply those that are receiving it at the time of the survey. It is also possible, due to the small numbers of patients included from the survey in each unit, that the data does not fully represent the hospital ETF population.
- In the UK an estimate of ETF activity in hospital was made to aid the calculation of the cost of malnutrition in England and potential cost savings from nutritional interventions by Elia et al. in 2015. They estimated that 148,684 patients are given ETF for a duration of 12 days under the current pathway of care (annual figure) which equates to over 1.7 million subject-ETF days per annum.[2]

ETF is frequently used in adult patients in the community

The use of ETF in the community or home enteral tube feeding (HETF) has become more common globally as a result of developments in technology, the development of the percutaneous endoscopic gastrostomy (PEG) and as a result of the need for more community care as governments attempt to refocus the delivery of healthcare away from the costly acute healthcare setting and closer to patients at home.[3]

Some countries, for example UK, Spain and Italy have developed national registers or undertaken surveys of patients receiving HETF. Although this information is not consistently available in all countries, data from these countries provides a longer-term picture allowing comparisons and trends in the HETF population over time. This is useful when planning and commissioning healthcare resources for this unique group of patients and can be used to monitor outcomes over a longer time frame.

Estimates of the prevalence of HETF have largely been obtained through national surveys or from large retrospective studies. Surveys generally rely on the co-operation of reporting centres/hospitals in providing accurate data and comparisons between surveys is often difficult due to the nature of reporting and the way in which the data is collected. A summary of prevalence data is shown in Table 3.2.

- In the UK the British Artificial Nutrition Survey (BANS) showed that 92 adult patients per million were receiving HETF (point prevalence) at the end of 2010.[4]
- The results of an Italian survey showed a point prevalence of 248 adult patients per million receiving HETF in 2012.[5]
- Results from the survey in Spain led by the Spanish Home Artificial Nutrition Group showed a prevalence of 67.1 per million of population receiving HETF during the year 2013.[6]
- A large retrospective analysis of data extracted from the National Health Insurance database in Taiwan of patients admitted for PEG insertion showed an incidence of 190 per million in 2010 in patients aged 65 years or over.[7]

[i]Worldwide reference data from nutritionDay national reports (https://www.nutritionday.org/en/about-nday/national-reports/index.html. Accessed 04.04.17).

- According to a year 2000 National Center for Health Statistics Home Survey in the US, 30,700 patients were on HETF,[8] although this figure excludes those patients in long-term care facilities. There is a lack of more recent data for the US.

The prevalence of ETF in adults in the community is growing

As awareness of the role of nutritional intervention has grown and the pressure on hospital beds leading to more care in the community, it is no surprise that this is reflected in an increase in the number of patients receiving ETF in the community (Table 3.5):

- UK data from the BANS shows a 5% increase in the number of new registrations in 2010 compared to 2009.[4]
- There was an eight-fold increase in the number of patients registered between 1997 and 2006 in the Spanish register of Home Enteral Nutrition, although it is worth noting that this figure includes patients receiving more than 1000 kcal/day from an enteral formula regardless of the access route (oral/tube feeding).[9]
- Data from Italy shows that the prevalence of HETF in 2012 had increased by a factor of 1.62 compared to 2005.[5]
- The incidence of PEG insertion in patients ≥ 65 years increased from 97 to 190/million of population from 2005 to 2010 in a large retrospective analysis of data extracted from the National Health Insurance database in Taiwan.[7]

Table 3.5 Prevalence and growth of HETF in specific countries

Reference	Country	Total/ Prevalence of HETF	Type of Enteral Nutrition	Data compiled	Age group	Growth
Annual BANS report 2011[4]	UK	5703 point prevalence (Industry adjusted data using figures obtained from home care companies [HCCs] provide an estimated point prevalence of 31,795) 92/million point prevalence 130/million period prevalence	Home Enteral Tube Feeding	2000-2010	≥16 years	5% increase in the number of new registered adult patients receiving HETF (*n* = 3430) compared with 2009. (Industry adjusted data using figures obtained from HCCs suggests growth of 28% from 2005-2010 [although this may also reflect growth in the use of HCCs providing HETF to patients]).
Wanden-Berghe et al. 2015[6]	Spain	67.1/million (period prevalence)	Home Enteral Tube Feeding	2013	All ages	Increased prevalence compared to 2011-2012 (64.5/million)
Chang et al. 2016[7]	Taiwan	472 point prevalence Incidence: 190/million (in 2010)	PEG insertion	1997-2004 and 2005-2010	≥65 years	Incidence of PEG increased from 97 to 190/million population from 2005-2010
Pironi 2017[5]	Italy	247.9/million (point prevalence)	Home Enteral Tube Feeding	2012	>18 years	Prevalence 1.62 x greater than 2005

ETF is used to support adult patients with a wide variety of conditions

The requirement for enteral tube feeding, particularly over the longer term, is determined by the clinical condition of the patient. Whilst in an acute setting enteral nutrition may be used across a broad spectrum of patients with varying clinical conditions, enteral nutrition provided at home or in a home care setting is often provided to similar groups of patients. National surveys and retrospective studies of tube fed patients provide a useful overview.

- In national surveys of HETF the main disease areas in which patients receive ETF are cancers, neurological disorders and non-malignant GI diseases (see Figure 3.33).[4-6;10]
- Head and neck cancer accounted for 77% of new HETF registrations with cancer in 2010 in the UK survey and this figure has grown from previous years.[4]
- In a retrospective study of patients admitted to hospital for PEG insertion in Taiwan between 2005-2010 the underlying diseases were neurological disease 29.1%, head and neck cancer 41.7% and miscellaneous conditions 29.1%.[7]
- A prospective study of 104 patients referred for PEG insertion at a hospital in Sweden, from 2005 to 2007 showed 75% had a diagnosis of cancer, 22% neurological diseases and 2% other conditions.[11]
- A retrospective multi-centre qualitative study of patients receiving HETF in Ireland showed that in adult patients (n = 50) the clinical conditions were classified as follows: malignancy 48%, neuromuscular degenerative disorder 16%, stroke 8%, respiratory disease 8%, brain injury 6%, congenital malformation 6%, and unknown 8%.[12]

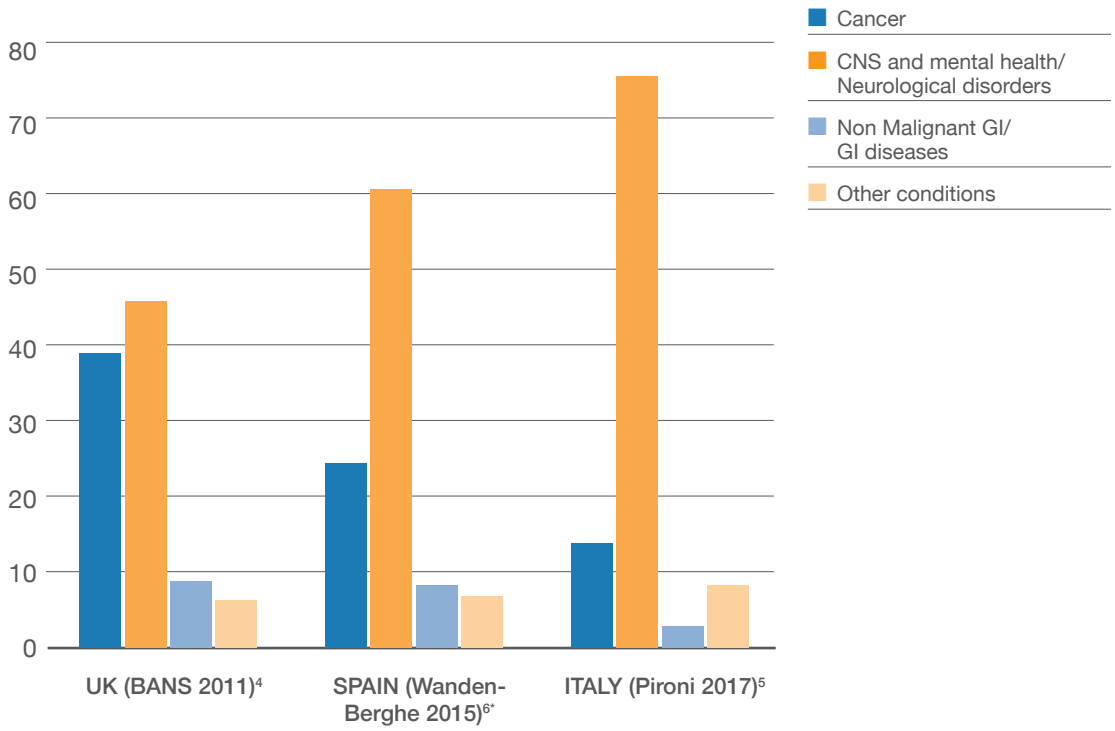


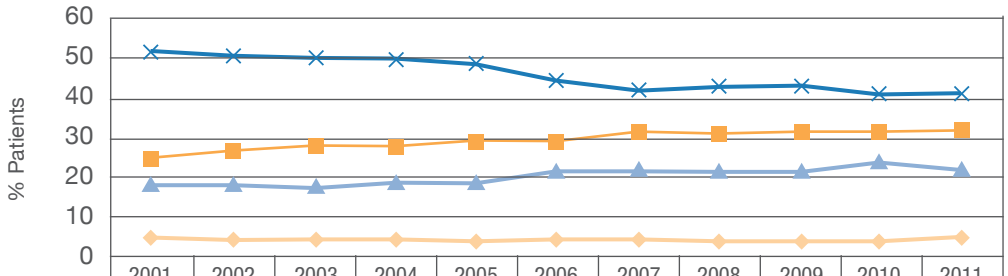
Figure 3.33 **Diagnostic groups of patients receiving HETF from three national surveys[4]**

*Data from Wanden-Berghe et al (2015), has been represented by the addition of the following categories in brackets: Cancer (head and neck tumour + GI tumour); Non-malignant GI/GI diseases (ORL and maxillofacial surgery + severe intestinal motility disorder + malabsorptive syndromes + non-neoplastic oseophageal stenosis).

ETF is used to support adult patients of all ages

Data on the prevalence of ETF in specific age groups in hospitals is not widely reported. However, there is useful data available from national registries of patients receiving ETF in the community.

- The BANS survey in the UK shows the largest group of adult patients receiving HETF are aged 71+ years.[4]
- Data from Spain shows a similar picture with the median age of adult patients receiving HETF being 73 years.[6]
- A large study of nursing home patients in Germany showed that the majority of patients with a PEG (48.6%) were aged over 80 years.[13]
- Whilst the majority of newly registered patients (63%) receiving HETF in 2010 were over 60 years in the UK BANS survey, the proportion aged between 31 and 60 years increased by 7% compared to 2000 (Figure 3.34). A possible explanation for the decreasing proportion of the oldest patients and the increasing proportion of the younger patients could be the change in the clinical conditions of patients newly registered with BANS (e.g. increase in the proportion of head and neck cancer patients; reduction in the proportion of CVA [cerebrovascular accident] patients).[4]
- A study of patients referred for PEG insertion in a hospital in Sweden showed that the majority of subjects (52%) were aged <65 years. This probably reflects the large proportion of these patients with malignancy as their underlying condition (75%).[11]



	2001 n = 6629	2002 n = 7187	2003 n = 6428	2004 n = 6585	2005 n = 5656	2006 n = 5978	2007 n = 5145	2008 n = 5182	2009 n = 4326	2010 n = 3282	2011 n = 3430
16-30 yrs	5.3	4.4	4.4	4.4	3.9	4.7	4.6	4.3	4.2	3.6	5.1
30-60 yrs	24.8	26.4	27.9	27.5	28.8	29.2	31.2	30.9	31.1	31.4	31.6
61-70 yrs	18.3	18.5	17.7	18.9	19.0	21.7	22.1	22.0	21.6	24.4	22.6
>70 yrs	51.5	50.6	50.0	49.1	48.3	44.3	42.1	42.8	43.1	40.6	40.6

Figure 3.34 **New adult HETF registrations in the UK (%) within age bands (2000-2010)** (adapted from Smith et al. 2011)[4]

The majority of patients receiving ETF in the community live in their own homes

There are little data on the comparative setting of patients receiving HETF except from the UK BANS survey which includes information on whether patients are in their own homes/ nursing homes or residential care and a regional survey in Italy which looked at patients receiving HEN either at home or in nursing homes over an 11 year period.[4, 14]

- Data from the most recent BANS report showed that the majority of newly registered patients on HETF lived in their own home (increase from 56% in 2000 to 69% in 2010). Less than one third (29%) of the patients lived in nursing homes or received residential care, which dropped from 40% in 2000.[4]
- An Italian epidemiological study over an 11 year period (2002-2012) which included 3246 subjects receiving HETF showed that 56% were living in their own homes and 44% were in nursing homes.[14]

Many adult patients on ETF in the community live independently and achieve full normal activity levels

Data from national registers and retrospective studies show that many people receiving ETF in the community live independently and self-manage their daily care whilst also achieving normal activity levels. In the UK there is an increasing trend towards ETF patients living independently which may reflect the younger age groups in which ETF is initiated. Unsurprisingly those ETF patients that live in nursing homes tend to require total care and are generally immobile.

- Data from the UK BANS report shows that the majority of newly registered patients (40.2%) achieve full normal activity levels whilst receiving HETF (Figure 3.35). This is an increase from 17% in 2000 (Figure 3.35).[4]
- This is mirrored by a reduction in the level of dependency in new HETF patients over the years. In 2000, 21% of new patients lived independently and 57% required total help. Data in 2010 showed an increase in patients who lived independently (40%), outnumbering the proportion of patients who required total help (39%) (Figure 3.36).[4]
- In a study of patients receiving HETF after discharge from hospital (n = 40) in Sweden thirty-two patients (80%) ran their daily care of HETF by themselves, while eight patients (20%), all using PEG, received help from their cohabitant, an adult, child or home health care services.[15]
- Data from Ireland from a retrospective multicenter study showed that a quarter of the patients felt that the use of HETF had a significant negative impact on daily activities, whilst in contrast 55% reported little or no impact.[12]
- Forty eight percent of patients referred for PEG insertion in a hospital in Sweden felt that the PEG placed no limitations on their activity levels, whereas 51% responded that it affected their activity to some extent. In the same study 63% were self-caring with respect to feeding assistance, 22% received care from care staff, 18% from their spouse and 2% from another relative.[11]
- Data from Spain led by the Spanish Home Artificial Nutrition Group show a slightly different picture with most of the HETF patients being chair- or bed-bound (49.4%) or limited in their activity (33.9%). In addition, most patients required partial (27%) or total help (56.5%) in their daily activities.[6]
- A study to investigate the prevalence of malnutrition in orally and tube-fed nursing home residents in Germany showed that 100% of the tube fed patients (n = 27) were "in need of care" and the overwhelming majority (96.3%) of tube fed patients were immobile.[16]

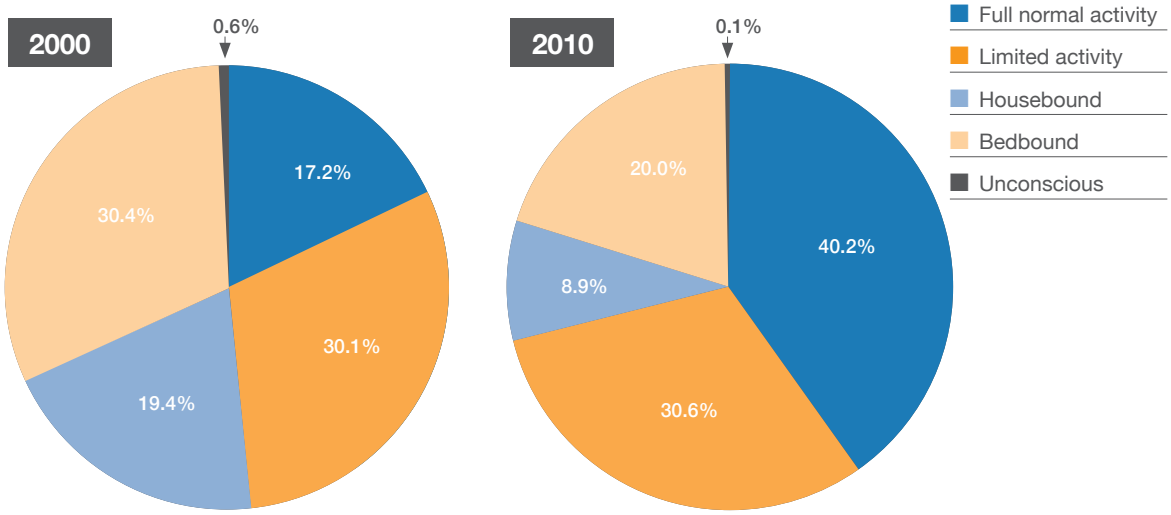


Figure 3.35 Activity levels of newly registered patients receiving HETF in 2010 and 2000 in the UK[4]

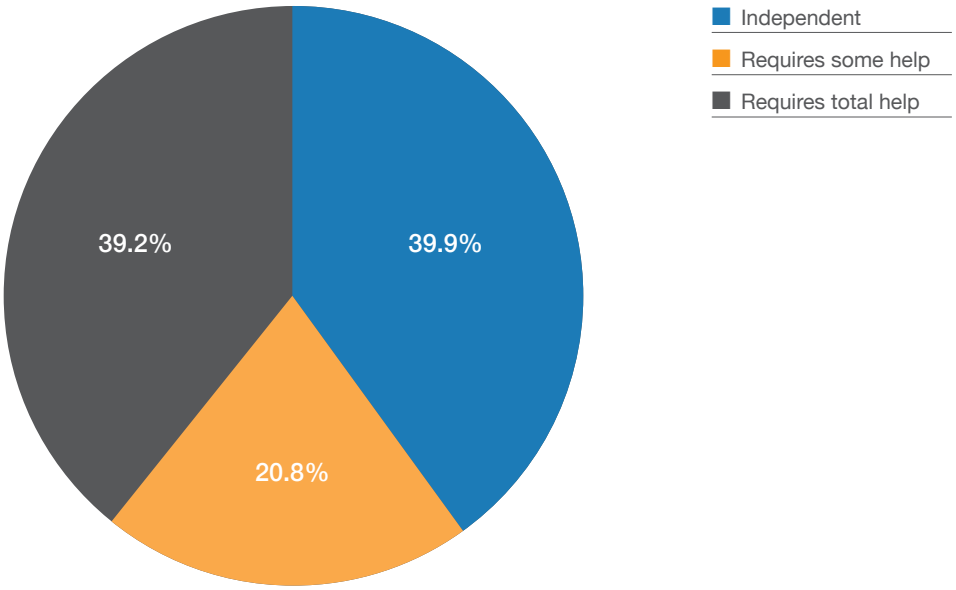


Figure 3.36 **Dependency levels of newly registered patients receiving HETF in 2010 in the UK**[4]

ETF via a gastrostomy tube is generally the most common feeding route used

- Data from the UK BANS report shows that gastrostomy was the primary route of feeding for HETF patients as it has been over the last ten years. In 2010, 75% of the HETF patients were fed by gastrostomy. Other routes of feeding are less common (jejunostomy 5%; nasogastric tube 17%). Feeding by naso-duodenal or naso-jejunal tube only occurred in 4% of the patients.[4]
- According to the data obtained through the Spanish HAN registry the principal route of administration was via a naso-gastric tube (48%) followed by gastrostomy (40.8%) in adults in the year 2013.[6]
- In a retrospective multi-centre qualitative study of patient experience and attitudes relating to HETF in Ireland (*n* = 50 Adults), 89% of patients were fed via a gastrostomy but there was no data on the access route of the remaining 11%.[12]
- A Polish observational multicenter study of 456 HETF patients (142 children and 314 adults) showed that EN was performed via percutaneous endoscopic gastrostomy (75.4%), surgical gastrostomy (8.5%), low-profile gastrostomy (0.7%), jejunostomy (2.6%), and nasogastric tube (12.7%).[17]

PAEDIATRICS

The indications for ETF in children are outlined in Table 3.6. As for adults, ETF may be required for a short period but for many children it can be long-term or even life-long.

Table 3.6 **Indications for ETF in children** (adapted from Shaw & Lawson 2008)[18]

Indication	Example
Inability to suck or swallow	Neurological handicap and degenerative disorders Severe developmental delay Trauma Critically ill child requiring ventilation
Anorexia associated with chronic illness	Cystic fibrosis Malignancy Inflammatory bowel disease Liver disease Chronic renal failure Congenital heart disease Inherited metabolic disease
Increased requirements	Cystic fibrosis Congenital heart disease Malabsorption syndromes (e.g. short gut syndrome, liver disease)
Congenital anomalies	Tracheo-oesophageal fistula Oesophageal atresia Orofacial malformations
Primary disease management	Crohn's disease Severe gastro-oesophageal reflux Short bowel syndrome Glycogen storage disease Very long chain fatty acid disorders

ETF is used widely to support children in the community

Published data on the prevalence of ETF in children in the community is increasing with more data available in recent years generally from those countries that conduct national surveys (see Table 3.7).

- Data from the UK BANS showed that in 2010, 448 new children were registered and 1336 were updated (period prevalence). The number of new registrations was lower than previous years, which was thought to be due to a reduction in the number of reporting centres as a result of a new method of reporting.[4] The survey also compares prevalence data obtained from the home care companies (HCCs) who supply HETF to give a more accurate picture of the numbers of children receiving HETF. The updated data gives a point prevalence estimate of 16,982 children receiving HETF in 2010, suggesting a large shortfall in reporting data (93.2% shortfall).[4]
- In 2007 the Register of Pediatric Outpatient and Home Enteral Nutrition (NEPAD) in Spain had recorded a total of 529 paediatric patients receiving HEN from 13 hospitals but recognized that this is likely to be an underestimate due to the small number of reporting centres.[19] It should also be noted that this register included a small number of patients receiving oral nutrition (96.3% tube fed, 3.7% oral).[19]

- The results of an Italian survey of Home Artificial Nutrition which included paediatric patients showed a point prevalence of 27.3/million inhabitants receiving HETF with a total number of cases of 1395 in 2012.[5]
- Another Italian survey including data from four Italian Regional Reference Centres for Paediatric Home Artificial Nutrition estimated the overall prevalence of HETF to be 34.7/million inhabitants in 2009 in children aged 0-18 years.[20]
- A survey sent to all regional centres providing paediatric HETF services in Poland showed that there were a total of 525 cases receiving HEN and an incidence of 13.75/million population at the end of 2010.[21]
- A national survey in New Zealand conducted in 2013 which was sent to all District Health Boards, showed a total of 630 children and young people receiving long-term EN, with a prevalence per 100,000 children aged <15 years of 66.5.[22]

The use of ETF in children in the community is growing

- In the UK the number of new registrations and the total number of children receiving HETF at the end of 2010 was lower than in previous years which was thought to be due to a 60% reduction in the number of reporting centres participating in the survey.[4] However, the data obtained from the Home Care Companies (HCCs) supplying HETF suggests that ETF continues to grow in the community with a growth of 39% in 2010 compared to the previous year and 41.5% growth compared to 2005.[4] This suggests that the BANS data is likely to be an underestimate of the real picture.
- Compared to 2005 the point prevalence of paediatric cases receiving HETF was 2.55 times greater in 2012 in the Italian survey of Home Artificial Nutrition.[5] Another Italian survey of children receiving HETF at four regional centres in Italy showed a steady increase from 1996-2009[20] (see Figure 3.37).
- In 2003 the Spanish Register of Pediatric Outpatient and Home Enteral Nutrition (NEPAD) registered only 124 children from six Spanish hospitals while in the last assessment, undertaken in 2007, both the number of patients and hospitals had increased (n = 529, 13 hospitals).[19] Note: the register includes a small number of patients receiving oral feeding (96.3% tube feeding, 3.7% oral feeding).
- A survey sent to all regional centers providing paediatric HETF services in Poland which included an analysis of the number of pediatric patients who received HETF on January 1st 2010 and December 31st 2010, showed that the number of children receiving HETF at the end of 2010 increased by 21% (from 433 to 525 patients) compared to the beginning of that year.[21]

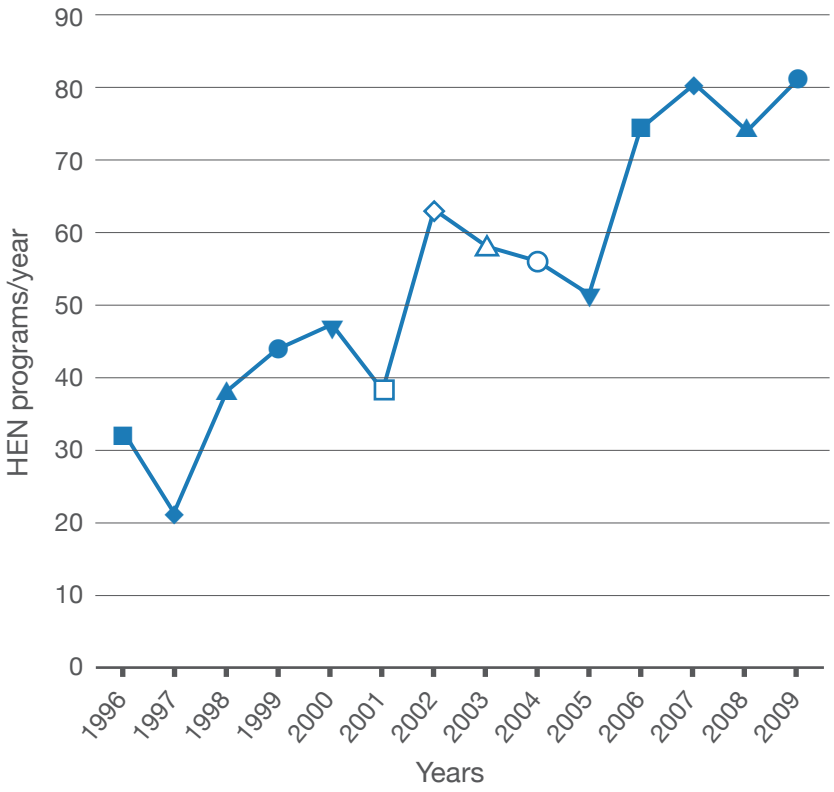


Figure 3.37 **Number of children started on HETF in Italy in four regional centres each year for the period 1996-2009** (adapted from Diamanti et al, 2013)[20]

Table 3.7 **Prevalence and growth of paediatric Home Enteral Tube Feeding (HETF)**

Reference	Country	Total/Prevalence of HEN	Data compiled	Age group	Growth
Jelleyman 2013[22]	New Zealand	Total: 630 (575 <15 years) 65.9 per 100,000 (<15 years)	2013	<15 years	Not reported
Gómez-López et al. 2010[19]	Spain	Total: 529	2003-2007	Paediatric-Not further defined	Growth from 124 patients in 2003 (6 reporting centres) to 529 patients (13 reporting centres) in 2007[a]
Szlagatys-Sidorkiewicz et al. 2012[21]	Poland	Total: 525 (13.75 per 1,000,000)	2010	≤18 years[b]	21% (from 433 to 525 patients) compared to January 1st 2010
Annual BANS report 2011[4]	United Kingdom	Total: 1336 (Industry adjusted data from Home Care Companies (HCCs) suggests total point prevalence in the UK is 16,982)	2010	<16 years	Shortfall in data due to reduction in number of reporting centres. (Industry adjusted data from HCCs suggests growth of 41.5% since 2005, although this could also reflect growth in the use of HCCs to provide HETF)
Pironi 2017[5]	Italy	Total: 1395 (27.3/million)	2012	≤18 years	Comparison between 2005 and 2012 point prevalence (expressed as 2012:2005 ratio) was 2.55

[a]The register includes a small number of patients receiving oral feeding (96.3% tube feeding, 3.7% oral feeding)
[b]Based on the age range reported in the paper which was up to 18 years

ETF is used to support children in the community with a wide variety of conditions

As for adults, HETF is used to support children in the community with a wide variety of medical conditions (see Figure 3.38).

- Data from the BANS report in the UK of new registrations in 2010 were grouped into 4 disease categories: cancer (6%), central nervous system (CNS) & mental health (31%), non-malignant gastrointestinal (GI) (13.8%) and other conditions (49.1%).[4]
- The results of an Italian survey of Home Artificial Nutrition which included paediatric patients showed that, of the disease categories, oncological disease accounted for 5% of total HETF in children, neurological disease 63%, GI disease 11% and other conditions 21%.[5]
- Another Italian survey of children receiving HETF at four regional centres showed the main disease areas for which children received HETF were neuro-genetic diseases (52%) and digestive diseases (21%) in the period 2003-2009.[20]
- In 2007 the Register of Pediatric Outpatient and Home Enteral Nutrition (NEPAD) in Spain had recorded the following disease categories: neurological diseases 28.3%, oncological disease 17.9%, gastrointestinal diseases 15% and other conditions 39%.[19]
- In a Polish survey of 525 paediatric HETF patients, in most cases, HETF was prescribed due to neurological disorders (64.2%).[21]
- A national Irish survey showed that cerebral palsy (18.9%), cystic fibrosis (13.5%), developmental delay (13.5%) and chromosomal or metabolic disorders such as Cri du Chat (24.3%) were the most common underlying pathologies in a sample of 37 children receiving HETF.[12]

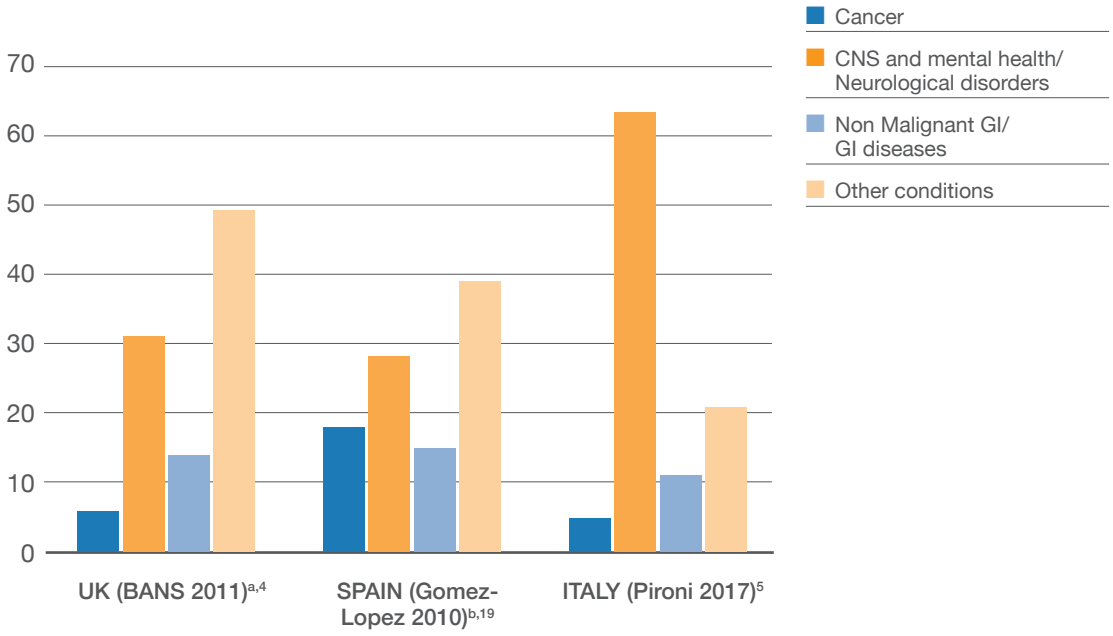


Figure 3.38 Diagnostic groups of paediatric patients receiving HETF from three national surveys

[a]Data from BANS is based on new registrations only. [b]Data from Spain includes a small number of patients receiving oral feeding (96.3% tube feeding, 3.7% oral feeding)

ETF is used to support children of all ages in the community but particularly children under the age of 5 years

- Data from the UK BANS report showed that in 2010, 69% of all newly registered children were less than 2 years old and 80% were 5 years or under. There was an overall trend of children being initiated on HETF at a younger age.[4]
- In the Register of Pediatric Outpatient and Home Enteral Nutrition (NEPAD) in Spain the average age of children receiving HEN was 3.79 years and the average age at initiation was 19.3 months.[19]
- Data from an Italian survey of children receiving HETF from four regional centres showed that the vast majority of children were aged 0-5 years (81%) at initiation of HETF, with fewer being in the older age categories (6-10 years 14%; >10 years 5%) between the period 2003-2009.[20]
- In a Polish survey of 525 paediatric HETF patients the median age of patients receiving HETF in 2010 was 6 years (range: 9 months–18 years).[21]
- A national survey in New Zealand conducted in 2013 showed a total of 630 children receiving long term ETF of which the largest age category was in the 5-14 year age group (37.4%) followed by the 1-3 year age group (21%).[22]

Most children on ETF in the community live at home with family

- There is little data on the care setting of children receiving HETF, this is probably because it is assumed that the vast majority of these children are cared for at home with a family member/carer being the principal carer. This is supported by data from the UK BANS report which showed that in 2010 only 2 out of 448 new children registered were documented to live in a location other than their own home.[4]

Little data exists on the impact of ETF in the community on daily activities in children

Few studies have been conducted to assess the impact of HETF on level of activity/dependence in a paediatric population probably because of the assumption that children are inherently dependent on a carer anyway. However, when a child is diagnosed with a chronic illness requiring nutritional support at home, this usually involves radical changes in family life, often implying extensive use of healthcare resources and changes in family activity. Better understanding these changes may allow for better targeting of healthcare services for this population.

- In an Irish survey of 37 children receiving HETF, respondents were more likely to report that HETF impacted on completion of activities of daily living “quite a bit”, or “very much” ($p = 0.06$). However, it is not clear if this response refers to the carer’s or child’s perspective.[12]

Route of feeding

- According to the UK BANS report, 63% of new paediatric registrations were fed via a naso-gastric tube in 2010. The use of naso-gastric (NG) tube feeding is an accepted and routinely used method to offer fluids and nutrition in children and as 80% of new registrations were under 5 years of age, the data suggest that NG feeding is more frequently used in very young children, with many returning to oral feeding.[4]
- Data from Spain in 2007 show that the majority of HETF paediatric patients were fed using an NG tube (64%), 34% are fed via a percutaneous endoscopic gastrostomy (PEG) whilst less than 2% were fed via the jejunal route.[19]

- Italian data from four regional centres shows a similar picture with 59% of children receiving HETF being fed via an NG tube, 38% fed via a gastrostomy and 3% fed via a jejunostomy in the period 1996-2009.[20]
- In contrast, results from a survey in Poland show that 85.7% of children receiving HETF in 2010 were fed via a gastrostomy tube, whilst only 11.2% were fed via a NG tube.[21]

The decision to initiate enteral tube feeding (ETF) is usually made when a patient can no longer consume sufficient food orally and, if relevant, attempts to increase oral intake from ONS have been unsuccessful (see Section 2 Figure 2.4 [Patient algorithm NICE 2006]). Enteral tube feeding may also be initiated when it is unsafe to continue oral intake such as in patients with dysphagia. In the majority of cases, there are clear benefits of the intervention as without it patients would ultimately face death from lack of nourishment.

Ethical aspects of ETF in relation to the available evidence base

From a clinical perspective it is clear that enteral tube feeding (ETF) is indicated for particular clinical conditions. Its value is generally undisputed in patients who are likely to recover from a period of unconsciousness or in those who have swallowing difficulties but otherwise are in good health or have a good quality of life. Because of the value of ETF in sustaining life it is often considered unethical to withhold treatment. This also means undertaking randomised controlled trials, whereby one group of subjects are randomised to receive ETF whilst the other group don't, would also be considered to be unethical. Randomised controlled trials using ETF therefore tend to focus on other aspects of enteral nutrition (EN) treatment such as feed composition, mode of feed delivery, route of access and timing of EN. As a result, the evidence base for ETF tends to be restricted to outcomes from studies in these specific areas often undertaken in hospitalised patients.

Data on the benefits of ETF in children are lacking. Studies are difficult to undertake in this population for the same ethical reason as in adults i.e. randomisation to a control group, receiving no ETF would be unethical. It is also challenging to recruit a homogeneous group of ETF children into a study due to small numbers. The data that does exist tends to focus on children with cystic fibrosis and children with neurological disorders who represent some of the larger groups of ETF children.

A key systematic review of the evidence base for ETF in hospital undertaken by Stratton et al in 2003 included 74 trials (n = 2769) of which only 45% were RCTs (33 trials, n = 1358). Many had low Jada scores and small samples sizes. In the same review, but for ETF in the community, 47 trials (n = 1321) were included of which <1% were RCTs (3 trials, n = 52). The majority of trials reviewed were small non-randomised trials, partly due to the ethical difficulties of withholding or withdrawing ETF in patients with severe chronic disease, for whom ETF is usually the sole or predominant source of nutrition.[23]

The following section provides an overview of the evidence base, reflected mainly by meta-analyses of studies.

3.2.2 Nutritional benefits of ETF

3.2.2.1 NUTRITIONAL INTAKE

ETF can substantially increase nutritional intake in hospital patients

- In a systematic review of ETF across a wide group of hospital inpatients by Stratton et al. in 2003 (74 trials, *n* = 2769; 45% were RCTs [33 trials, *n* = 1358]) 98% percent of trials (and all RCTs) assessing intake with ETF showed improvements in total energy intake (of which 62% were significant). On average, ETF increased energy intake by ~1000 kcal/day compared with routine care in the RCTs reviewed. ETF does not substantially suppress food intake.[23]

Medical inpatients receiving ETF have higher protein and calorie intakes than those receiving oral feeding or no intervention

- In a systematic review and meta-analysis by Bally et al. in 2016 on types of nutritional support and outcomes in malnourished medical inpatients, a subgroup analysis including patients receiving ETF had higher protein and calorie intakes vs. those receiving oral feeding/non-intervention (48.6 g/d [36.2 to 61.0] vs. 17.8 g/d [10.9 to 24.8] and 613 kcal/d [318 to 908] vs. 383 kcal/d [261 to 505] respectively).[24]

ETF can improve or maintain nutritional intake in patients in the community

- In the review by Stratton et al. in 2003, all trials that assessed total energy intake, indicated that it was improved by ETF (*n* = 14). When used as a supplement to food intake, ETF did not suppress appetite and dietary intake substantially. ETF was also used effectively as a sole source of nutrition for prolonged periods of time (e.g. stroke patients, patients with inflammatory bowel disease).[23]

ETF increases calorie intakes in patients with cystic fibrosis

- As part of a systematic review, a study on patients with cystic fibrosis demonstrated an increased caloric intake by approximately 40% of the recommended daily intake after the start of enteral tube feeding.[25]

3.2.2.2 NUTRITIONAL STATUS

ETF typically attenuates loss of body weight and lean tissue in hospital patients

- The review by Stratton et al. (2003) showed that in 81% of RCTs in patients with burns, critical illness, cystic fibrosis, liver disease and those post-surgery, ETF produced weight gain or attenuated weight loss relative to a control group (of which 53% were significant). The effect on weight appears to involve improvements or better retention of lean and fat tissue mass. Meta-analysis of % weight change suggested a mean effect size with ETF of 1.41 (95% CI 0.66–2.16) compared with routine care, but with significant heterogeneity between studies (Figure 3.39).[23]

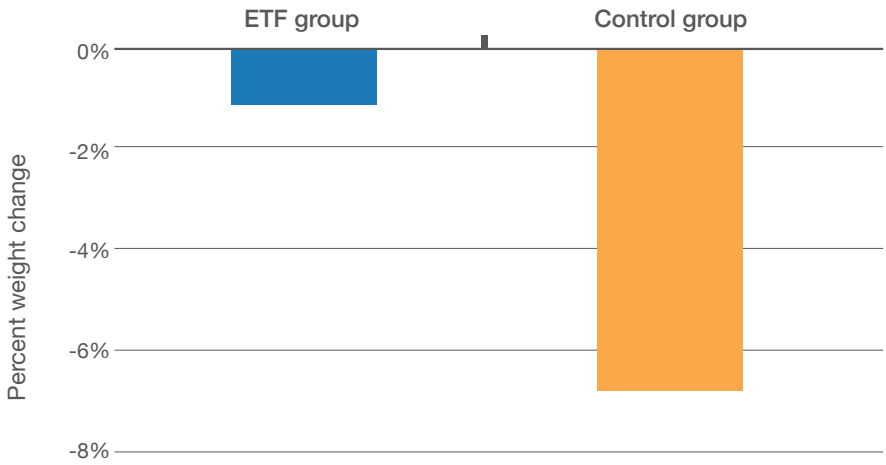


Figure 3.39 **Attenuation of weight loss with ETF in the hospital setting**
(results from 9 RCT, *n* = 312; weighted mean analysis) (adapted from Stratton et al. 2003)[23]

In community patients ETF can improve body weight and lean tissue mass

- In a systematic review of ETF in community patients by Stratton et al. ETF increased or maintained weight over variable periods of time in all trials that made assessments (significant improvement in all three RCTs). In trials that assessed body composition, 88% indicated improvements in fat mass and/or muscle mass in a variety of patient groups, such as COPD, cystic fibrosis, HIV and renal disease.[23]

Prophylactic gastrostomy feeding in head and neck cancer patients may reduce percentage weight loss compared to usual care

- In an evidence update by the National Institute for Health and Care Excellence in the UK, prophylactic gastrostomy feeding in head and neck cancer patients resulted in a lower percentage body weight lost at 6 months (among only those patients who had lost weight) in the group receiving prophylactic gastrostomy feeding (11.4%) than the control group receiving usual care (13.6%, $p = 0.03$).[26] Note: usual care included nutritional advice and enteral feeding when necessary.

ETF can improve growth in children in the community

- In the systematic review of ETF in community patients by Stratton et al. (2003). ETF improved growth in infants and children with cancer, cystic fibrosis, HIV and gastrointestinal disease.[23]

Enteral tube feeding improves weight variables in specific groups of children

- A systematic review assessing the effects of nutritional interventions in patients with cystic fibrosis found that in 5 studies, a significant improvement in weight variables was evident after the start of enteral tube feeding, with follow-up periods lasting from 1-4 years.[25]
- A systematic review of 13 studies looking at the effects of gastrostomy tube placement on the quality of life and physical benefits of care givers and children with neurological impairment, found no overwhelming conclusions but reported improvements in weight gain in a thematic analysis.[27]

3.2.3 Functional benefits of ETF

ETF can improve functional outcomes in hospital patients

- In a systematic review of ETF in hospital patients by Stratton et al. ETF was found to produce functional benefits in 67% of RCTs in patients with COPD, cystic fibrosis, liver disease, cancer and in post-surgery patients. Depending on the patient group these included significant improvements in:[23]
  - ~ respiratory function
  - ~ liver function
  - ~ bowel function
  - ~ wound healing
  - ~ well-being
  - ~ immune function
- The benefits were typically accompanied by substantial improvements in weight (~6% difference between ETF and control patients).[23]

Early ETF is associated with improved functional outcomes in patients with traumatic brain injury

- A meta-analysis which assessed 5 RCTs and 3 non-randomized prospective studies (NPSs) all on patients with traumatic brain injury showed that, compared with delayed feeding, early feeding was associated with a significant reduction in the rate of poor functional outcome (RR = 0.70; 95% CI, 0.54–0.91;p<0.05) as assessed by the Glasgow Outcome Scale.[28]

ETF can improve functional outcomes in patients in the community

- In the systematic review of ETF in the community by Stratton et al. 80% of trials reported improvements in function with ETF. These varied with the patient group and included:[23]
  - ~ improved well-being/quality of life
  - ~ improved pulmonary function
  - ~ reductions in pressure-ulcer surface area

Prophylactic gastrostomy feeding in head and neck cancer patients may improve some aspects of quality of life compared to usual care

- In an evidence update by the National Institute for Health and Care Excellence in the UK, prophylactic gastrostomy feeding in head and neck cancer patients improved some aspects of quality of life at 6 months (as measured by the European Organization for Research and Treatment of Cancer 30-item Questionnaire): physical functioning (p = 0.02), role functioning (p = 0.05), cognitive functioning (p = 0.008), Global Health Status (p = 0.02), and fatigue (p = 0.01) compared to patients receiving usual care. However, these differences were not significant at 12 or 24 months.[26] Note: usual care included nutritional advice and enteral feeding when necessary.

Enteral tube feeding may be associated with stabilization of pulmonary function in CF patients and improvements in perceived quality of life of children with neurological impairment.

- A systematic review assessing the effects of nutritional interventions (including ETF) in patients with cystic fibrosis assessed five studies which described pulmonary function as an outcome measure in CF patients receiving ETF. Two of the five studies showed stabilisation in pulmonary function in the intervention group after 6 and 12 months enteral tube feeding. Two studies demonstrated a gradual decline in pulmonary function after 1 and 2 years of gastrostomy feeding whilst one study found a significant reduction in the rate of pulmonary decline after the start of enteral tube feeding in girls, as well as in adult men (all $p < 0.05$).[25]
- A systematic review of 13 studies looking at the effects of gastrostomy tube placement, on the quality of life of care givers and children with neurological impairment, found no overwhelming conclusions but reported some improvements in perceived quality of life of the child in a thematic analysis.[27]
- In contrast, a Cochrane systematic review on enteral tube feeding in cystic fibrosis found no eligible randomised controlled trials in 2012.[29] The authors acknowledged that such trials would be very difficult to undertake as ethical approval is unlikely to be granted for a trial withholding an intervention which will probably be of benefit.

3.2.4 Clinical benefits of ETF

3.2.4.1 MORTALITY

ETF can reduce mortality rates in hospital patients

- A systematic review by Stratton et al. found that mortality rates were significantly reduced by ETF compared with routine care in some patient groups. Mortality was significantly lower with ETF (11% vs. 23%) (Figure 3.40), with meta-analysis suggesting an odds ratio of 0.48 (95% CI 0.30–0.78). The reduction in mortality occurred to a similar extent in trials with a mean BMI <20kg/m^2 or >20kg/m^2. Weight change (+6-8% difference between ETF and control patients) was associated with improvements in mortality but there was no clear relationship with the duration of ETF.[23]

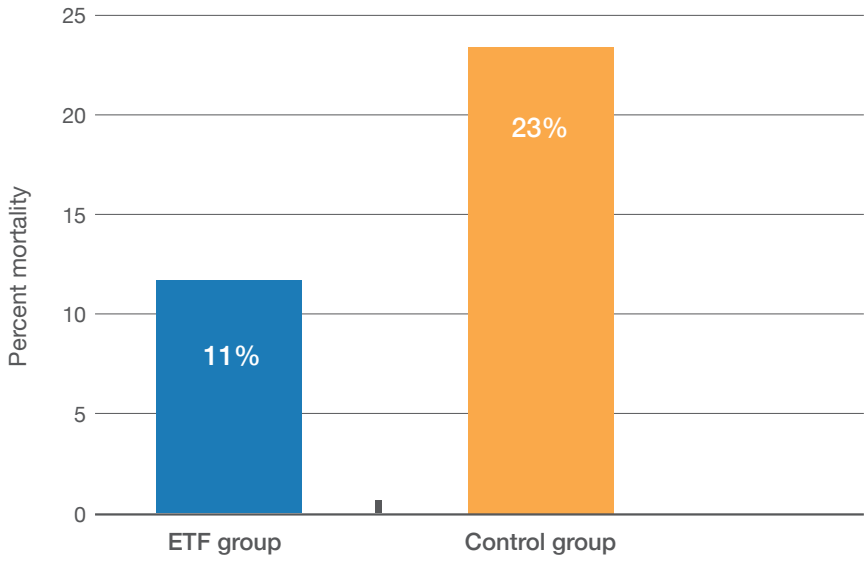


Figure 3.40 **Lower mortality rates with ETF compared with routine clinical care** (12 RCT, *n* = 600) (adapted from Stratton et al. 2003)[23]

Early enteral nutrition is associated with lower mortality in critically ill patients

- In formulating recent international guidelines on nutritional support therapy in adult critically ill patients, a meta-analysis of 21 studies was undertaken and showed that provision of early ETF was associated with a significant reduction in mortality (RR = 0.70; 95% CI, 0.49–1.00; *p* = 0.05) compared with withholding early ETF (delayed ETF or standard therapy) (see Figure 3.41).[30]
- Other meta-analyses have made similar conclusions based on mortality outcomes but patient groups included and definitions of early enteral nutrition vary between studies (see Table 3.8).

Study or subgroup	Early EN Events	Early EN Total	Delayed/None Events	Delayed/None Total	Weight	Risk ratio M-H, random, 95% CI	Year
Sagar 1979	0	15	0	15		Not estimable	1979
Moore 1986	1	32	2	31	2.3%	0.48 [0.05, 5.07]	1986
Chiarelli 1990	0	10	0	10		Not estimable	1990
Schroeder 1991	0	16	0	16		Not estimable	1991
Eyer 1993	2	19	2	19	3.7%	1.00 [0.16, 6.38]	1991
Beier-Holgersen 1996	2	30	4	30	4.9%	0.50 [0.10, 2.53]	1996
Carr 1996	0	14	1	14	1.3%	0.33 [0.01, 7.55]	1996
Chuntrasakul 1996	1	21	3	17	2.7%	0.27 [0.03, 2.37]	1996
Watters 1997	0	14	0	14		Not estimable	1997
Singh 1998	3	21	4	22	8.2%	1.05 [0.30, 3.66]	1998
Kompan 1999	0	14	1	14	1.3%	0.33 [0.01, 7.55]	1999
Minard 2000	1	12	4	15	3.0%	0.31 [0.04, 2.44]	2000
Pupelis 2000	1	11	5	18	3.2%	0.33 [0.04, 2.45]	2000
Pupelis 2001	1	30	7	30	3.1%	0.14 [0.02, 1.09]	2001
Dvorak 2004	0	7	0	10		Not estimable	2004
Kompan 2004	0	27	1	25	1.3%	0.31 [0.01, 7.26]	2004
Peck 2004	4	14	5	13	11.0%	0.74 [0.25, 2.18]	2004
Malhotra 2004	12	100	16	100	26.5%	0.75 [0.37, 1.50]	2004
Niguyen 2008	6	14	6	14	17.5%	1.00 [0.43, 2.35]	2008
Moses 2009	3	29	3	30	5.6%	1.03 [0.23, 4.71]	2009
Chourdakis 2012	3	34	2	25	4.4%	1.10 [0.20, 6.12]	2012
Total (95% CI)		**469**		**467**	**100.0%**	**0.70 [0.49, 1.00]**	
Total events	41		66				

Heterogeneity: Tau^2= 0.00; Chi^2=7.23,, df=15 (P=0.95); I^2=0%

Test for overall effect: Z=1.97 (P=0.05)

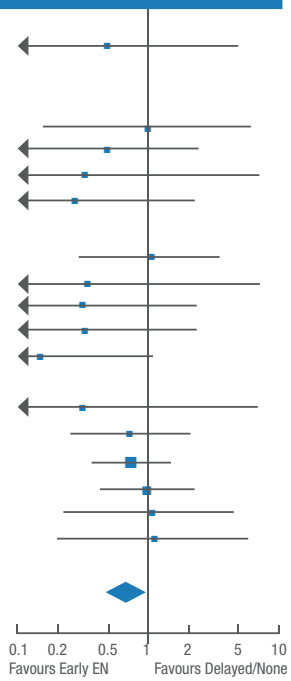


Figure 3.41 **Early Enteral Nutrition (ENN) vs. Delayed enteral nutrition (DEN) associated with a reduced risk of mortality** (adapted from McClave et al. 2016)[30]

Table 3.8 **Overview of meta-analyses looking at timing of enteral nutrition with respect to mortality as an outcome**

Author (year)	Type of study (no. of RCTS)	Patient group	EEN definition	Outcome mortality
McClave et al. (2016)[30]	Meta-analysis (*n* = 21)	Not reported	Not reported	EEN was associated with a significant reduction in mortality (RR = 0.70; 95% CI, 0.49–1.00; *p* = 0.05) compared with withholding early EN (delayed EN or standard therapy)
Li et al. (2014)[31]	Meta-analysis (*n* = 12 RCTs, 625 subjects)	Acute pancreatitis	Within 24 hrs of admission	EEN was associated with a lower mortality rate (16/300 vs. 36/323) (RR: 0.51, 95% CI: 0.30–0.86, *p* = 0.01, I^2 = 34%) compared to TPN or delayed enteral nutrition (DEN)
Li et al. (2013)[32]	Meta-analysis (*n* = 11RCTs, 775 subjects)	Acute pancreatitis	Within 48 hours of admission	EEN was associated with a significant reduction in mortality (OR 0.31; 95%CI 0.14–0.71, *p* <0.05)
Wang et al. (2013)[28]	Meta-analysis (*n* = 5 RCTs and 3NPSs)	Traumatic brain injury	Within 72 hours of admission (5 studies) and within 7 days post injury (2 studies)	EEN was associated with a significant reduction in the rate of mortality (relative risk [RR] = 0.35; 95% CI, 0.24–0.50) *p* = 0.05; I^2 = 44%) compared to delayed feeding
Doig et al. (2011)[33]	Meta-analysis (*n* = 3 RCTs 126 subjects)	Adult trauma patients in intensive care	Within 24 hours of injury	EEN associated with a significant reduction in mortality (OR = 0.20, 95% confidence interval 0.04–0.91, *p* = 0.04, I^2 = 0)

CI Confidence interval; DEN delayed enteral nutrition EEN Early enteral nutrition; EN enteral nutrition; NPSs non-randomized prospective studies; RCTs Randomised controlled trials TPN Total parenteral nutrition

Higher energy and protein intakes in critically ill septic patients over the course of their ICU stay are associated with a lower 60-day mortality

- In a secondary analysis of pooled data collected prospectively from international nutrition studies (*n* = 2,270) in critically ill septic patients with a median length of ICU stay of 11 days, receiving total enteral tube feeding, an increase in energy intake via ETF of 1,000 kcal was associated with reduced 60-day mortality (odds ratio (OR) 0.61; 95% confidence interval (CI) 0.48 to 0.77, *p* <0.001). An increase of 30g protein delivered by ETF was also associated with a reduced 60-day mortality (OR 0.76; 95% CI 0.65 to 0.87, *p* <0.001).[34]
- The same analysis showed that the lowest tertile of energy and protein intake received per day (patients receiving ≤865 kcal/d and ≤39.5 g/d, respectively) was associated with increased 60-day mortality as compared to the highest tertile (patients receiving ≥1,294 kcal/d and ≥58.9 g/d, respectively).[34]

3.2.4.2 COMPLICATIONS

ETF can reduce complication rates in hospital patients

- A systematic review by Stratton et al. found that complication rates were significantly reduced by ETF compared with routine care in some patient groups. Complication rates, including sepsis, wound and urinary infections and pneumonia, were significantly lower with ETF than with routine care (33% vs 48%), with meta-analysis suggesting an odds ratio of 0.50 (95% CI 0.35–0.70). Significant reductions in infective complications were also noted (odds ratio 0.26 [95% CI 0.15–0.44]). Weight change may be associated with the improvements in complications.[23]

Early enteral nutrition is associated with lower complication rates in critically ill patients

- As part of recent guidelines on nutritional support therapy in adult critically ill patients a meta-analysis of 21 studies was undertaken and showed that provision of early EN was associated with a significant reduction in infectious morbidity (RR = 0.74; 95% CI, 0.58–0.93; p = 0.01), compared with withholding early EN (delayed EN or STD) (see Figure 3.42).[30]

Study or subgroup	Early EN Events	Early EN Total	Delayed/None Events	Delayed/None Total	Weight	Risk ratio M-H, random, 95% CI	Year
Sagar 1979	3	15	5	15	3.1%	0.60 [0.17, 2.07]	1979
Moore 1986	3	32	9	31	3.3%	0.32 [0.10, 1.08]	1986
Schroeder 1991	1	16	0	16	0.5%	3.00 [0.13, 68.57]	1991
Carr 1996	0	14	3	14	0.6%	0.14 [0.01, 2.53]	1996
Beier-Holgersen 1996	2	30	14	30	2.5%	0.14 [0.04, 0.57]	1996
Singh 1998	7	21	12	22	7.6%	0.61 [0.30, 1.25]	1998
Minard 2000	6	12	7	15	6.6%	1.07 [0.49, 2.34]	2000
Malhotra 2004	54	100	67	100	20.9%	0.81 [0.64, 1.01]	2004
Kompan 2004	9	27	16	25	9.4%	0.52 [0.28, 0.96]	2004
Peck 2004	12	14	11	13	17.7%	1.01 [0.74, 1.39]	2004
Niguyen 2008	3	14	6	14	3.5%	0.50 [0.15, 1.61]	2008
Moses 2009	17	29	19	30	14.5%	0.93 [0.61, 1.39]	2009
Chourdakis 2012	13	34	12	25	9.8%	0.80 [0.44, 1.44]	2012
Total (95% CI)		**358**		**350**	**100.0%**	**0.74 [0.58, 0.93]**	
Total events	130		181				

Heterogeneity: Tau² = 0.05; Chi² = 19.58, df = 12 (p = 0.08); I² = 39%

Test for overall effect: Z = 2.54 (p = 0.01)

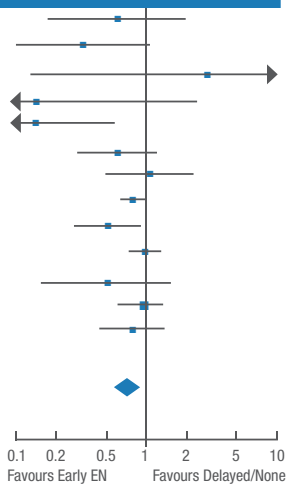


Figure 3.42 **Early enteral nutrition (EEN) vs. Delayed enteral nutrition (DEN) associated with a reduced risk of infectious complications** (adapted from McClave et al. 2016)[30]

High energy and protein intakes delivered by ETF reduce the risk of infectious complications in critically ill patients

- In a meta-analysis of randomised controlled trials (8 RCTS, *n* = 1,895) comparing initial hypocaloric EN versus hypercaloric EN, with different protein intakes, in critically ill patients, there was no statistical difference between the low-energy and high-energy groups in infectious complications (RR, 1.09; 95% CI, 0.92 to 1.29; *p* = 0.32), or the risk of gastrointestinal intolerance (RR, 0.84; 95% CI, 0.59 to 1.19; *p* = 0.33). However, sub group analysis within the same review showed that high-energy intake combined with high-protein intake delivered by ETF reduced the risk of infectious complications (RR, 1.25; 95% CI, 1.04 to 1.52; *p* = 0.02).[35]

Higher protein and energy intakes delivered by ETF are associated with more ventilator free days in critically ill septic patients

- In a secondary analysis of pooled data collected prospectively from international nutrition studies (*n* = 2,270) in critically ill septic patients receiving total ETF, an increase in energy intake via ETF of 1,000 kcal was associated with more ventilator-free days (2.81 days, 95% CI 0.53 to 5.08, *p* = 0.02) as was an increase of 30g protein delivered by ETF per day (95% CI 0.58 to 3.27, *p* = 0.005).[34]

Early enteral nutrition is associated with a reduced rate of complications in critically ill patients

- In a meta-analysis including 12 RCTs, complications associated with early initiation of EN (EEN) in patients with acute pancreatitis were assessed by stratifying relevant RCTs into subgroups according to the starting time of EN (<24 h or between 24 and 72 h after admission). Results showed that EEN, but not TPN or delayed enteral nutrition (DEN), was associated with reduced risk of:[31]
  - ~ pancreatic infection (21/186 vs. 53/206) (RR: 0.44, 95% CI: 0.28–0.69, *p* = 0.0004, I^2 = 0%);
  - ~ organ failure (51/297 vs. 90/317) (RR: 0.59, 95% CI: 0.44–0.79, *p* = 0.0003, I^2 = 10%) (see Figure 3.43);
  - ~ hyperglycaemia (18/116 vs. 51/120) (RR: 0.38, 95% CI: 0.24–0.59, *p* <0.0001, I^2 = 0%);
  - ~ catheter-related septic complications (5/113 vs. 23/117) (RR: 0.29, 95% CI: 0.13– 0.64, *p* = 0.002, I^2 = 0%).

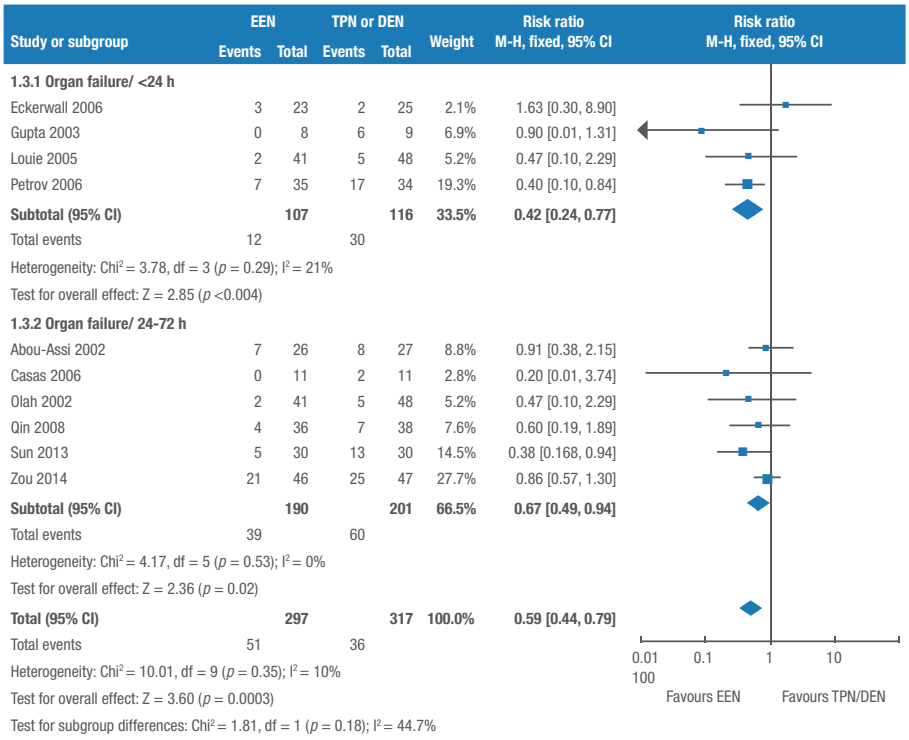


Figure 3.43 **Early Enteral Nutrition (EEN) (vs. Parenteral Nutrition (PN) vs. Delayed Enteral Nutrition (DEN)) associated with reduced risk of organ failure** (adapted from Li et al. 2014)[31]

- Eleven studies containing a total of 775 patients with acute pancreatitis were included in a meta-analysis to assess the effect of EEN on ICU outcomes. Early enteral nutrition was associated with significant reductions in:[32]
  - ~ all infections as a whole (OR 0.38; 95%CI 0.21–0.68, *p* <0.05) (see Figure 3.44);
  - ~ catheter-related septic complications (OR 0.26; 95%CI 0.11–0.58, *p* <0.05);
  - ~ pancreatic infection (OR 0.49; 95%CI 0.31–0.78, *p* <0.05);
  - ~ hyperglycemia (OR 0.24; 95%CI 0.11–0.52, *p* <0.05);
  - ~ the length of hospitalization (mean difference -2.18; 95%CI -3.48-(-0.87); *p* <0.05);
  - ~ no difference found in pulmonary complications (*p* >0.05).

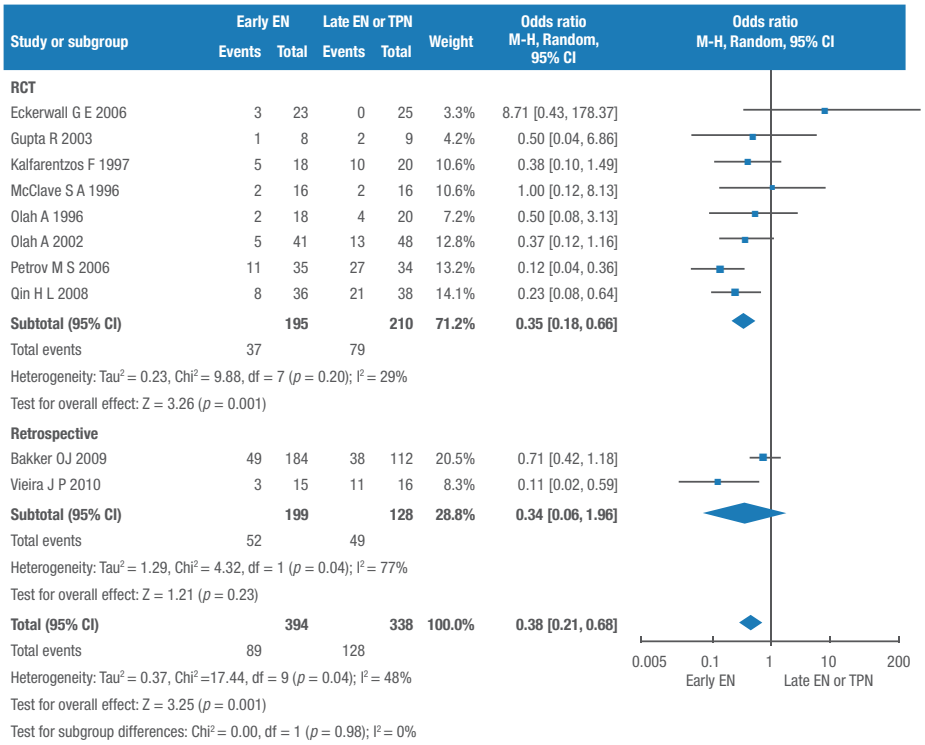


Figure 3.44 **Early Enteral Nutrition (EEN) associated with reduced risk of all infectious complications as a whole in acute pancreatitis** (adapted from Li et al. 2013)[32]

- A meta-analysis which assessed 5 RCTs and 3 non-randomized prospective studies (NPSs) all on patients with traumatic brain injury showed that, compared with delayed feeding, early feeding was associated with a significant reduction in the rate of infectious complications (RR = 0.77; 95% CI, 0.59–0.99).[28 i]
- In a meta-analysis of studies assessing the effect of early enteral nutrition in adult trauma patients in intensive care, the provision of early EN (within 24 hours of injury) significantly reduced the incidence of pneumonia compared to standard EN care provided >24hrs (9/27 vs. 16/25, $p = 0.050$) in one eligible trial.[33]
- In a meta-analysis of individuals from the EN arm of randomised studies, EEN within 24 hours of admission was associated with a lower incidence of complications compared with EN started after 24 hours.[36]
  - ~ EEN within 24 hours of admission was associated with a lower incidence of the primary composite endpoint (adjusted OR of 0.44 [95% CI 0.20-0.96] and an NNT[ii] of 4 patients). The primary composite endpoint included infected pancreatic necrosis, organ failure, or mortality.

[i]This meta-analysis also included two studies that compared early PN vs. delayed EN. It is not possible from the data presented in the paper to separate out the results specific to the early EN studies only. [ii]NNT Number needed to treat

~ The same analysis showed a significant reduction in the rate of organ failure following EN within 24 h of admission (16% compared to 42%; adjusted OR 0.42; 95% CI 0.19-0.94, NNT 4).

ETF can improve clinical outcomes in patients in the community

- In the review by Stratton et al. (2003) some trials suggested improvements in clinical outcome, such as fewer and shorter hospitalizations, lower mortality rates and reduced use of medication in certain patient groups.[23]

PEG placement does not appear to be associated with increased gastro-oesophageal reflux disease (GORD) symptoms in children

- In a systematic review of 8 studies (case series and retrospective reviews) looking at the symptoms of GORD following PEG placement in children there was no difference or a decrease in the severity of GORD following PEG placement in 6 of the reviewed studies.[37]

3.2.5 Economic benefits of ETF

Elia et al. 2015 summarised some of the issues regarding the evaluation of the economic benefit of ETF:[2]

> *'It can be argued that use of ETF/PN in certain groups of hospitalised patients can produce at least some favourable budgetary consequences by aiding recovery from illness and reducing the length of hospital stay. It can also be argued that a cost impact analysis is of limited value when applied to treatments such as home ETF/PN, which are often used to save lives rather than save money. It may be more appropriate to assess the value of home ETF/PN using a cost-effectiveness analysis, based on societal thresholds for willingness to pay, rather than using a budget impact analysis.'*

ETF in the hospital setting may lead to cost savings

- A systematic review of ETF in the hospital setting by Stratton et al. concluded that small reductions in hospital stay may accompany ETF and that cost savings are likely to occur when complication rates are markedly reduced.[23]
- The report from the Malnutrition Action Group of BAPEN and the National Institute for Health Research Southampton Biomedical Research Centre estimated the potential savings from reduced length of hospital stay associated with use of ETF and PN to be approximately €12.4 million[iii] (£11 million) in England (see Table 3.9).[2]

Table 3.9 **Potential annual cost saving from reduced healthcare utilization** (adapted from Elia et al. 2015)[2]

Cost saving	Amount
Reduced length of hospital stay (oral, mainly ONS)	£89,682,364
Reduced length of hospital stay (ETF + PN)*	£11,122,060
Reduced healthcare use (from extra OP activity)**	£11,355,100
Reduced hospital admissions	£9,717,306
Reduced GP visits	£3,866,242
Reduced OP visits	£906,915
Total potential cost saving	**£126,649,987**
	(£115,527,927)†
	(£101,806,313)‡
	(£112,928,474)+

The values shown do not reflect the net balance. They represent the cost savings, from which the costs need to be subtracted to establish the overall net balance or budget impact. The blue shaded areas represent cost savings only when it assumed that the financial benefits are equal to additional costs so that the final budget impact or net cost saving remains cost neutral. Without a cost saving from these sources the potential budget impact is £104,172,827

* Assumed to be equal to the cost of the extra ETF and PN in hospital

** Assumed to be equal to the cost of the extra outpatient (OP) activity, the benefit of which could occur in multiple settings, part of a sensitivity analysis). Other models assumed no cost saving from ETF and PN

† All forms of oral nutrition support only

‡ ONS only

+ Without oral (non-ONS), i.e. ONS, ETF, and PN only

[iii] Calculated based on an exchange rate of 1 GBP = 1.1245 EUR (Source: Interbank 12/07/2017)

- The same report indicates that the use of nutritional support **including ONS, EFT and PN** ultimately saves rather than costs money €134,000 - €486,000[iv] (£119,000 – £432,000 per 100,000 depending on the model used) (see Figure 3.45). It is necessary to make a commitment to invest money before the financial benefits can be reaped.

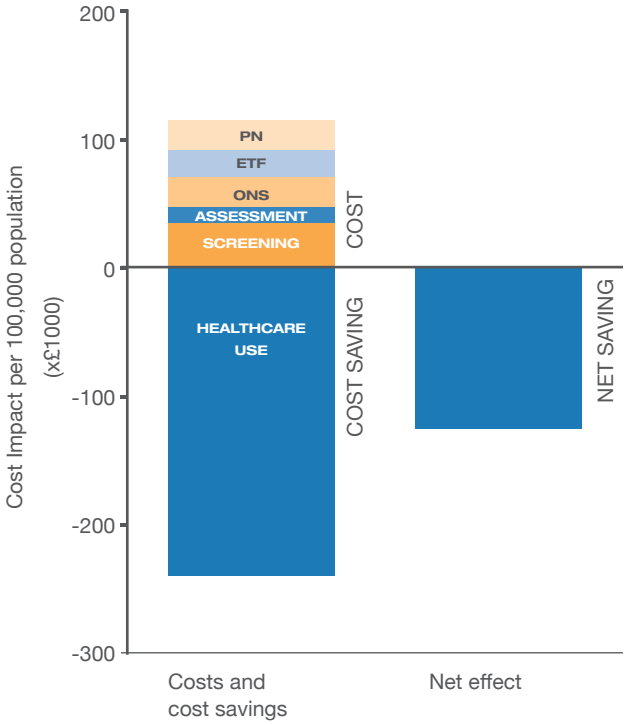


Figure 3.45 **The costs, cost savings and budget impact (net effect) of providing nutritional support to 85% of subjects with high risk of malnutrition.**
(Adapted from Elia et al. 2015)[2]
PN = parenteral nutrtion, ETF = enteral tube feeding, ONS = oral nutritional supplements.

ETF in the community can be cost-effective in adults and children

- A systematic review of ETF in the community by Stratton et al. concluded that the increasing use of ETF at home provides substantial cost saving to the hospital but places greater demands on carers in the community, who are often family members.[23]
- A multi-centre observational study was undertaken in 4 Polish medical centres after the introduction of reimbursement for commercial ETF (n = 456, 142 children and 314 adults). Before this point all patients who required HETF used 'homemade blenderised kitchen diets' administered via their feeding tube. Data was collected retrospectively for a 12-month period on homemade feeds and prospectively for a 12 month period on commercial feeds. In terms of healthcare resource use there were significant reductions in:[17]
  - ~ Number of hospital admissions (1.98 ± 2.42 vs 1.26 ± 2.18, p <0.001)
  - ~ Length of hospital stay (39.7 ± 71.9 days vs 11.9 ± 28.5 days, p <0.001)

  Use of ETF for over one year decreased the average length of stay by 27 days (39.7 vs 11.9 days, p <0.001). Mean (± SD) annual costs for hospitalisation were reduced from €5663 ± 9063 to €1806 ± 4789[v] ($6500 ± 10403 to $2073 ± 5497). The authors attribute the reduction in complications and hospital stay to the introduction of commercial ETF products which are nutritionally complete minimising the risk of inadequate or incorrect nutrient delivery and saving carer time, along with the introduction of professional complex care.[17]

[iv]Calculated based on an exchange rate of 1 GBP = 1.1245 EUR (Source: Interbank 12/07/2017). [v]Calculated based on an exchange rate of 1 USD = 0.8712 EUR (Source: Interbank 12/07/2017)

Home enteral tube feeding in stroke patients is cost-effective

- A systematic review looking at the economic value of enteral medical nutrition in the management of disease-related malnutrition included one study[38] that focused on long term home enteral tube fed CVA patients living in the community (own home and nursing homes). Enteral tube feeding at home was found to be cost-effective using the cost threshold of €22,490 - €33,735/QALY[vi] (£20,000 - £30,000/QALY) set by the National Health Service in England. The incremental cost-utility ratio (extra costs/extra QALY) of €14,413[vi] £12,817/QALY €11,640 - €18,921[vi] [£10,351-£16,826 using 95% CI for quality of life] was far below the used cost threshold. The same intervention given to patients with CVA in nursing homes was cost-effective only in terms of cost/QALY when the non-medical costs were paid privately (€11,587[vi] £10,304 [below the cost threshold] vs. €76,538[vi] £68,064 if paid by the state [above the cost threshold]).

[vi]Calculated based on an exchange rate of 1 GBP = 1.1245 EUR (Source: Interbank 12/07/2017)

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3 BENEFITS OF MEDICAL NUTRITION

3.3 Indications, use, and benefits of Parenteral Nutrition (PN)

Summary and recommendations

Parenteral nutrition (PN) is a life-sustaining therapy for patients who cannot be fed adequately and/or safely with food, oral nutritional supplements (ONS) or enteral tube feeding (ETF) for a long period, such as those with intestinal failure (IF). PN is primarily indicated to prevent or treat malnutrition in these patients; without PN, they would die from dehydration and starvation. PN is also used to aid recovery when the gastrointestinal (GI) tract requires rest, and perioperative PN may be used in patients who are malnourished or at high nutritional risk, to prevent nutrition-associated complications after surgery when sufficient oral and/or enteral intake is not feasible. PN can be used to supplement oral or enteral feeding or as the sole source of nutrition (total PN).

PN can be used for patients of any age, and across all healthcare settings (e.g., hospitals, nursing/residential homes, and patients' own homes). International and internationally recognized guidelines recommend that PN should be administered as soon as possible in critically ill adults and children who cannot be fed by the oral or enteral routes. Use of PN has transformed the prognosis for many patients with previously fatal conditions, and is considered one of the most important advances in therapeutics over the last four decades.

Because PN is a life-sustaining therapy for patients with IF, evaluation of its efficacy compared with no nutrition support in randomized controlled trials (RCTs) is not possible. Furthermore, clinical guidelines note that the ability of PN to preserve quality of life (QOL) and promote rehabilitation supports its use in the home setting.

Home PN (HPN) is the cornerstone of treatment for adults and children with chronic intestinal failure and is considered the best option for improving QOL in children with conditions that require long-term PN, and their families. Moreover, since its introduction in the 1970s, use of HPN has expanded to include patients with IF due to cancer or chronic radiation enteritis and also certain patients with incurable cancer. HPN is a life-saving therapy for patients with cancer who are at risk of death from malnutrition rather than disease progression.

There is little systematic review evidence for the efficacy of PN. However, a number of RCTs and many prospective and retrospective observational studies have shown nutritional (Section 3.3.2), functional (Section 3.3.3) and clinical (Section 3.3.4) benefits with PN in a variety of different age groups, conditions, and healthcare settings. Higher protein and energy intake in critically ill patients is associated with significant reductions in-hospital and 60-day mortality rates and shorter time to discharge alive. Nutrition guidelines recommend that critically ill patients who are malnourished or at nutritional risk receive adequate nutritional support to prevent the significant morbidity and mortality that is associated with starvation or underfeeding in these patients. Perioperative PN is also associated with a reduction in major and infectious complications following surgery in patients who are malnourished or cannot be fed via the oral or enteral routes.

Development of evidence-based guidance on the safe management of PN in the hospital and community settings, together with the introduction of multichamber bag (MCB) technology and alternative IV lipid emulsions, has made PN safe and effective for both short- and long-term use. Recently published studies, including two multicentre randomized studies involving 2,338 and 1,372 critically ill patients, found no increased risk for infectious complications with PN compared with ETF. Published data about the potential cost savings and cost-effectiveness of PN across healthcare settings and in different countries are limited. However, the cost of PN has been shown to compare favourably with the cost of other

supportive treatments used in the intensive care unit (e.g., dialysis). Furthermore, a cost-minimization analysis from the US acute care perspective showed that timely use of PN significantly and meaningfully reduced the total cost of acute hospital care by US$3,150 per patient. Timely use of supplemental parenteral nutrition (ETF + PN) has also demonstrated cost-effectiveness in patients who are not able to achieve at least 60% of their target energy intake by day 3 of admission to ICU, through a reduction in the incidence of hospital-acquired infections. Use of premixed MCBs, which are suitable for most patients requiring PN, also realize considerable cost savings by reducing manpower costs and the risk of bloodstream infections (reducing morbidity, mortality, and costs). HPN also plays a key role in shortening the length of hospital stay for patients who are ready for discharge but who require intravenous nutrition, which may yield considerable cost savings for the healthcare system.

Conclusion

PN is an important life-sustaining therapy that is used across all healthcare settings in patients of all ages with a variety of medical conditions. The use of HPN is increasing, particularly in patients with cancer and in children with chronic conditions. PN has demonstrated nutritional, functional, and clinical benefits, and data are accumulating to show that it is a cost-saving therapy and compares favourably with other supportive therapies used in the ICU (e.g., dialysis).

Recommendations

On the benefits of **PN**, the MNI makes the following recommendations.

Action	Issues to consider
The available evidence demonstrates the benefits of PN, in a wide range of patients, and it is life-saving in those who cannot achieve adequate nutrition (as defined in guidelines) through the oral or enteral routes. This should be translated into practice, to ensure that patients who need PN receive it in a timely and appropriate manner.	• Information about the benefits of PN and how it should be used in practice, including appropriate use of commercial multichamber bags, should be included as part of education and training on the management of nutrition • Patients' progress should be monitored regularly and documented in their nutritional care plan, including the types of nutritional intervention used • PN is a life-saving technique and should be available to all patients when needed; access or ability to pay should not be a constraint

3.3.1 Indications for PN

Parenteral nutrition (PN) is a life-sustaining therapy for adults and children when oral and enteral nutrition are contraindicated or inadequate

- PN refers to the IV infusion of nutrients directly into the bloodstream, bypassing digestion in the bowel and stomach. PN solutions comprise amino acids, glucose (dextrose), and lipids, and should also include electrolytes, vitamins, and trace elements.[1] PN solutions are preferably administered using either individually compounded all-in-one (AIO) admixtures or standardized commercial MCBs.[1]
- PN is a life-sustaining therapy for patients who cannot be fed adequately and/or safely with food, oral nutritional supplements (ONS) and/or enteral tube feeding (ETF) for a long period, such as those with intestinal failure (IF);[2] Its primary role is to prevent or treat malnutrition. PN is also used in conditions where rest of the GI tract is required to aid recovery, for example, when there is inflammation, fistulae, or obstruction,[3; 4] and perioperatively for certain patients who are malnourished or are at risk of malnutrition,[5] to reduce the risk of preventable post-surgical nutrition-associated complications. PN may be required short term, long-term, or sometimes for the patient's lifetime, depending on the underlying disease or condition.
- PN can be administered in children and adults through either a central or peripheral vein, depending on the duration of treatment and indication. Patients who are not severely malnourished, require PN for less than 2 weeks, and who have no other need for central venous access may be fed via a peripheral vein (PPN).[6; 7] When used appropriately, PPN may provide benefits over centrally administered PN, such as ease in establishing peripheral access, which may prevent delays in initiating nutrition support, and avoidance of complications (e.g., sepsis) and costs associated with use of a central venous catheter.[8] However, PPN may not meet the energy and protein needs of all patients (e.g., patients who are fluid restricted or require long-term PN support) because the osmolarity of the solutions limits the macronutrient concentrations.[9; 10] Peripheral vein thrombophlebitis is often the rate-limiting factor when trying to optimize peripheral PN solutions;[11] ESPEN and ASPEN guidelines recommend that, to reduce the risk of thrombophlebitis, the osmolarity of peripheral solutions should not exceed 850 mOsm/L or 900 mOsm/L, respectively.[12-14] PN solutions with osmolarity below 850 mOsmol/L are available.
- Most patients receiving PN require a central line, which allows delivery of nutrients directly into the superior vena cava or the right atrium—the tip of the catheter is placed in the lower third of the superior vena cava (at the trio-caval junction, or in the upper portion of the right atrium).[12] In hospital, PN can be administered through a dedicated peripherally inserted central catheter (PICC) or a non-tunnelled central venous catheter (CVC).[12; 15] However, a tunnelled catheter or a totally implantable device is recommended for long-term use (>30 days) as these devices are associated with a lower risk of thrombosis and infection.[12; 15-17]

PN can be used to supplement dietary intake, ONS, and/or ETF (supplemental PN—SPN) or may be used as the sole source of nutrition (total parenteral nutrition—TPN)

- Depending on the patient's needs, PN may be used as the sole source of nutrition (TPN or exclusive PN) or in addition to ETF (SPN, partial PN, complementary PN).
- The major indication for TPN is failure of the GI tract due to conditions such as short-bowel syndrome (SBS), severe gut dysfunction, mesenteric vascular insufficiency, bowel obstruction, GI bleeding, severe diarrhoea, high-output fistula, sepsis, severe burns, and trauma associated with continuous haemodynamic instability or severe fulminant acute or chronic pancreatitis.[18] TPN does not require a functioning GI tract or access to the gut, nutrient delivery is not affected by abdominal distension, fistula drainage, ischemia, or nausea/vomiting.[18] TPN may be life-saving for patients with GI tract failure.[19; 20] TPN can also be used to delay surgical intervention in patients that cannot be fed adequately via the oral or enteral routes, avoiding prolonged, progressive malnutrition which greatly increases the risk of peri- and post-operative complications.[18]
- SPN is typically indicated when oral or enteral routes cannot alone achieve the patient's energy and protein targets defined in their nutritional care plan.[1]

PN is an established therapy in children, and has transformed the outcomes for many previously fatal conditions

- Children are particularly susceptible to starvation because they require nutrients for normal growth and development as well as for maintenance of body tissues, particularly during infancy and adolescence when growth is rapid.[21] Small preterm infants (<1 kg) can survive only 4 days' starvation, and less than 2 days if there is underlying disease that increases energy expenditure. Withholding nutrition for just 1 day may therefore have negative consequences.[21] Suboptimal feeding may slow or stunt growth, resulting in long-term adverse effects such as extrauterine growth restriction and poor neurodevelopment.[22; 23] A growing body of evidence also suggests that undernutrition during early critical periods of development is associated with significant adverse effects that may persist into adulthood, a concept known as programming.[24-27]
- PN is considered to be one of the most important advances in paediatric therapeutics over the last four decades. It is life-saving for children who cannot be adequately fed by the oral or enteral route, because, for example, severe IF or functional intestinal immaturity.[21]

Home PN (HPN) has a key role in shortening the hospital stay in patients who are ready to be discharged but who require intravenous nutrition

- PN can be administered in both the hospital and community settings. HPN is not a treatment in itself but allows the provision of PN outside the hospital, typically the patient's own home or residential care/nursing home. HPN was introduced in the early 1970s, primarily for patients with benign chronic IF (i.e., with no underlying malignancy).[28] Before this, effective delivery of long-term PN was not possible and patients with permanent IF due to major intestinal resection, fistulas, or immature development of the GI tract, died within a few months of diagnosis from malnutrition, dehydration, and/or electrolyte disturbances.[29] However, advances in the preparation and administration of HPN over the past four decades have led to dramatic improvements in survival for these patients (now measured in decades[30]) and enables many to resume normal activities, including employment, within the constraints of their underlying disease.[31] A large proportion of patients on HPN improve over time and are able to resume normal feeding, such as those with hyperemesis gravidarum (100%), CD (70%), chronic pancreatitis (82%), or chronic adhesive obstruction (47%).[30]

- The indications for HPN have expanded beyond benign chronic IF to include appropriate patients with cancer, including certain patients with incurable disease (see Section 3.3.1.1). However, this varies across countries (see Section 3.3.1.2).
- HPN also has a key role in shortening the length of hospital stay for patients who are ready to be discharged medically but who still require IV nutrition; this may yield considerable cost savings for healthcare systems (see Section 3.3.5).[32]

HPN is considered the best option for improving quality of life (QOL) in children with diseases requiring long-term TPN or SPN, and their families

- Long-term TPN or SPN is indicated to preserve nutritional status and facilitate normal growth and development in children when oral or enteral feeding is not sufficient to meet nutritional needs.[21] SBS, mostly congenital, accounts for at least 30% of cases of IF in children. Other diseases that impair digestive function include intractable diarrhoea of infancy, chronic intestinal pseudo-obstruction, and inflammatory bowel disease (IBD), particularly Crohn's disease (CD). The main non-digestive indications for long-term PN in children are HIV/AIDS, cancer, metabolic diseases, and end-stage liver disease prior to transplantation, which account for about 20% of all patients. However, the need for HPN is typically shorter for these non-digestive conditions than for primary digestive diseases. HPN provides an alternative to prolonged hospitalization for children requiring long-term PN and is recognized as the best option for improving the QOL for both the child and their family, within the constraints of the underlying disease.[21]

3.3.1.1 INDICATIONS FOR PN IN SPECIFIC PATIENT GROUPS

PN is used to provide nutritional support to adults and children with a variety of diseases and conditions. This section provides a summary of the main indications for PN in specific patient groups and a comparison of ASPEN and ESPEN guideline recommendations for each condition. Please refer to tables in Section 4.3 for recommendations and guidance from other international and internationally recognized guidelines.

GASTROINTESTINAL DISEASE

PN provides critical short- or long-term nutrition to patients with gastrointestinal dysfunction and is potentially life-saving in children with chronic intestinal failure

- Diseases and conditions that involve the digestive system (oesophagus, stomach, small and large intestines, rectum, liver, gallbladder, and pancreas) can make it challenging to achieve adequate nutrition using the oral or enteral routes.[33] PN may be required short term (see Table 1) when the gut is temporarily unavailable (known as transient intestinal insufficiency).[34] In such cases, when gut function begins to recover, food, ONS or ETF can be carefully reintroduced whilst PN is slowly reduced, ensuring that total nutritional requirements continue to be met.2 However, PN may be required long term, or even permanently, for conditions that result in chronic IF, such as SBS (see Table 1).[34] SBS results from an inadequate length of intestine after surgical resection (<200 cm).[35] The prevalence of SBS is estimated to be 3 to 4 cases per million population, depending on geographical region.[36]

Table 1 Gastrointestinal conditions that may require short- or long-term PN[34]

Short-term PN required	Long-term PN required
• Post-operative ileus (a delay in gut motility that can occur after major abdominal surgery) • Severe pancreatitis • Mucositis (pain and inflammation of the mucous membrane lining the GI tract) caused by intensive chemotherapy • Multi-organ failure where nutritional requirements cannot be met by ETF alone • Prolonged nil by mouth (e.g., following surgical resection) • High output fistula—an abnormal opening in the digestive tract that causes a large amount of gastric fluids to leak through the lining of the stomach or intestines (≥500 mL/day)	• Short bowel syndrome (SBS) • Unresolved high output fistula • Inflammatory bowel disease with concomitant fistula or SBS • Chronic radiation enteritis (inflammation of intestinal lining following radiation therapy) • Motility disorders (e.g., scleroderma) • Chronic malabsorption

Abbreviations: ETF, enteral tube feeding; GI, gastrointestinal; SBS, short bowel syndrome

PN (TPN or SPN) is typically used to maintain nutritional status in patients with acute intestinal failure (AIF) and enterocutaneous fistula (ECF)

- ESPEN defines IF as reduction in GI function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes, such that IV supplementation is required to maintain health and/or growth.[35] IF is an umbrella term that includes surgical SBS due to intestinal resection for congenital or acquired GI diseases and disorders of gut motility. IF is functionally classified as Types I, II, and III, based on onset, metabolic, and expected outcome criteria.[37] Types I and II IF are considered acute conditions. Type I is considered short term and is typically self-limiting, whereas Type II is prolonged and may require PN over weeks or months.
- Patients with Type II AIF usually have a high output fistula or enterostomy, sepsis, and complications associated with SBS.[38; 39] Optimization of nutritional status is a key aspect of therapy alongside treatment of the underlying condition.[38] In patients with AIF who develop sepsis it is important to minimize negative energy and protein balance and muscle loss (by preventing starvation) and maintain tissue function, particularly in the liver, immune system, skeletal muscles, and respiratory muscles.[38; 40]
- ESPEN guidelines note that although ETF is the route of choice for nutritional support in patients with AIF and ECF, it is unlikely to be sufficient because of the extent of injury to the GI tract.[38] Therefore, PN is typically used, either alone (TPN) or in combination with ETF (SPN). Additionally, guidelines jointly published by ASPEN and the Federación Latino Americana de Terapia Nutricional, Nutrición Clínica y Metabolismo (FELANPE) state that PN (TPN or SPN) may be required for patients with high-output ECF (>500 mL/day) to meet fluid, electrolyte, and nutrient requirements to support spontaneous (or surgical closure) of the ECF.[3]

- Although ASPEN has not published specific guidance relating to type II AIF, these patients often require admission to an ICU. Therefore, ASPEN–SCCM guidelines on nutrition support therapy in adults with critically illness apply (see subsection CRITICAL ILLNESS), as do ASPEN consensus recommendations on appropriate PN use.[14] These guidelines state that PN should be used in patients who are malnourished or at risk for malnutrition when there is a contraindication to ETF (or the patient cannot tolerate adequate ETF) or if gut function is not sufficient to preserve or restore nutrition status.[14]

PN is a life-sustaining therapy for children and adults with conditions resulting in chronic intestinal failure (CIF)

- Type III IF is a chronic condition that requires PN over months or years.
- Five main pathophysiological conditions underlie CIF: SBS, intestinal fistula, intestinal dysmotility, mechanical obstruction, and extensive small bowel mucosal disease,[35] which may occur as a result of various GI or systemic diseases.[35] In patients with SBS, intestinal fistula, or extensive small bowel disease, IF is caused by surgical (or disease-related) reduction or bypass of the absorptive mucosal surface, resulting in malabsorption of ingested food. In patients with intestinal dysmotility or intestinal mechanical obstruction, IF is caused by feed-related digestive symptoms or episodes of mechanical or non-mechanical intestinal obstruction, resulting in limited tolerance of ONS or ETF.[35] CIF is the rarest form of organ failure and may be caused by severe benign GI or systemic disease or the end stage of intra-abdominal or pelvic cancer.[35]
- Regardless of the underlying aetiology, PN is a life-saving therapy for children and adults with CIF and may be needed for the patient's lifetime unless the condition can be reversed surgically.[35] ASPEN guidelines on nutrition support therapy in critically ill adults note that PN should be continued in patients with SBS upon admission to the intensive care unit (ICU) unless bacteraemia is suspected.[41]

HPN is the cornerstone of treatment for adults and children with CIF

- HPN allows the provision of nutrients for individuals with CIF; it is associated with 5 year survival rates of about 80% for adults and 90% for children.[42] HPN enables many patients to live a normal life within the constraints of their condition. About two-thirds of adults are able to partly or fully resume normal social and working activities while on HPN.[43]
- US and European guidelines recommend that HPN be considered for adults with IF who are clinically stable and able to receive therapy outside of the acute care setting.[14; 28] ESPEN guidelines recommend that HPN should be administered without delay in malnourished patients with chronic GI motility dysfunction resulting from chronic intestinal pseudo-obstruction and in malnourished patients with radiation enteritis if ONS/ETF is not adequate.[35] Additionally, ETF or ONS may be used alongside PN in adults with SBS and a low-level of HPN dependence, if the expected gain with ETF could enable the patient to be weaned off HPN.[35]
- ESPGHAN guidelines recommend that all children who need long-term PN should be discharged on HPN as long as social and familial requirements are met.[21] Similarly, ASPEN consensus recommendations state that HPN should be considered in carefully selected clinically stable paediatric patients who are expected to require PN for a prolonged period; however, PN should be initiated in the hospital setting.[14]

PN is life-saving in patients with Crohn's disease (CD) who have prolonged gastrointestinal failure

- IBD comprises Crohn's disease (CD) and ulcerative colitis (UC). CD can involve any section of the GI tract from the mouth to the rectum whereas UC is restricted to the colon. Therefore, malnutrition is more common in patients with CD (20–85% of patients) and is particularly prevalent in patients with IF resulting from SBS due to CD.[44-46] Malnourished patients with IBD are at increased risk for hospitalization following emergency department attendance[47] and are more likely to be admitted to hospital with infection (27.5% of all IBD hospitalizations).[48] Infections account for significant morbidity and mortality in patients with IBD.[48]
- Patients with IBD are at risk of protein–energy malnutrition as a result of poor oral intake, malabsorption due to active disease or bowel surgery, high protein catabolism due to systemic inflammation, and the adverse effects of treatment.[49] Protein requirements are therefore increased in patients with active IBD (1.2–1.5 g/kg per day).[4]
- Malnutrition is frequent in children and adults with CD and may result in impaired muscle function and growth retardation in up to 40% of children and adolescents.[50] Two-thirds of hospitalized paediatric patients with CD have negative nitrogen balance at presentation.[51] Therefore, nutrition support has become an important adjunctive therapy for these patients.[50]
- In patients with IBD who are unable to maintain or recover nutrition status because of an impaired GI function, PN is essential to prevent further nutritional loss, restore homeostasis, and prevent long-term sequalae of malnutrition.[51]
- ESPEN guidelines on clinical nutrition in IBD, published in 2017, recommend PN in patients with IBD when ONS or ETF is not sufficient (e.g., when the GI tract is dysfunctional or in CD patients with SBS) and for patients with an obstructed bowel when there is no possibility of placing a feeding tube beyond the obstruction, or this has failed, or other complications arise such as an anastomotic leak or a high-output intestinal fistula.[4] PN is also indicated in surgical patients with the aforementioned conditions and in patients who cannot tolerate ETF or in whom nutrition cannot be maintained with ETF.
- The ESPEN IBD guidelines[4] highlight that recently published guidance by ESPEN on nutrition in the surgical patient[5] (see subsection on SURGERY) also applies to patients with IBD undergoing surgery, namely, if energy and nutrient needs cannot be met by oral and enteral intake (<50% of caloric requirement) for more than 7 days, combined EN and PN is recommended. Moreover, PN should be administered as soon as possible if nutrition therapy is indicated and there is a contraindication for EN (e.g., intestinal obstruction). ESPEN IBD guidelines recommend that patients admitted for emergency surgery should receive ETF or PN if they are malnourished or oral diet cannot be resumed within 7 days after surgery. Furthermore, non-emergency surgery for IBD should be delayed for 7–14 days, if possible, if the patient is malnourished to allow intensive artificial feeding[4]—studies in patients undergoing GI surgery (non-IBD) [52-57] show that malnutrition has a negative impact on clinical outcomes, rate of postoperative complications, and mortality. ETF should be used in preference to PN in the perioperative phase; however, SPN should be considered in patients requiring nutrition support if >60% of their energy needs cannot be met with ETF.4 TPN should only be used if ETF is not possible or contraindicated. However, ESPEN recommends that patients with CD undergoing surgery should receive early nutritional support (independently of the route of administration),[4] as it reduces the risk for postoperative complications.[58; 59]

- For patients with active CD undergoing surgery, ESPEN guidelines[60] recommend that preoperative PN is used to improve nutritional status only when other modes of nutrition are not possible;[61] however, patients with a proximal and/or very-high-output fistula should receive SPN or TPN,[60] as preoperative optimization of nutritional support increases the likelihood of successful surgical correction of this condition.[62]
- CD is one of the most common reasons for SBS in adults (along with mesenteric artery thrombosis and irradiation damage),[50] resulting from frequent surgery and bowel resection;[63; 64] younger patients with CD who have undergone multiple small-bowel resections are at particularly increased risk for SBS.[65] ESPEN guidelines state that PN is a mandatory and life-saving therapy in patients with CD and prolonged GI failure, such as those with SBS, at least in the early stages of IF.[4] Patients with UC are less likely to require PN because they are typically well-nourished when in remission.[50] ESPEN guidelines recommends PN in patients with UC only if they have IF.[4]
- ASPEN has not published any recent guidance specifically addressing the use of PN in patients with IBD. Consensus recommendations published by ASPEN in 2017 state that use of PN in adults should not be based solely on disease state but should be used in patients who are malnourished or at risk for malnutrition when ETF is contraindicated or not tolerated or the patient has inadequate bowel function to maintain or restore nutrition status.[14] Similarly, TPN or SPN should be initiated in paediatric patients, when indicated, if ETF is not feasible or sufficient to meet total nutrient needs.[14] ASPEN–SCCM guidelines on nutrition in patients with critical illness (discussed in the subsection CRITICAL ILLNESS) will also apply to patients with IBD who are admitted to the ICU.[41]

CRITICAL ILLNESS

Many critically ill patients are malnourished or will become malnourished while in the ICU, leading to poor clinical outcomes and higher healthcare costs

- Critically ill patients are often malnourished when admitted into the ICU.[66] Rates of malnutrition at admission of 20–68% have been reported for acutely ill patients,[67-71] and rates of about 50% for critically ill patients admitted to the ICU.[72-74] Furthermore, failure to provide optimal calories and protein during critical illness can result in deterioration of nutritional status in patients who are not malnourished and can promote further nutritional decline in patients with existing malnutrition.[75]
    - Critical illness typically induces a state of catabolism[41] which promotes a systemic inflammatory response and nutritional deterioration. Systemic inflammation has been shown to alter both the structure and function of the GI tract,[41] leading to inadequate nutritional intake.[76] Studies suggest that up to 60% of patients in the ICU experience impairments in GI motility, digestion, or absorption, which can result in an energy deficit and loss of skeletal muscle.[77-79] Critical illness is also associated with increased energy expenditure, the magnitude of which is positively related to the severity of injury.[75] Insufficient energy provision in patients with critical illness leads to the breakdown of protein tissues such as muscles and organs.[75; 80] Thus, energy requirements should be accurately assessed in critically ill patients, and balanced nutrition provided in order to avoid the adverse effects of under-or overfeeding.[75]

- Malnutrition and loss of muscle tissue in critically ill patients, whatever the cause, is associated with worse outcomes, such as weakness, respiratory failure, increasing dependency on ventilatory support, increased risk of pressure ulcers, delayed wound healing, insulin resistance, compromised immune function, resistance to infections, higher healthcare costs, and increased mortality.[81-93] Patients who have lost skeletal muscle also require longer rehabilitation to resume normal life.[94] The cost of treating a malnourished patient is estimated to be 2–3 times higher than for a non-malnourished patient.[95] By contrast, sufficient energy and protein provision during critical illness is associated with fewer infectious complications,[96] shorter duration of mechanical ventilation,[91] faster recovery,[97] and reduced mortality,[91; 92; 97; 98] especially in patients with poor nutritional status. Provision of nutrition support in patients who are malnourished or at high nutritional risk is also cost-saving by reducing requirements for healthcare resources.[99]

- Worldwide, most adults in the ICU, including those at high nutritional risk, do not achieve protein and energy targets, even though clinical guidelines highlight the importance of adequate nutrition during critical illness.[100-102] Data from the 2013 International Nutrition Survey (INS) of clinical practice in 201 ICUs from 26 countries, involving some 4,000 patients, showed that, on average, critically patients received approximately 60% of prescribed calories and 58% of prescribed protein.[100] It is estimated that 43–88% of critically ill patients have a protein-energy deficit.[103; 104]
  - Underfeeding is common in the ICU because of prolonged periods nil by mouth, feeding intolerance, interruptions to feeding and inappropriate use of nutrition support. Appropriate and timely nutrition support may also be avoided because of traditional concerns about the safety of feeding during critical illness.[101] Studies have been carried out to identify the reasons for feeding interruptions in the ICU. One prospective observational study conducted in three ICUs found that presumed feeding intolerance (gastric residual cutoff 120–200 mL across the three centres) was the primary reason for interruption of feeding, followed by intubation/extubation and tests/procedures. Another prospective observational study conducted over 3 months in a medical ICU reported an average of 5 hours' feeding interruption per day.[105] As a result, patients received only about 64% of their daily energy requirements. Interruptions for tests and procedures accounted for approximately 36% of the total interruption in feeding time, followed by changes in body position (15%), unstable clinical conditions (13.5%), high gastric residual volume (11.5%), and nausea and vomiting (9.2%). Similar findings have been reported in other observational studies.[106-109]

- To prevent muscle loss in critically ill patients,[84] sufficient protein and non-protein energy is required.[110] Nutrition guidelines therefore recommend that critically ill patients who are malnourished or at nutritional risk receive adequate nutritional support to prevent the significant morbidity and mortality that is associated with starvation or underfeeding.[111]
  - ESPEN and ASPEN-SCCM guidelines[41; 90] and expert opinion[112] recommend that sufficient (high-dose) protein should be provided to critically ill patients. Protein requirements in critically illness are expected to be 1.2–2.0 g/kg actual body weight per day, and are likely to be higher in patients with burns or multiple trauma.[41; 90; 112]
  - ESPEN guidelines recommend that, during acute illness, energy provision should be as close as possible to measured energy expenditure, in order to improve negative energy balance.[90] In the absence of indirect calorimetry, patients should receive 25 kcal/kg per day increasing to target over 2–3 days. Similarly, ASPEN–SCCM guidelines recommend that if indirect calorimetry is unavailable, a published predictive equation or a weight-based equation (25–30 kcal/kg per day) should be used to determine energy requirements.[41]

Critically ill infants and children often accumulate substantial energy and protein deficits while in the ICU that are associated with deterioration in nutritional status

- Underfeeding in critically ill children is common during the initial days of ICU admission, and nutrition support is often delayed until patients are clinically stable, which may be several days.[113; 114] However, adequate nutrition and restoration of energy balance are crucial to ensure a good clinical outcome and survival in critically ill children,[115] especially because of their intrinsically high anabolic drive and lower nutrient reserves compared with adults.[116]
- Children admitted to the ICU are at risk of deterioration of nutritional status because energy and protein intake is often less than recommended.[117] A prospective observational study that assessed daily nutritional intake in a mixed population of 261 critically ill children admitted to a tertiary PICU in the Netherlands reported substantial cumulative energy and protein deficits during the first 14 days of admission.[118] Moreover, these deficits had significant negative effects on growth parameters, such as mid-upper arm circumference (energy: $p = 0.025$ for term neonates and older children; protein: $p = 0.033$ for cumulative deficit of 10 g/kg) and weight (energy and protein both $p < 0.001$).
- Many studies have shown that infants and children who have impaired nutrition status and nutrient delivery during critical illness are more likely to experience adverse clinical outcomes, such as longer periods of ventilation, infectious complications, longer PICU and hospital stay, and increased risk of dying.[73; 119-122]

Guidelines agree that in critically ill patients who are malnourished or at nutrition risk, TPN should be started within 24–48 hours of ICU admission if ETF is not feasible or is contraindicated

- ESPEN recommends that TPN should be administered within 24–48 hours if ETF is contraindicated and the patient is not expected to resume oral nutrition within 3 days of ICU admission.[111] Similarly, ASPEN–SCCM guidelines recommend that TPN is administered as soon as possible following admission to the ICU in patients who are severely malnourished or at high risk for malnutrition if ETF is not possible.[41]

Whilst there is no consensus on when to start SPN in the ICU, many experts suggest timely initiation where nutritional intake from other routes is inadequate

- International guidelines differ regarding the timing of SPN in patients with critical illness. ESPEN intensive care guidelines recommend that SPN should be considered after 2 days if ETF is not providing adequate nutrition.[111] By contrast ASPEN–SCCM guidelines recommend that in patients at low or high nutrition risk, SPN should be considered after 7–10 days if at least 60% of energy and protein requirements cannot be met by ETF alone[41] whereas PN should be initiated as soon as possible after ICU admission in patients at high nutrition risk who are unable to receive nutrition through the enteral route.
- The ASPEN–SCCM recommendation on the timing of SPN in the ICU was informed by studies showing that provision of SPN within 48 hours of admission to the ICU had little or no benefit.[123-126] However, it has been highlighted.[101; 127; 128] that these studies have methodological limitations that result in a high risk of bias which may confound the results. For instance, many patients included in large studies evaluating different levels of nutrition provision are not considered to be at high nutritional risk and therefore may not respond to optimal nutrition intake.[127] By contrast, a meta-analysis of studies that enrolled patients with short-term relative contraindications to EN found that patients randomized to receive PN within the first 24 hours of ICU admission had a significantly reduced risk of mortality compared with patients receiving standard care

(i.e., no nutrition support for 2–5 days).[129] Recently published studies have also provided evidence to support timely initiation of SPN in critically ill patients with relative contraindications to ETF, [130-132] such as improved nutrition intake[130; 131; 133] and nutrition status (i.e., less muscle wasting),[134] shorter duration of mechanical ventilation (Early PN Trial),[132] and fewer hospital-acquired infections (The Swiss SPN study).[130] Reducing the incidence of hospital-acquired infections[135] and dependence on mechanical ventilation with SPN are also likely to yield economic benefits.[136] Results from a recently published randomized controlled pilot study (TOP-UP trial)[133] in mechanically ventilated adult ICU patients (BMI <25 or ≥35 kg/m^2) who received SPN to reach 100% of their prescribed nutrition goal showed significantly increased energy and protein delivery over the first week of ICU admission, with no increased infection risk and non-significant trends in reduced hospital mortality and improved QOL and functional outcomes; these findings may warrant investigation in a suitably powered large-scale trial.

- It has also been suggested that RCTs in which many patients spend only a short time in the ICU may be too short to demonstrate a benefit with early SPN.[137] Indeed, a prospective multicentre multinational cohort study demonstrated that greater nutritional intake in high-risk longer-stay patients is associated with both lower mortality and shorter time to discharge alive—every 10% increase in protein intake relative to goal was associated with a significant 6.6% decrease in mortality for high-risk patients who remained in the ICU for at least 4 days, and 10.1% for those remaining in the ICU for at least 12 days (both p = 0.003).[138] The authors concluded that, as it is not possible to predict which patients are likely to have longer ICU stays, best clinical practice would be to feed all critically ill patients at target protein and calorie levels, while accepting that patients with less severe disease or at lower nutritional risk may not receive additional benefit from this approach. The decision to start SPN timely in ICU patients is also supported by other medical nutrition experts.[139]
- ASPEN guidelines on nutrition support in the critically ill paediatric patient (i.e., age>1 month and <18 years) recommend that protein is provided early in the course of critical illness, to meet protein targets and promote positive nitrogen balance.[117] PN should be considered when ETF is not feasible or is contraindicated and may be used to supplement ETF in the first week of hospitalization if the patient is severely malnourished or at risk of nutrition deterioration or if the patient is unable to advance on low volumes of ETF. The time when PN should be initiated to supplement insufficient EN is also unknown. The threshold for and timing of PN initiation should be individualised. On the basis of a single RCT (PEPaNIC),[140] ASPEN guidelines do not recommend initiation of PN within the first day of PICU admission. Current European guidelines on paediatric PN recommend that the decision to initiate PN depends on individual circumstances and the age and size of the infant or child. In the small preterm infant starvation for just one day may be detrimental and where it is clear that enteral feeds will not be tolerated soon PN must be instituted shortly after birth. However older children and adolescents may tolerate up to 7 days of inadequate nutrition depending on age, nutritional status, underlying disease, surgery, and medical intervention.[21] This document was however prepared before the completion of the new European (ESPGHAN) PN guidelines and the reader should refer to these new guidelines for the latest recommendations when published.

SURGERY

Patients undergoing surgery have a high risk of developing malnutrition and severe protein loss due to catabolism and prolonged periods nil by mouth

- Full recovery after surgery can take weeks or months, even after ambulatory surgery,[142] and may be hindered by preoperative organ dysfunction, surgical stress and catabolism, pain, postoperative nausea and vomiting, ileus, fluid excess, semistarvation and immobilization.[142; 143] Interventions to reduce surgical stress and improve recovery include afferent neural blockade, medication, fluid and temperature management, nutrition, and exercise.[144]
- Patients undergoing major surgery are at heightened risk for malnutrition due to hypermetabolism, inflammation, and protein catabolism.[145] Resting energy expenditure in surgical patients can increase by up to 40% within the first week of hospital admission, and exceeds 100% during the second week.[146; 147] Furthermore, surgical patients often require periods of starvation before procedures and in the event of perioperative complications such as ileus and inability to tolerate oral or enteral feeding,[146; 148] further increasing the risk for malnutrition. Nutritional status in patients undergoing abdominal surgery is also influenced by the presence of cancer or chronic diseases that affect nutrient metabolism.[142] Malnutrition in surgical patients is an independent risk factor for postoperative complications such as infections and delayed healing, as well as increased mortality, length of hospital stay, and healthcare costs.[5; 146] Development of malnutrition during the hospital stay confers an even greater risk for negative outcomes, especially if the patient is already malnourished, has chronic disease, or is elderly.[146] A large evidence base shows that targeted nutrition therapy is associated with fewer infectious complications, reduced requirement for mechanical ventilation, decreased length of hospital stay, and lower mortality in surgical patients admitted to the ICU.[146]

PN is an important modality for patients undergoing surgery to maintain nutrition status and prevent postoperative complications when nutritional targets cannot be met with oral and/or enteral nutrition

- ESPEN surgery guidelines state that nutritional support is indicated in surgical patients who are malnourished or at nutritional risk, in order to prevent and treat catabolism and malnutrition, and reducing the risk for postoperative complications.[5] ONS and ETF are preferred; however, PN should be administered as soon as possible if nutrition therapy is indicated and there is a contraindication for EN. When indicated, nutrition therapy is typically administered perioperatively to maintain nutritional status and should start as soon as nutritional risk is identified, in order to reduce the risk of postoperative complications.[5; 149] ESPEN recommends that perioperative nutritional support should also be initiated without delay in patients who are not expected to be able to eat for more than 5 days perioperatively and in patients who are expected to have low oral intake and who are not able to maintain more than 50% of recommended intake for more than 7 days.[5] Furthermore, SPN is recommended if energy and nutrient requirements cannot be met by oral and enteral intake alone (<50% of caloric requirement) for more than 7 days. ESPEN considers improvement in nutritional status and functional recovery (including QOL) to be the most important nutritional goals in the late postoperative period.[5] ASPEN–SCCM critical care guidelines suggest that PN should be initiated in patients who have undergone major upper-GI surgery if ETF is not possible and the duration of therapy is anticipated to be ≥7 days.[41] However, unless the patient is at high nutrition risk, PN should not be started in the immediate postoperative period but should be delayed for 5–7 days.

Enhanced Recovery After Surgery (ERAS) protocols support the use of PN for certain patients undergoing surgery

- The ERAS protocol, introduced in 2001, was developed by academic surgeons in Europe to optimize outcomes in patients undergoing surgery.[150] ERAS protocols have been (or are being developed) for many surgical procedures, including colonic/rectal resection, pancreaticoduodenectomy, gastric resection, bariatric surgery, liver resection, head and neck cancer surgery, and esophageal resection (complete list available from http://www.erassociety.org). Each protocol lists the actions to be performed by different professionals and disciplines at different phases of the surgical patient's journey (pre-admission, pre-, intra-, and post-operative).[150]
- ERAS guidelines on perioperative care following pancreaticoduodenectomy recommend that PN should be used preoperatively in patients who are significantly malnourished, if the enteral route is not feasible, and postoperatively in patients who cannot eat and drink normally and who are unable to tolerate EN.[151] ERAS guidelines for head and neck cancer surgery state that PN is indicated in patients with a non-functioning gut and when enteral access is not possible.[152] For patients undergoing liver surgery, perioperative PN is indicated in severely undernourished patients who cannot be fed adequately through the oral or enteral routes; postoperative enteral EN or PN is indicated in malnourished patients and those with prolonged fasting due to complications (e.g., ileus >5 days or delayed gastric emptying).[153] The ERAS protocol for patients undergoing gastrectomy recommends that significantly malnourished patients should receive preoperative oral or enteral nutritional support and that PN may be warranted if the tumour prevents access to the duodenum. The guidelines highlight that patients undergoing total gastrectomy are likely to be at higher risk of malnutrition and cachexia during surgery than other groups of patients with abdominal cancer. Thus, it is expected that total calorie intake will be low for the first few days following surgery and that some patients with need additional nutrition support. Therefore, in patients who are clearly malnourished or are unable to meet 60% of daily requirements by postoperative day 6, nutrition support with ETF is indicated when oral intake is not possible and with PN if the gut is not functional or cannot be accessed [154]

CANCER

Malnutrition is highly prevalent in patients with cancer; it reduces tolerance and response to anticancer therapy, leading to poor clinical outcomes and shorter survival

- As described in Section 1.1 (Identifying malnutrition), malnutrition is highly prevalent in patients with cancer, and occurs in up to 70% of patients with solid tumours (e.g., pancreas, lung, gastric, colorectal, head and neck).[155] Weight loss is often the first presenting symptom in patients with cancer[89; 156] and results from reduced food intake and metabolic derangements that promote the loss of lean muscle mass.[157] Cancer-associated weight loss impairs patients' ability to receive, tolerate, and respond to anticancer therapy and predicts poor clinical outcomes independently of other risk factors.[158-162] Studies suggest that malnourished patients have a 2–5-fold higher risk of dying than patients with little or no evidence of malnutrition.[163-165] Two multivariate analyses have shown that undernutrition is an independent risk factor for complications in patients undergoing surgery for cancer, as well as increased mortality, length of hospital stay, and healthcare costs.[5; 166; 167] Moreover, even minimal weight loss during chemotherapy and/or radiotherapy is associated with significantly shorter survival.[168]

PN is indicated in patients with cancer who are malnourished or at nutritional risk during active cancer treatment (surgery, chemotherapy, and/or radiotherapy) and in certain patients with incurable cancer, to preserve nutritional status and QOL when oral intake or EN are insufficient to meet nutritional needs

- The aim of nutrition therapy in patients undergoing cancer treatment is to maintain or improve nutritional intake and reduce metabolic dysfunction in order to preserve skeletal muscle mass, physical function, and QOL, to prevent treatment-related complications, and to enable completion of planned treatment.[157] ESPEN and ASPEN–SCCM guidelines highlight that their recommendations for nutrition therapy in patients undergoing surgery are equally applicable to patients with cancer who are undergoing tumour resection.[5; 41] Moreover, the ESPEN surgery guidelines[5] highlight that management of nutrition in the preoperative period may be critical for long-term outcomes in patients with cancer.
- ESPEN and ASPEN have also published cancer-specific guidelines.[157; 169] ESPEN cancer guidelines recommend that PN should be administered when ETF is not sufficient or feasible in patients undergoing anticancer treatment who are unable to eat for >1 week or who are likely to achieve <60% of their nutritional target for more than 1–2 weeks.[157] Similarly, the ASPEN cancer guidelines recommend nutrition therapy during active anticancer treatment for patients who are malnourished and who are unlikely to achieve adequate nutritional intake for 7–14 days; the enteral route is recommended for patients with a functioning gut.[169]
- Nutrition support is also indicated in patients undergoing cancer-related surgery, radiation therapy, or chemotherapy who experience complications or chronic adverse effects, such as severe radiation enteritis, malabsorption, mucositis, intractable vomiting, ileus, protracted diarrhoea, or GI graft versus host disease following haematopoietic stem cell transplantation (HSCT).[157; 170] ESPEN guidelines on CIF in adults recommend that HPN should not be delayed in patients with radiation enteritis who are malnourished if oral or enteral nutrition is inadequate, noting that most patients requiring HPN because of radiation enteritis have type III IF[37; 39] due to structuring and/or fistulizing disease (often associated with surgical complications). Up to 20% of patients receiving pelvic radiotherapy are estimated to have chronic radiation enteritis,[171] 5% of whom develop CIF;[172] ESPEN guidelines note that HPN may be superior to surgical intervention for these patients.[173; 174] Likewise, ESPEN cancer guidelines highlight that when PN is indicated in patients undergoing intensive chemotherapy and HSCT, it should be administered early in order to prevent or minimize further loss of weight and body cell mass.[157] Patients undergoing HSCT are typically malnourished at admission, particularly those receiving allogeneic HSCT.[157] Nutrition status may be further compromised because of the GI adverse effects associated with high-dose radiotherapy/chemotherapy (e.g., nausea, vomiting, mucositis, diarrhoea, and infections) which lead to weight loss, particularly in the first 40 days after admission, compromising clinical outcomes.[175; 176]
- The ESPEN and ASPEN guidelines agree that PN may improve QOL and prolong survival in patients with incurable cancer (including cachectic patients) who are unable to receive nutrition via the oral or enteral routes.[157; 169] It is noted that some cancer patients may survive many months or even years on TPN.[157; 172; 177] However, both guidelines caution that the decision to implement PN in patients with incurable cancer should be taken in consultation with the patient (and close relatives or partners) and should consider both the expected benefit on QOL, and potentially survival, as well as the burden associated with nutritional therapy.[157; 169] Ethical considerations for PN in patients with cancer relate to its use during the terminal phase of the disease. In general, the risks of PN are considered likely to outweigh the benefits in patients who are near the end of life (i.e., life expectancy of weeks rather than months).[157; 169] However, it is important to note that provision of nutrition and hydration, whether by natural or artificial means, is considered essential in certain cultures.

HPN is a life-saving therapy for patients with cancer who are at risk of death from malnutrition rather than disease progression

- HPN is generally recommended in patients with CIF due to end-stage cancer if predicted life expectancy is greater than 2–3 months.[28; 157; 178] Patients with incurable cancer may also enter a HPN program if they are unable to achieve nutritional targets with oral in take or EN and are at risk of dying from malnutrition. HPN is not contraindicated in patients with cancer who are no longer receiving anticancer treatment but should not be initiated if the patient is likely to die from the underlying disease rather than from malnutrition.
- ASPEN and ESPEN have not published PN guidelines specifically for paediatric patients with cancer, although the ASPEN Nutrition Support Practice Manual states that indications for PN in children with cancer are similar to those for adults.[179]

KIDNEY DISEASE

Malnutrition is common in hospital patients with acute kidney injury (AKI) and is associated with an increased risk of in-hospital morbidity and mortality

- Malnutrition is frequent in hospital patients with AKI180 and is associated with increased morbidity (e.g., infection, poor wound healing, longer dependence on mechanical ventilation, and increased length of hospital stay) and mortality.[116; 180-183] Together, ARF and critical illness result in intense and prolonged catabolism and sustained inflammation.[116; 184] Continuous renal replacement therapy (CRRT), used to support critically ill patients with AKI, is associated with significant amino acid loss (10–15 g per day).[185]

The goals of nutrition support for patients with AKI are the same as those for other critically ill patients

- ESPEN guidelines highlight that the primary goals of PN in adults with AKI are the same as for patients for other catabolic conditions in the ICU: to prevent protein-energy wasting (PEW) and further metabolic dysfunction, maintain skeletal muscle mass and nutritional status, enhance wound healing, support immune function, and reduce mortality.[186] Additional goals are to reduce systemic inflammation and oxidative stress and to improve endothelial function.[186] Thus, ESPEN[90] and ASPEN–SCCM[41] recommendations for PN in critically ill patients (see subsection CRITICAL ILLNESS) apply to patients with AKI. Specifically, ESPEN guidelines state that PN is appropriate in AKI when ETF is not possible or not sufficient to meet nutritional targets.[186] PN should be slowly withdrawn when GI function returns, and ETF or oral nutrition introduced.

The goals of PN in patients with chronic kidney disease (CKD) are to prevent and treat PEW, provide optimum nutrition support, and attenuate disease progression

- Patients with CKD who are not on haemodialysis (HD) are unlikely to require PN outside of the ICU unless they have severe PEW or GI (or other) complications.[186] However, PEW has been reported in up to 70% of adults with CKD who are on HD and is an independent predictor of morbidity and mortality in these patients.[186; 187] The actual prevalence of PEW may be even higher, as published studies typically include only clinically stable patients.[187] The risk and severity of PEW increase the longer a patient remains on HD,[188] due to declining nutritional intake and metabolic dysfunction associated with renal failure.[189; 190] GI symptoms such as constipation, impaired gastric emptying, and motility disorders, which occur frequently in patients with CKD, also contribute to PEW.[187]

- The indications for PN in patients with CKD are similar to those for patients without kidney disease, such that PN should only be considered in malnourished patients requiring nutritional support if oral or enteral intake are not feasible or insufficient to meet nutritional targets.[191] ESPEN considers PN to be a "desired choice" in patients with conservatively treated CKD who cannot achieve adequate nutrition through oral intake or ETF or who have severe GI complications that preclude enteral access.[186] However, PN should be slowly withdrawn when GI function returns and ETF or normal nutritional intake resumed. ESPEN guidelines note that special attention should be given to surgical patients with CKD who require PN during the perioperative period.[191] The goals of PN in patients with CKD are to prevent/treat PEW in order to prevent cachexia, provide optimum nutrition support, and attenuate disease progression through protein or phosphate restriction.[186]
- ESPEN states that the decision to initiate PN in acutely ill patients with CKD on HD should be based on the same criteria as for patients with ARF.[191] Intradialytic PN (IDPN), which provides nutrition support directly via the venous access for HD, is recommended for non-acutely ill patients who are exhibiting severe PEW and are unable to comply with ONS.[186] Many studies, including RCTs, have demonstrated improvements in nutritional parameters with IDPN[186] and it is considered a safe and convenient treatment for patients who cannot meet their nutritional needs orally.[187] However, EN can be necessary if ONS or IDPN do not improve nutritional status.[191] Indeed, ESPEN guidelines point out that ONS and IDPN are unlikely to be sufficient in patients with severe PEW in whom spontaneous intake is <20 kcal/day (or in stress conditions) and are therefore not recommended. ESPEN recommends central venous PN in these patients when ETF is not possible or sufficient to meet nutritional targets. ASPEN guidelines on adult renal failure state that IDPN should not be used as a nutritional supplement in malnourished patients with stage V CKD (i.e., kidney failure, dialysis or kidney transplant needed). The 2017 ASPEN consensus recommendation on the appropriate use of PN recommend that IDPN should not be used as the sole source of nutrition support in malnourished patients with CKD[14] but should be considered for adult and paediatric patients who are unable to tolerate adequate oral intake or ETF.[14]
- ESPEN guidelines note that the prevalence and consequences of PEW are similar for patients on continuous ambulatory peritoneal dialysis (CAPD) and HD. For patients on CAPD, ESPEN guidelines highlight that, based on current data, PN should be limited to those who are malnourished and stressed, or with severe encapsulating peritonitis, when nutritional requirements cannot be ensured by ONS or ETF.[186]
- Finally, ESPEN guidelines recommend that, in patients undergoing kidney transplantation, early intake of normal food or ETF should occur within 24 hours of surgery, and, if necessary PN should be combined with ETF (SPN).[5]

LIVER DISEASE

In patients with acute liver failure, PN ensures provision of sufficient energy and optimizes protein synthesis when ETF is inadequate

- Acute liver failure results in severe metabolic dysfunction and is almost always accompanied by multiple organ failure.[192] Resting energy expenditure in patients with acute liver failure is increased 1.2–1.3-fold compared with healthy individuals. Nutritional therapy in these patients therefore aims to ensure adequate provision of energy and optimal rates of protein synthesis by providing sufficient intake of protein or amino acids.[192] ESPEN guidelines state that artificial nutrition is indicated in patients with acute liver failure, irrespective of nutritional status, when normal oral nutrition is not likely to be resumed within 5–7 days, and that PN is a safe second-line option to adequately feed patients in whom ETF is not possible or sufficient.[192] ASPEN–SCCM critical care guidelines state that ETF should be used in preference to PN in ICU patients with acute and/or chronic liver disease.[41]

Malnutrition is highly prevalent in patients with chronic liver disease, due to decreased nutrient intake, metabolic derangement, and malabsorption, and is associated with a poor prognosis

- Patients with chronic liver disease are particularly susceptible to malnutrition because of central role of the liver in maintaining normal nutrition and energy balance and the synthesis and degradation of key proteins.[193] Chronic liver disease is also associated with poor appetite, leading to a reduction in nutritional intake and further compromising nutrition status.[193] Up to 90% of patients with cirrhosis, which is the most common indication for transplantation, are malnourished.[193-195] Protein malnutrition in patients with liver disease is associated with higher rates of complications, mortality, and reduced survival following liver transplantation.[192; 196; 197]

PN should be administered in patients with cirrhosis who are moderately or severely malnourished and who cannot be fed adequately with oral or enteral nutrition

- ESPEN guidelines highlight that PN is safe for patients with cirrhosis, and improves mental recovery in those with hepatic encephalopathy.[192] PN should be started immediately in moderately or severely malnourished patients with cirrhosis who cannot be adequately fed by diet and ONS or ETF[192] and when fasting exceeds 72 hours. Furthermore, PN should be considered in patients with unprotected airways and hepatic encephalopathy if cough and swallow reflexes are impaired. Early postoperative PN is indicated for patients with cirrhosis who are undergoing surgery if they cannot be adequately nourished by diet and ONS or ETF.[192]
- ESPEN guidelines highlight that PN improves nutrition status and liver function in patients with alcoholic steatohepatitis (ASH) and should be started immediately in moderately or severely malnourished patients who cannot be fed sufficiently with diet and ONS or ETF[192] and should also be initiated when fasting exceeds 72 hours.

PN is safe and effective for patients undergoing liver transplantation

- The ESPEN hepatology guidelines state that perioperative PN (including during liver transplantation) is safe, and reduces the rate of postoperative complications.[192] In these guidelines ESPEN recommends that postoperative nutrition should be provided early after liver transplantation, and that PN is a secondary option to ETF,[192] whereas the 2017 surgical guidelines consider ETF and PN to be equally “important” in patients after liver transplantation.[5; 198]

PANCREATITIS

PN should be administered early in patients with severe pancreatitis when ETF is not feasible or sufficient

- Metabolic derangements in patients with acute pancreatitis (or an acute episode of chronic pancreatitis) can promote hypermetabolism and negative nitrogen and energy balance, leading to progressive nutritional decline.[199] Although the impact of nutrition status on the prognosis for patients with acute pancreatitis is not completely understood, it is expected to be same as in other critical illnesses.[200; 201] Patients with severe pancreatitis, which is characterized by the development of major organ failure, are more likely to require nutrition support than patients with mild disease.[199]
- ESPEN pancreatitis guidelines state that nutritional support is indicated in acute pancreatitis if oral intake is, or is anticipated to be, inadequate for 5–7 days; patients who are already malnourished may require earlier nutritional intervention.[201] PN or ETF are unlikely to be required in patients with mild acute pancreatitis unless malnutrition is evident or when therapeutic fasting for >5–7 days is indicated. In these cases, PN is indicated if ETF is not feasible—because of intestinal failure, prolonged ileus, complex pancreatic fistulae, abdominal compartment syndrome, for example—or is not tolerated.[201] However, If it is anticipated that ETF cannot be started early or will not be fully tolerated, PN (preferably SPN) should be started as soon as possible and decreased as ETF tolerance increases.[201] ESPEN guidelines[201] note that PN does not significantly stimulate pancreatic secretion or impair pancreatic function.[202-204]
- ASPEN–SCCM critical care guidelines suggest that, based on expert consensus, PN should be considered in patients with severe acute pancreatitis after 1 week from the onset of the attack when ETF is not feasible.[41] Similarly, International Consensus Guidelines on pancreatitis[205] recommend that if nutrition support is indicated, such as in mild-to-moderate disease with complications, severe disease, or fasting >5–7 days, PN should be used when ETF is contraindicated or not tolerated. The guidelines also note that PN does not have any complications specific to patients with pancreatitis.[205] Nutrition support should be started early in patients with severe pancreatitis.

Preoperative PN is indicated in patients with chronic pancreatitis who are malnourished and is also indicated in those patients with gastrointestinal obstruction or complex fistulating disease

- Chronic pancreatitis is a serious disease that can have long-term and life-threatening consequences, such as diabetes and pancreatic cancer, and can severely impair QOL.[206] The incidence in Europe is around 5–10 cases per 100,000, and prevalence approximately 120 per 100,000 population.[207] Alcohol is the causal factor in 60–70% of cases.[208] PEW is common in these patients, particularly during the terminal phase, and is partly due to pain-induced anorexia and ongoing alcohol misuse.[201] Furthermore, resting energy expenditure is increased in up to half of all patients with chronic pancreatits.[208]
- ESPEN guidelines[201] and United European Gastroenterology guidelines[206] state that in patients with chronic pancreatitis, PN is indicated for gastric outlet obstruction secondary to duodenal stenosis and in patients with complex fistulating disease. The United European Gastroenterology guidelines also state that PN is also indicated in patients with apparent severe malnutrition prior to pancreatic surgery if ETF is not possible.[206]

3.3.1.2 PREVALENCE OF PN USE

The prevalence of PN in hospital patients varies across countries

- Data on the prevalence of PN in hospital patients are scarce. The 2016 worldwide NutritionDay prevalence study of nutrition practice in intensive care, which included all patients present on the morning of the annual one-day audits from 2007 to 2013, found that about 10% of patients received TPN during their stay in ICU, with usage peaking at day 5–6 (~12% of patients). Use of combined PN and ETF (i.e., SPN) increased with length of ICU stay, reaching a maximum of 12% of patients during week 2 of ICU stay.[209] Table 2 summarizes the data on use of PN from national reports uploaded to the NutritionDay survey website (www.nutritionday.org). These reports contain data from participating units in each country for a given year compared with the worldwide average (reference data). Reports are publicly available for countries with at least six participating hospitals. Data from selected countries are presented to illustrate variability in PN prescribing across countries; these data include all hospital-administered PN and are not reported separately for the ICU—the prevalence of PN is likely to be higher for ICU patients.

Table 2 NutritionDay country-specific data on use of ETF, PN and SPN (ETF + PN)*

Country	No. of patients	Patients with any ICU stay (%)	Patients receiving nutrition support, all hospital (includes ICU) (%)		
			ETF	PN	ETF + PN
Australia	198	9.09	1.52	0.51	–
Austria	321	3.43	7.17	2.8	0.93
Belgium	2,514	12.1	4.73	2.23	0.4
Brazil	700	17.4	8.86	1.0	0.29
Canada	737	10.4	1.76	1.76	0.54
China	253	31.6	9.09	10.3	7.91
France	396	16.2	11.1	4.04	2.53
Germany	533	22.9	18.2	5.07	2.25
Great Britain	97	12.4	10.3	3.09	5.15
India	286	28.7	4.55	–	0.35
Italy	122	0.82	34.4	9.02	4.92
Japan	1,313	6.93	2.44	14.0	1.29
Norway	634	16.4	10.9	7.41	1.74
Spain	339	5.9	6.78	2.36	–
Sweden	182	7.14	1.10	8.79	0.55
US	2,806	8.8	1.67	1.03	0.25
United Arab Emirates	85	22.4	12.9	4.71	–

Reference data from units with comparable patients: 2014 (*n* = 14,603): EN, 5.9%; PN, 3.2%, ETF + PN, 0.62; 2011 (*n* = 14,207): EN: 8.0%, PN: 4.5%, ETF + PN: 0.99.
*Data are from 2014 NutritionDay survey except for Canada, which are from the 2011 survey.
Source: Data taken from individual country reports uploaded to www.nutritionday.org

- Analysis of data (2002–2011) from the Nationwide Inpatient Sample and the Kid's Inpatient Database in the US found that of 2.1 million paediatric patients (aged 1 month–17 years) hospitalized per year, more than 54,600 had a coded diagnosis of malnutrition. Of these patients, 15.7% received artificial nutrition (PN or EN) and 8.7% received PN, compared with 2.8% and 2.1%, respectively, for patients with no coded diagnosis of malnutrition (*n* = 2,089,755). Patients diagnosed with protein-calorie malnutrition (*n* = 7,203) were most likely to receive artificial nutrition (enteral or parenteral) (22.0%), and in particular PN (14.5%).[210]

SPN may be underused in critically ill patients who do not receive adequate nutrition intake from ETF alone

- The Screening Day study—an observational study on ICU nutrition support practices in Latin America (Argentina, Brazil, Chile, Colombia, Ecuador, Mexico, Panama, and Peru) involving critically ill adults who received artificial nutrition (ETF and/or PN) on both the screening day and the previous day, reported that fewer than 1 in 10 patients (9.4%) received PN alone and 10.7% received PN in combination with ETF.[211] However, the authors noted that 40% of patients receiving nutrition therapy did not achieve their target caloric intake, and that use of PN and SPN should have been higher given the clinical characteristics of the study population (75% of patients required mechanical ventilation; 74% had suspected moderate or severe malnutrition; one-third had a contraindication or intolerance to ETF).
- A large study that analysed claims data from the Premier Perspective database (the largest inpatient clinical database in the US) found that PN was used more frequently in non-critical care settings than in the ICU, based on data from 106,374 patients (all ages) who received PN during the study period (January 2005 to December 2007).[212] PN was most frequently used in the non-critical care setting (*n* = 66,217), followed by the neonatal ICU (*n* = 28,06) and the adult ICU (*n* = 20,140). The most common primary diagnosis requiring PN was intestinal or peritoneal adhesions with obstruction, followed by acute pancreatitis, septicemia, and diverticulitis. Malignancy was the most common comorbidity in patients requiring PN, for both adult (38.9%) and paediatric (25.6%) patients. The average duration of PN was similar for non-critical care and critical care (6.5 vs 6.1 days) but was longer in the neonatal ICU (8.9 days).

Use of PN in the ICU may be declining in some countries after decades of growth

- Examination of US trends in hospital PN using data from the Healthcare Cost and Utilization Project (Agency for Healthcare Research and Quality) showed that use more than tripled during 1993–2010 but has declined in the following four years (Figure 1), even after adjusting for total number of hospital discharges, which have also decreased in recent years (Figure 2).[14] However, when stratified by age, PN use has not changed for paediatric patients <1 year of age (0.3% of hospital stays). It is suggested that this apparent decline in PN use in the ICU may be due in part to its expanded use outside of the critical care setting.

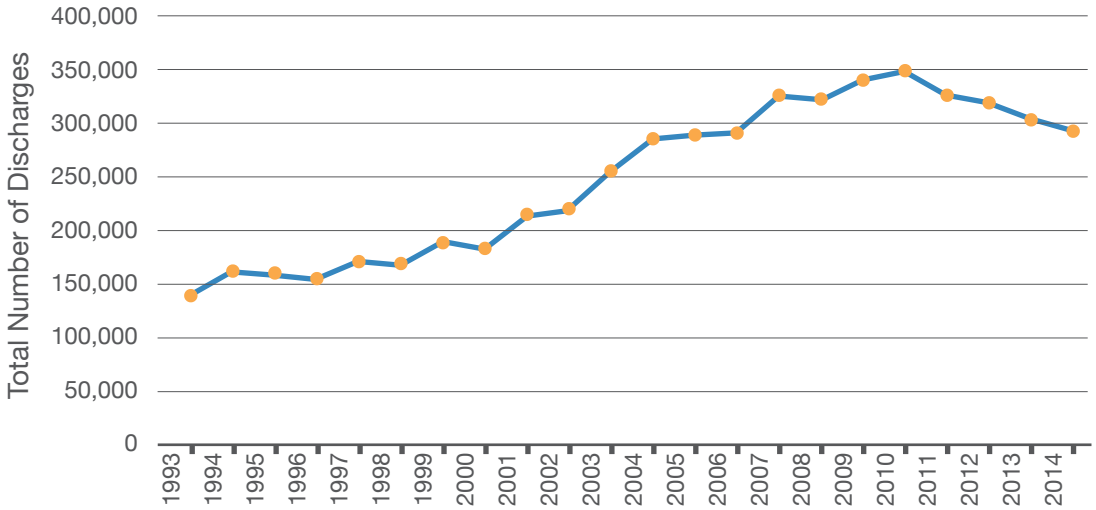

Figure 1 **Total number of hospital discharges with the ICD-9 code of 99.15, parenteral nutrition, 1993–2014. Data from National Inpatient Sample of the Healthcare Cost and Utilization Project from the Agency for Healthcare Research and Quality (http://hcupnet.ahrq.gov/),** adapted from Worthington et al. 2017[14]

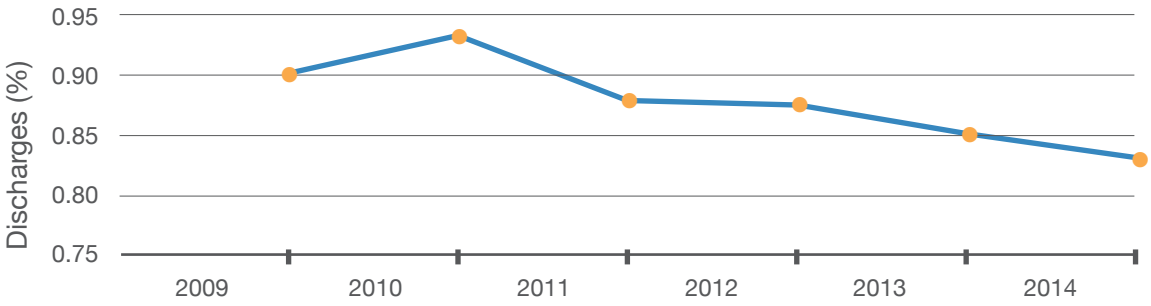

Figure 2 **Parenteral nutrition use as a proportion of total hospital discharges. Data from National Inpatient Sample of the Healthcare Cost and Utilization Project from the Agency for Healthcare Research and Quality,** adapted from Worthington et al. 2017[14]

- Similarly, a retrospective analysis of data from the Project IMPACT database in the US, a voluntary fee-based ICU registry, showed that use of PN has decreased from 7.2% in 2001–2002 to 5.5% in 2007–2008 ($p < 0.001$).[213] Decline was most evident for emergent surgical patients, patients with moderately severe illness, patients in the surgical ICU, and patients admitted to an academic facility ($p \leq 0.01$ for all interactions with year).

- Again, this decline in PN in the ICU may be partly explained by its expanded use outside of the acute setting. In addition, current guideline recommendations are based on meta-analyses of predominantly older studies that show an increased rate of infections with PN compared with EN, which may influence perception of the risks versus the benefit with PN in current clinical practice.[14] Also, when PN was introduced, it was prescribed extensively across a wide range of indications – and often irrespective of the patient's nutrition status or the functional status of the gut, suggesting that PN use was not always appropriate.[14] However, evidence-based guidance on the safe management of PN in both the hospital and community setting has helped to maximize the clinical benefit of PN while minimizing harm. Indeed, more recent studies in which PN is administered using modern protocols indicate that PN can be safely administered to critically ill patients without impairing outcomes.[14] For instance, two multicentre randomized studies involving 2,338 and 1,372 critically ill patients, found no increased risk for infectious complications with PN compared with ETF.[214; 215] Moreover, a systematic review of studies published up to July 2015 to compare rates of catheter-related (CR) bloodstream infection (BSI) in patients who did and did not receive PN reported that analysis was insufficient to determine whether patients receiving PN are at increased risk of CR BSI compared with ETF, and that gold-standard practices on the insertion and maintenance of central catheters are achievable in this population.[216] Likewise, prospective longitudinal data indicate that HPN is associated with a relatively low rate of CR complications,[217-219] even in patients with cancer who are likely to have compromised immune function. Innovative technologies in PN delivery, such as pre mixed ready-to-use MCBs have also been shown to reduce the risk for BSI,[220; 221] and recently published ESPEN guidelines on clinical nutrition in surgery recommend that all-in-one (three-chamber bag or pharmacy prepared) PN solutions should be used in preference to multibottle systems to reduce the risk for BSI.[5]

HPN provision varies across countries

- Baxter and colleagues estimated the prevalence of HPN based on a survey completed by members of the ESPEN Home Artificial Nutrition and Chronic Intestinal Failure (HAN CIF) group.[222] Period prevalence for 2010 and point prevalence (31st December 2010) were calculated for 16 countries, based on data from 9,200 patients (Table 4). Period prevalence ranged from 3.25 cases per million population in Spain to 66 per million in Denmark. The differences in prevalence were suggested to reflect differences in service organization and attitudes to the provision of HPN for patients with cancer. Period prevalence could not be calculated for Germany; however, the figure is expected to be high as large numbers of patients with cancer receive HPN here.[222]

Table 3 **Population, period, and point prevalence of HPN, and number of HPN centres in selected countries** (adapted from Baxter et al. 2012)[222]

Country	Population (mn)	2010 period prevalence/mn	31 Dec 2010 point prevalence/mn	No. HPN centres
Australia	22.2	6.7	5.1	9
Belgium	10.5	11*	8*	7
Denmark	5.3	66	47	3
Republic of Ireland	4.2	10.1	7.5	0
England	51.8	10	8.3*	21
France	63.1	6	Unknown	>14
Germany	82	Unknown	49*	Few
Israel	7.85	25.5	Not calculated	4
Italy	60	33.3*	Unknown	90*
Netherlands	17	14.7	Unknown	2
N. Ireland	1.7	18.8	14.1	1
New Zealand	4.2	7.2	5.3	1
Poland	38.2	25	22.3	26
Scotland	5.3	23	17.5	11
Spain	46.2	3.25	2.7	7
Wales	3.0	18	21	2

*Estimated prevalence
HPN, home parenteral nutrition; mn, million

The prevalence of HPN has increased in many countries over the past four decades

- Since HPN was introduced in the early 1970s, its use has substantially increased in many countries, possibly because its relatively low associated morbidity and mortality has promoted its extensive use in Western countries.[28]
- A national survey conducted in 2005 and again 2012 across Italian local health care units found a 66% increase in the prevalence of home artificial nutrition, with use of HPN increasing by 58%.[32; 223] The prevalence of HPN (including HPN + home EFT) was 50.2 per million population in 2012, compared with 31.7 (corrected prevalence) in 2005.[32; 223]
- Analysis of data from the largest Danish IF centre showed an exponential increase in the number of patients discharged with HPN, from one per year in 1970 to more than one per month in the 1980s and more than one patient per week in the 2000s.[29]
- A retrospective study in Switzerland on the use of HPN during 2005–2009, based on 13,000 adults, reported that the HPN use increased from 2.1% in 2005 to 4.0% in 2009 (overall prevalence, 3.2%).[224] However, follow-up data for the period 2010 to 2015, presented at the 2017 ESPEN Congress, found that 1.5% of HAN received HPN during this period.[225]

- Analysis of data from the Spanish Home Parenteral Nutrition for 2015 reported prevalence of home artificial nutrition (HAN) of 5.08 patients per million. Although not directly comparable, this figure is higher than that reported by Baxter and colleagues (2012) for Spain in 2010 (period prevalence, 3.25).
- The British Artificial Nutrition Survey (BANS) report produced by the British Association for Parenteral and Enteral Nutrition (BAPEN) in 2016 stated that the number of new adult HPN registrations increased steadily between 2008 and 2013, peaking in 2013 with 472 new registrations. Moreover, the point and period prevalence in 2015 were the highest ever recorded by BANS, at 1140 and 1360 patients, respectively. Relating these data to the UK population, the incidence of HPN was 6.5 per million in 2015, with a point and period prevalence of 17.1 and 21.1 cases per million, respectively. The true rates may be even higher, given underreporting.
- Analysis of US Medicare data from 9,228 patients estimated the average prevalence of HPN over the 4 year study period to be 238 patients per million.[226] However, a study published in 2017 suggests that the prevalence of HPN in the US has since declined: in 2013 6,778 Medicare beneficiaries received HPN. The ratio of Medicare to non-Medicare use of HPN was 0.271, leading to an estimated total of 25,011 patients receiving HPN in the US in 2013 (79 patients per million US population), with adults ac counting for approximately 80% of all HPN patients.[226]

The rising prevalence of HPN in many countries appears to be due largely to expanded use in patients with cancer

- In 1997, the most common indications for long-term HPN in Europe were CD, mesenteric vascular disease, cancer, and radiation enteritis[227; 228] whereas more recent data suggests that, in adults, malignancy is now the most common indication for HPN in Europe.
- The Italian national survey found that cancer was the most frequent underlying diagnosis for HPN in adults.[32] The prevalence of HPN in patients with GI disease increased the most during the study period (2005–2012) but this represented the smallest patient group.
- Analysis of 7 years of HPN data from the Spanish NADYA group registry showed that patients with a cancer diagnosis receiving HPN increased by 43% from January 2010 to December 2016.[229] Furthermore, half of these patients (51.3%) were receiving palliative cancer therapy.
- Retrospective analysis of survey data from Switzerland for 2005–2009 showed that cancer was the underlying disease in half of all HAN patients.[224] Follow-up data from 2010–2015 confirmed that patients with cancer represented the largest group of patients receiving HAN (46.0%).[225]
- The 2016 BANS report states that cancer is a major diagnostic indication for HPN, ac counting for one-quarter of all new HPN registrations. CD remains a leading diagnosis for adults receiving HPN, accounting for 14% of newly registered patients (point prevalence, 21%). Data from the largest UK single-centre series of adults requiring HPN for Type 3 IF showed a significant reduction in the prevalence of HPN for CD-related IF, from 45% in 1978–1998 to 22% in 2006–2011; the prevalence of HPN for cancer-related IF increased from 2.2% to 9.5% over the same period (both $P < 0.05$).[230]
- A retrospective analysis of data from the Canadian HPN registry (established in 2005)[231] showed significant changes in the indications for HPN between 2005–2008 and 2011–2014), with an increased proportion of patients with cancer (37.9% vs 16.7%) and but fewer with SBS (32% vs 65.5%).

Use of HPN in patients with cancer varies by tumour type

- A cross-sectional study in France estimated the one-day prevalence of malnutrition and nutrition support in patients with cancer. Based on data on nutrition status collected for 1,903 patients, 39% were identified as being malnourished (likely to be an underestimate as strict criteria were used to define malnutrition). A total of 39.9% of patients received nutrition support (Table 5), and of these 9.6% (4% overall) received HPN.[156] Cancer of the pancreas (24.3%), uterus/ovaries (21.3%), and oesophagus/stomach (19.6%) were the leading diagnoses for patients receiving HPN. Importantly, more than 40% of patients who were identified as being malnourished did not receive any nutrition support.

Table 4 **Prevalence of nutrition support and HPN use in adults with cancer in 154 non-critical care wards in France** (adapted from Hébuterne et al. 2014)[156]

Tumour type (n)	% of patients with nutrition support	% of patients receiving HPN
Pancreas (42)	66.7	24.3
Uterus/ovaries (87)	32.2	21.3
Oesophagus/stomach (103)	65.0	19.6
Blood (377)	34.5	16.2
Colon/rectum (191)	30.4	10.9
Others (160)	31.9	10.2
Lung (247)	42.9	8.1
Kidney/bladder (29)	41.4	7.7
Head and neck (366)	63.7	6.1
Prostate (72)	13.9	4.5
Breast (229)	14.8	4.1
Total (1,903)	39.8	9.6

HPN, home parenteral nutrition (i.e. PN administered outside of the critical care setting)

Prevalence of paediatric HPN continues to rise in many countries; intestinal failure is the most common indication

- A cohort study conducted in France, in 2015 involving 307 paediatric patients showed a 14.5% increase in the prevalence of HPN use from the previous year, with 95% of patients being treated for primary digestive disease.[232]
- Analysis of data from the Italian national survey found that IF was the most frequent diagnosis for paediatric HPN in 2012 (58% of patients).[32] The prevalence of paediatric HPN increased from 1.2 patients per million population (total prevalence) in 2005[223] to 4.1 per million in 2012 (point prevalence).[32] Furthermore, the increase in HPN use for paediatric patients during the study period (2005–2012) was double that for adults.[32]
- A survey of the 32 nutrition support teams that register patients with British Intestinal Failure (BIF) showed that the point prevalence of paediatric HPN has risen four-fold in the last two decades.[233] In this study data were requested for children (<16 years) with Type II IF (≥28 days inpatients days on PN) and Type III IF (HPN or being prepared for discharge with HPN); 95 Type II and 195 Type III patients were identified. Comparison with data from previous years showed that the point prevalence of Type III IF has risen significantly, from 4.4 patients per million at risk population in 1993 to 16.6 per million in 2012 ($P < 0.001$). More recently, point prevalence data on paediatric IF from the Paed eBANS National Digital Registry in the UK showed an increase in the number of paediatric HPN patients to 312 in 2015, a rise of 64% from 2012.

3.3.2 Nutritional benefits of PN

This section summarizes relevant studies reporting improved nutritional intake and/or nutritional status with PN. Functional and/or clinical benefits reported in these studies are summarized in Section 3.3.3 and Section 3.3.4 .

3.3.2.1 NUTRITIONAL INTAKE

- Delivery of nutrition via the parenteral route is efficient, as research indicates that most patients prescribed PN receive their planned nutritional intake. For instance, data from the nutritionDay ICU survey, an annual one-day cross-sectional audit from 2007 to 2013, showed that 97% of patients prescribed PN received their planned nutritional intake.[234]

CRITICAL ILLNESS

Timely initiation of PN in hospital patients who cannot be fed adequately with enteral tube feeding (ETF) improves energy and protein provision, enabling more patients to meet their nutritional targets

- Doig and colleagues (2013) conducted a large multicentre single-blind RCT in Australia and New Zealand to evaluate the nutritional and clinical benefits of early PN in critically ill adults with a short-term relative contradiction to early ETF.[132] A total of 1,372 surgical (65%) and medical (35%) patients admitted to the ICU were randomized to receive either pragmatic standard care (i.e., current practice in individual ICUs; n = 686) or PN provided within 24 hours of ICU admission (n = 686). Nine patients subsequently withdrew consent (4 standard care and 5 early PN). The mean time from ICU admission to enrolment was 13.8 hours. Of the 681 patients allocated to early PN, 679 (99.7%) started PN within 44 minutes of enrolment and 59.6% progressed to ETF within a mean of 3.83 days of starting PN. In total, 274 of 681 patients (40.2%) received ETF at some point during their ICU stay. Of the 682 patients who received pragmatic standard of care, 29.2% started ETF within a mean of 1.98 days after enrolment and 24.1% received supplemental PN (SPN) within 5.58 days after the start of ETF. Additionally, 27.3% initiated PN within 1.99 days after enrolment, with 43.0% progressing to ETF within 5.08 days after starting PN. Therefore, 40.8% of patients receiving standard care never received ETF or PN during their ICU stay (average 3.72 days). Patients who received early PN had significantly higher energy and amino acid/protein intakes on each of the first 6 days of admission to ICU after study enrolment (p values not reported).
- Heidegger and colleagues (2013) conducted an RCT ('Swiss SPN study') to assess whether delivering 100% of energy targets with SPN (ETF + PN) on days 4–8 of the ICU stay would optimize clinical outcome.[130] This study involved 305 medical and surgical ICU patients; patients who received <60% of their energy target on ETF alone on day 3 of ICU admission were enrolled and randomized to receive ETF alone or SPN. SPN significantly increased mean energy and protein delivery over days 4–8 (both $p < 0.0001$) compared with ETF alone; 103% and 100% of the energy and protein target, respectively, was achieved in the SPN group, compared with 77% and 71% in the ETF group.
- A cross-sectional retrospective observational study in eight Latin American countries found that patients receiving SPN (ETF + PN) were significantly more likely to achieve >90% of their daily energy and protein targets than patients receiving ETF alone (odds ratio [OR] 1.56; 95% CI 1.02–2.39; p = 0.038).[211] SPN was associated with 64% and 56% increases, respectively, in the likelihood of achieving >90% of target daily energy and protein intake. Most patients (79.9%) received ETF alone, 9.4% received PN alone, and 10.7% received SPN. However, the authors argued that use of PN should have been higher, given that 74.1% of patients were assessed as having moderate or severe malnutrition and more than one-third had a contraindication or intolerance to ETF.

- The International Study Group of Pancreatic Surgery highlights that delayed gastric emptying and/or intestinal paralysis can occur after pancreaticoduodenectomy, leading to insufficient post-operative calorie intake and prolonged hospitalization.[235] Therefore, Probst and colleagues (2016) retrospectively evaluated the safety and efficacy of post-operative SPN in 69 consecutive patients who received pancreaticoduodenectomy between 2003 and 2012. Early SPN (ETF + PN) initiated immediately after surgery was safe, and provided comprehensive coverage of nutritional needs during the post-operative period after pancreaticoduodenectomy.[236] The median nutritional balance (i.e., coverage of calorie target per patient during hospitalization) was 93.4%. Moreover, calorie targets were achieved for 71.3% of 1,516 patient-days and for 6 of the first 7 days after surgery, when catabolic stress is most intense.
- Kutsogiannis and colleagues (2011) reported an international multicentre observational study (29 countries) that evaluated the early use of SPN (ETF + PN) in 2,920 mechanically ventilated patients with GI dysfunction who spent more than 72 hours in the ICU.[124] Outcomes were compared for patients receiving early ETF alone, early SPN, and early ETF + late PN. The early SPN group were most likely to achieve energy and protein targets (81.2% and 80.1%, respectively vs 63.4% and 59.3% with ETF/late PN and 63.4% and 59.3% with early ETF; $p < 0.0001$).
- An international multicentre observational study by Cahill and colleagues (2011) evaluated the effects of timely initiation of PN on nutritional adequacy in critically ill patients who were not fed adequately with ETF.[237] The analysis included data from 703 patients who spent >72 hours in the ICU and were eligible to receive ETF 48 hours after admission. Most patients (77%) received late ETF without PN. In patients receiving late ETF and PN, 11.8% received early PN and 11.2% received late PN. Patients receiving early PN were most likely to achieve adequate energy and protein intake (74.1% and 71.5%, respectively) whereas patients in the late ETF group were least likely to achieve adequate energy and protein intake (42.9% and 38.7%; $p < 0.001$).

3.3.2.2 NUTRITIONAL STATUS

- ESPEN oncology guidelines[157] highlight that that PN has been shown to maintain nutritional status in patients with severe intestinal insufficiency caused by radiation enteritis, chronic bowel obstruction, SBS, peritoneal carcinomatosis, or chylothorax.[172; 238; 239]

CRITICAL ILLNESS AND SURGERY

Timely administration of PN (SPN or TPN) in hospital patients has been shown to preserve nutritional status and prevent skeletal muscle wasting and fat loss

- In the large, multicentre, single-blind RCT conducted by Doig and colleagues (2013) to evaluate the nutritional and clinical benefits of early PN in critically ill adults with a short-term relative contradiction to early ETF,132 patients randomized to receive standard care (usual clinical practice in individual ICUs), experienced significantly greater muscle wasting (0.43 vs 0.27 increase in subjective global assessment [SGA] score per week (mean difference, 0.16; 95% CI 0.038–0.28; $p = 0.01$)) and significantly greater fat loss (0.44 vs 0.31 increase in SGA score per week; mean difference, 0.13; 95% CI 0.01–0.25; $p = 0.04$) during their ICU stay than patients receiving PN within 24 hours of admission. This suggests that early administration of PN may protect against both muscle wasting and fat loss. In addition, mid-arm circumference was significantly reduced by day 2 in patients receiving standard care (0.2 cm loss) whereas patients receiving early PN did not experience any reduction (0.0 cm loss; $p = 0.04$); however, these differences did not remain significant for the whole of the ICU stay (0.8 vs 0.4 cm loss per week; $p = 0.28$).

- An open-label single-centre RCT conducted by Wu and colleagues (2016) evaluated the efficacy and safety of early SPN (within 24 hours of surgery) in 80 patients undergoing oesophagectomy. Patients receiving SPN to meet caloric targets, but not those receiving ETF alone, had preserved fat free mass (1.46 ± 2.97 vs –2.08 ± 4.16 kg) and body weight (0.18 ± 3.38 vs –2.15 ± 3.19 kg; $p < .05$) relative to preoperative measurements.[240]
- Bauer and colleagues carried out a double-blind RCT to determine whether early SPN (ETF + PN) improves nutrition status and clinical outcomes compared with ETF alone.[241] This study included 120 critically ill adults (60 in each group) who were admitted to the ICU for at least 3 days and were expected to survive for at least 3 days; patients must have consumed <20 kcal/kg daily. Patients with a contraindication to ETF or PN were excluded. Patients received their assigned therapy for 4–7 days after initiation of nutritional support. Overall, 32% of patients were moderately malnourished and 9% were severely malnourished. Nutritional status, measured using levels of retinol-binding protein (RBP) and prealbumin, was significantly higher in patients receiving SPN; RBP and prealbumin corrected more rapidly from day 0 to day 7 in the SPN group than in the ETF group ($p = 0.0496$ and $p = 0.0369$, respectively), as did levels of Vitamin E ($p = 0.031$).
- A retrospective analysis of data from 90 consecutive patients who underwent total gastrectomy for malignancy found that post-operative nutrition support with TPN reduced in-hospital weight loss and attenuated weight loss post discharge.[242] In this study, 42% of patients received postoperative TPN and 53% received IV fluids alone. At preoperative assessment, patients receiving TPN were significantly more malnourished than those who received IV fluids. However, the latter patients lost significantly more weight during their hospital stay (5.2 kg, vs 3.1 kg in those on TPN; $p = 0.008$). Furthermore, 69% of patients receiving only IV fluids lost a severe amount of weight (measured using Blackburn criteria) compared with 34% of the TPN group ($p = 0.01$). Patients who received only IV fluids continued to lose significantly more weight after discharge (7.5 kg, vs 2.9 kg in TPN patients; $p = 0.01$). From pre-surgery to outpatient follow-up (3 months), patients who received IV fluids lost an average of 17.8 kg, compared with 9.6 kg in TPN patients ($p < 0.01$).
- Liebau and colleagues evaluated the effects of supplementing EN with parenteral amino acids (equivalent to 1 g/kg per day), infused over 3 hours, on whole-body protein turnover in critically ill patients during their first week in the the ICU.[243] Patients were assessed at baseline during ongoing nutrition ($n = 13$) and then during amino acid supplementation if they were still in the ICE 2–4 days later ($n = 7$). Parenteral amino acid supplementation significantly improved protein balance at both timepoints ($p = 0.001$ and $p = 0.0018$, respectively), attributed to increased protein synthesis, which attained significance during the first measurement ($p = 0.007$). Importantly, amino acid oxidation did not increase during the 3 hour amino acid infusion. There was also a positive correlation ($r = 0.80$; $p < 0.0001$) between total amino acids and/or protein administered and whole-body protein balance.

Use of PN (TPN and SPN) in critically ill surgical patients may promote the recovery of immune function and improve nutritional status

- Yao and colleagues (2005) evaluated the effect of perioperative PN on nutritional status and postoperative outcome in 32 severely malnourished patients with CD who underwent bowel surgery for obstruction; 16 patients received perioperative PN and 16 received IV fluids alone (isocaloric diet).[244] PN was started 1 week before surgery and continued for 2 weeks after. BMI increased significantly in the PN group (from 13.9 ± 0.6 to 15.3 ± 0.7 kg/m^2, $p = 0.02$) but not in the IV fluids group. In addition, serum immunoglobulin M levels, which had increased significantly in both groups before surgery ($p = 0.04$), returned to normal 3 weeks after surgery in patients receiving PN ($p = 0.02$) but not for those receiving IV fluids only, suggesting that PN had a positive effect on humoral immunity.[244] The rate of postoperative complications was similar in both groups, but at 6 months' follow up, more patients in the PN group had returned to work, suggesting that perioperative PN had a long-lasting effect on recovery.[244]
- A prospective RCT in China reported by Fan and colleagues compared the effects of SPN (ETF + PN), ETF alone, and PN alone on immune function, nutritional status, complications, and clinical outcomes in 120 patients with undergoing surgery for severe traumatic brain injury (40 patients in each group). Measures of immune function (certain T-lymphocyte subsets and plasma immunoglobulin) were significantly increased from baseline after 20 days of treatment in patients receiving SPN ($p < 0.01$) and were significantly higher than for patients receiving PN or ETF alone ($p < 0.05$ and $p < 0.01$). Nutritional status (Nutritional Risk Screening tool) was also significantly higher in the SPN group and the EN alone group (both, $p < 0.01$) except for serum prealbumin which was higher in the SPN group.[245]

PAEDIATRIC PATIENTS

Timely protein and energy intake is associated with improved developmental outcomes in preterm and extremely low birth weight (LBW) infants, providing rationale for early initiation of TPN

- A systematic review and meta-analysis by Moyses and colleagues (2013) showed that early administration of PN improves short-term growth outcomes in preterm infants.[246] Eight RCTs ($n = 533$) and 13 observational studies ($n = 1,796$) met the inclusion criteria. The analysis showed that early PN reduced the time to regain birth weight by 2.2 days (1.1–3.2 days) in RCTs and 3.2 days (2.0–4.4 days) in observational studies (both $P < 0.001$). Furthermore, maximum percentage weight loss was lower with early PN by 3.1 (1.7–4.5) percentage points in RCTs and by 3.5 (2.6–4.3) in observational studies (both $p < 0.001$). Early PN also improved weight at discharge or 36 weeks postmenstrual age by 14.9 g (5.3–24.5 g) in the observational studies ($p = 0.002$); however, no benefit was shown for length or head circumference.
- An open-label randomized controlled multi-intervention trial found that supplementing the enteral supply of energy, protein, essential fatty acids, and vitamin A with PN in very low birthweight (VLBW) infants (<1,500 g) resulted in postnatal growth in-line with birth percentiles for weight and head circumference.[247] The SPN group had a lower mean birth weight ($p = 0.03$) and contained a higher proportion of infants who were small for gestational age ($p = 0.04$) than the group who received EN alone. Mean energy and protein delivered in the SPN group over the first 4 weeks of life were significantly higher in the SPN group (139 vs 126 kcal/kg per day [$p < 0.001$] and 4.0 vs 3.2 g/kg/day [$p < 0.001$], respectively). Infants receiving SPN regained birth weight significantly faster ($p = 0.001$) and maintained their z-scores for weight and head circumference from birth to 36 weeks' postmenstrual age (both $p < 0.001$). Median growth velocity was also significantly higher in the SPN group (17.4 [interquartile range 16.3–18.6] vs 13.8 [13.2–15.5]] g/kg per day; p 0.001). The proportion of growth-restricted infants at this time point did not differ from baseline in the SPN group (11 of 23 infants) but increased in the control group from 4 to 13 infants ($n = 21$).

- An open-label, multicentre, non-comparative Phase 3 trial by Rigo and colleagues in preterm infants evaluated PN (administered for 5–10 consecutive days) containing amino acids and energy intake within the range of "aggressive" nutrition recommendations for VLBW infants,[248] Mean nutrient intake and mean weight gain were within the range recommended by guidelines[249] for preterm infants.
- A chart review of daily protein and energy intakes during the first 4 weeks of life in 148 extremely LBW infants showed that, after adjusting for confounding variables, week 1 energy and protein intakes were both independently associated with improvement in score on the Mental Development Index (MDI),[250] such that every 42 kJ (10 kcal)/kg per day was associated with a 4.6-point increase in the MDI and each g/kg per day in protein intake was associated with an 8.2-point increase. Furthermore, higher protein intake was associated with a lower likelihood of body length <10th percentile.[250]

Short-term PN accelerates weight gain and head growth, even in healthy Very LBW infants

- Morisaki and colleagues (2014) analysed registry data 4,005 hospitalized Very LBW preterm infants from the Neonatal Research Network of Japan to determine whether PN had any benefits on growth in infants who reached full enteral feeding by day 14.[251] PN was administered to 40% of infants. After adjusting for maternal, infant and institutional characteristics, infants who received PN had greater weight gain (0.09 SD; 95% CI 0.02–0.16) and head growth (0.16 SD; 95% CI 0.05–0.28), and lower odds of extra-uterine growth restriction by head circumference (OR 0.66, 95% CI: 0.49, 0.88), suggesting that even infants who can be enterally fed within 2 weeks may benefit from SPN.

Timely amino acid supplementation in preterm infants may improve clinical outcomes

- A Cochrane review conducted by Trivedi and colleagues (2013) evaluated the impact of early versus late administration of amino acid solution, with or without other PN components, on various outcomes in preterm infants. Evidence for improved nitrogen balance with amino acid supplementation was seen in four of the seven studies included.[252] One of these studies (Tang et al. 2009[253]) found that infants who received amino acids with 24 hours of birth had shorter PICU stay (by 5.5 days), fewer days to enteral nutrition (by 4.2 days), shorter duration of admission ($p < 0.05$) and fewer days to regain birth weight (11.7 vs 14.1 days).

CANCER

PN has been shown to improve or stabilize nutritional status in patients with cancer, including those with cachexia

- Cachexia (skeletal muscle loss with or without fat loss) is common in patients with upper GI cancer.[254] Pelzer and colleagues (2010) showed a positive effect of PN on measures of nutritional status in patients with advanced cancer and progressive cachexia. In this Phase 2 study, 32 patients with advanced pancreatic cancer and progressive cachexia who were experiencing ongoing weight loss despite ETF received additional overnight HPN for 5 out of 7 days. Nutritional status was measured using bioelectrical impedance analysis (BIA) including phase angle, which is a potential predictor of survival in cancer patients,[255] the ratio of extracellular mass (ECM) to body cell mass (BCM) index, and BMI. Median treatment duration was 18 weeks (8–35 weeks). Nearly half of patients had a temporarily improved phase angle (the main parameter). Median BMI increased from 19.7 to 20.5 kg/m^2 during nutrition therapy, median ECM/BCM index decreased from 1.7 to 1.5, and phase angle increased by 10% (from 3.6 to 3.9). A follow-on study involving a larger patient cohort is currently being conducted to correlate the level of nutritional improvement with overall survival and QOL.[254]

- Richter and colleagues (2012) prospectively evaluated the addition of PN during chemotherapy in patients with advanced pancreatic cancer in Germany.[256] Two groups of patients were retrospectively defined based on survival following initiation of PN: Group 1, ≥5–>37 months (n = 10) and Group 2, 1–4 months (n = 7). Eighty percent of patients in Group 1 showed an increase in body weight with initial PN and the other patients after dose adaption. This positive effect of PN was also confirmed at the cellular level using BIA (i.e., phase angle), BCM, ECM, cell content, and the ECM/BCM index. Moreover, results were reproducible in two patients who received two or three episodes of PN: when PN was interrupted, all BIA parameters worsened before improving when PN was restarted. In Group 2, PN was started in the late stage of the disease (i.e., after failure of final chemotherapy). Importantly, the results indicated that weight loss could be reversed, even if the effects on body weight and BIA parameters were less pronounced than in patients in Group 1.[256]

Use of HPN improves nutritional status in patients with cancer

- Culine and colleagues (2014) reported a prospective observational study in 767 patients with cancer (65.3% with metastatic disease) to evaluate the benefit of HPN.[257] After 28 days of HPN, mean body weight had increased by 2.5% ($p < 0.001$), with most patients (67%) gaining weight. The nutrition status (measured using the Nutrition Risk Index and serum albumin) also increased significantly ($p < 0.001$), as did glycaemia and serum haemoglobin (both $p < 0.05$).[257]
- A longitudinal study reported by Vashi and colleagues (2014) of patients with advanced cancer (various tumour types) found significant improvements in nutritional status, measured by increased body weight from baseline at 1 month (from 61.5 to 63.1 kg; $p = 0.03$), 2 months (from 57.6 to 60 kg; $p = 0.04$), and 3 months (from 61.1 to 65.9 kg; $p = 0.04$) and in SGA scores ($p < 0.05$ for all time points), irrespective of tumour type.[258] Each month of HPN was associated with 1.3 kg increase in body weight ($p = 0.009$).
- Lundholm and colleagues conducted a randomized prospective study in 309 cancer patients with progressive cachexia (primarily due to GI tumours), to evaluate whether specialized nutrition-focused care (including HPN) improved integrated whole-body metabolism and functional outcome; patients were receiving systemic anti-inflammatory treatment and erythropoietin.[259] Approximately, 50% of patients received HPN; the other half were dependent on spontaneous oral intake alone. The intent-to-treat analysis showed an improvement in energy balance for HPN patients ($p < 0.03$). Furthermore, the as-treated analysis showed an improved energy balance ($p < 0.001$), an increase in body fat ($p < 0.05$; which was lower in the HPN group than in the control group at baseline), a greater maximum exercise capacity ($p < 0.04$), and a trend toward increased metabolic efficiency at maximum exercise capacity ($p < 0.06$) for patients receiving HPN, suggesting that nutritional support may protect both integrated metabolism and metabolic function in patients with progressive cancer-related cachexia.[259]
- Senesse and colleagues (2015) conducted a prospective observational study in 370 patients with GI cancer (71% with metastatic disease), to evaluate the impact of HPN on QOL and nutritional status.[260] HPN was used to supplement oral intake in 84% of patients. After 28 days of HPN, body weight improved by 2.7% from baseline ($p < 0.001$) while nutrition risk decreased (NRI scores, 3.2 ± 1.1 vs 2.8 ± 1.3, $p = 0.003$).

- Drissi and colleagues conducted a large retrospective analysis of data from 53 oncology centres in Germany, to determine current PN practice in the outpatient setting, with a view to improving patient-centred nutritional care. Two patient cohorts were analysed: all oncology patients treated during the fourth quarter of 2004, and all patients administered PN during the whole study period (July 2010–March 2011). In the first cohort, 2.46% (*n* = 626) of 25,424 cancer patients received PN; the most frequent diagnosis was gastric cancer. In the second cohort (*n* = 1,137), impaired GI motility was a frequent indication for PN—60.3% of patients received SPN and 37.3% received TPN (2.4% missing data). Patients in the second cohort showed a stable or slowly increasing BMI (from 21.6 ± 3.8 to 21.8 ± 3.5 kg/m^2): patients on TPN had a mean increase in BMI points of 0.4 ± 1.6 (range –6.0 to 6.1) during the observation period whereas patients on SPN had an increase of 0.3 ±1.5 (–6.9 to 7.0).[261]

PN improves nutritional status in children with cancer and in those undergoing high-dose chemotherapy and stem cell transplantation

A number of early paediatric RCTs examined the impact of PN on nutritional status in children with cancer.[179] These studies show that in primarily well-nourished cancer patients, administration of PN for 17–104 days significantly increases body weight, nitrogen balance, and anthropometric measures of nutrition status, such as arm-muscle circumference and triceps skinfold measurement. PN also promoted maintenance of total leukocyte and absolute granulocyte counts compared with those of control groups.[262-264] Similarly, early non-randomized studies in which PN was administered for approximately 4 weeks showed a significant increase from baseline in anthropometric measures (e.g., arm muscle area, triceps and subscapular skinfold measurements, and percentage of diagnosis weight) as well as serum transferrin, albumin, prealbumin, and RBP levels.[179; 265-269]

Initiating TPN in the early post-transplant period in paediatric patients undergoing autologous HSCT may improve nutritional status and contribute to recovery of haematopoiesis. Wędrychowicz and colleagues (2010) evaluated the impact of TPN on nutritional status in 22 children and adolescents (median age 5.4 years) undergoing high-dose chemotherapy followed by autologous HSCT.[270] Patients received isoenergetic and isonitrogenous TPN with electrolytes (based on individual requirements). Mucositis was observed in 82% of patients. Assessment of nutrition parameters showed an increase in serum albumin levels after TPN (p 0.0005). Additionally, TPN duration correlated with recovery of leukocytes (p = 0.05) and platelets (p = 0.04).

KIDNEY DISEASE

IDPN improves nutritional status in adults on maintenance haemodialysis (HD)

- PEW is a significant cause of morbidity and mortality in patients on maintenance HD.[271] A multicentre open-label Phase 4 RCT conducted by the German IDPN-Trial group showed that IDPN, administered three times weekly in a 16-week intervention resulted in a statistically significant and clinically relevant increase in mean serum prealbumin (a surrogate marker for outcome and survival in HD patients with PEW) and was superior to nutritional counseling.[272] IDPN significantly increased serum prealbumin ($p < 0.05$) compared with nutritional counselling, with rapid increases during the first 16 weeks of therapy and stabilizing thereafter. Analysis of the full dataset (*n* = 83) showed that 40.0% of 39 patients receiving IDPN had a relevant (i.e., ≥15%) increase in prealbumin from baseline at week 4, compared with 20.5% of 44 patients in the control group, and more patients on IDPN achieved an increase in prealbumin >30 mg/L at week 16 (48.7% vs 31.8%). Furthermore, prealbumin response to IDPN was greater for patients with moderate malnutrition (SGA score B) than with severe malnutrition (SGA score C).

- Cano and colleagues (1990) conducted a non-randomized study to evaluate the impact of nutrition delivered by peridialytic PN (PDPN) in 26 malnourished patients on HD.[273] Compared with control patients, patients receiving PDPN showed increases in body weight ($p < 0.01$), arm-muscle circumference ($p < 0.02$), serum transthyretin and albumin concentrations ($p < 0.05$), interdialytic creatinine appearance ($p < 0.01$), skin-test reactivity ($p < 0.02$), plasma leucine ($p < 0.05$) without modifications of other amino acids, and plasma apolipoprotein A-I ($p < 0.01$) but without significant changes in levels of apolipoprotein B, cholesterol, triglyceride, or phospholipid.
- Navarro and colleagues (2000) investigated the effects of intradialytic amino acid supplementation on nutritional status in a randomized study of 17 stable HD patients; 10 were randomized to receive amino acid supplementation.[274] After 3 months, patients receiving amino acid supplementation had a significant improvement from baseline in protein catabolic rate and serum albumin and transferrin (all $p < 0.05$) whereas significant changes in these measures were not observed in control patients. Furthermore, these improvements occurred without any change in the dialysis dose.

IDPN has been shown to promote weight gain and increase BMI in children on haemodialysis (HD) with protein-energy malnutrition (PEM)

- Orellana and colleagues (2005) evaluated the benefit of providing supplementary nutrition via IDPN to adolescent patients on maintenance HD with PEM.[271] IDPN was administered to all patients with >10% weight loss and who were at <90th percentile of ideal body weight. Nine patients received IDPN three times weekly for 3–22 months. Six of these patients experienced significant increases in both weight and BMI (both $p < 0.01$) and one patient stopped losing weight. The other two patients continued to lose weight during the initial 5 months of IDPN. Normalized protein catabolic rate also increased significantly in patients who responded to IDPN ($p = 0.03$) but there was no change in serum albumin. Cohort analysis determined that all patients with organic PEM responded to IDPN therapy, whereas patients with psychosocial causes of PEM did not.

3.3.3 Functional benefits of PN

CRITICAL ILLNESS AND SURGERY

Higher protein intake, as recommended in nutrition guidelines, may lead to clinically significant improvements in the functional status of critically ill patients

- Ferrie and colleagues (2016) compared standard amino acid intake versus the higher level recommended amino acid intake (0.8 vs 1.2 g/kg) in a double-blind RCT involving 120 critically ill (mostly surgical) patients requiring PN; all patients had received mechanical ventilation.[275] Data were available for 59 patients who received high protein and 60 who received standard protein. Actual amino acid delivery from PN was 0.9 and 1.1 g/kg in the two groups, respectively. The primary endpoint of handgrip strength at discharge did not quite meet statistical significance ($p = 0.54$); however, the high-protein group showed a significant improvement in handgrip strength at day 7 (secondary endpoint; $p = 0.025$). These patients also experienced less fatigue, measured using the Chalder score (mean [SD]: 5.4 [2.2] vs 6.2 [2.2]; $p = 0.045$) and greater forearm-muscle thickness (3.2 [0.4] vs 2.8 [0.4] cm; $p < 0.0001$).

Supplementing ETF with PN to achieve target caloric intake leads to functional benefits in hospital patients

- In an open-label single-centre RCT reported by Wu et al. (2016), timely (within 24 hours) initiation of SPN (ETF + PN) following surgical resection of oesophageal cancer resulted in significant improvements at 90 days post-surgery in physical functioning (Medical Outcomes Survey Short-Form versus ETF [MOS-SF 36] scores 71.5 ± 24.3 vs 60.4 ± 27.4 [$p = 0.0387$])) and energy/fatigue (62.9 ± 19.5 vs 54.2 ± 23.5 [$p = 0.0482$]).[240] Further more, multivariate regression analysis showed that changes in body weight ($p = 0.015$; 95% CI 1.544–2.808 kg) and fat-free mass ($p = 0.048$; 95% CI 0.761–2.612 kg) were independent predictors for improvement in physical functioning score, while change in fat-free mass ($p < 0.001$; 95% CI 3.006–4.018 kg) was an independent predictor for improvement in energy/fatigue score.

Patients undergoing abdominal surgery for Crohn's disease (CD) were more likely to resume work within 6 months if they had received preoperative PN

- Yao and colleagues (2005) evaluated the effect of perioperative PN on nutritional status and postoperative outcome in 32 severely malnourished patients with CD who had undergone bowel surgery for obstruction. Patients who received preoperative PN for 3 weeks were more likely return to work within 6 months than those who did not (p value not reported).[244]

CANCER

HPN improves functional status in patients with cancer

- A randomized prospective study that investigated the impact of specialized nutrition-focused patient care (including PN) in 309 cancer patients with progressive cachexia (primarily due to GI tumours) showed that those receiving PN had greater maximum exercise capacity (measured by treadmill walking test that progressively increased speed and incline) than control patients who did not receive nutrition support ($p < 0.04$).[259]
- Culine and colleagues (2014) reported a prospective observational study that assessed the impact of HPN on QOL in cancer patients ($n = 767$). Functional capacity (evaluated using performance status [PS] score) improved in 22% of patients and was stable in 58% after 28 days of HPN (p values not reported).[257] Moreover, there was a significant association between functional capacity and measures of nutritional status, including body mass index (BMI) ($p = 0.006$), serum albumin ($p = 0.005$), Nutrition Risk Index ($p = 0.01$), and weight loss ($p < 0.0001$). Decline in PS correlated with deterioration in nutritional status (p value not reported), suggesting that poor nutritional status may compromise functional capacity.
- A longitudinal study by Vashi and colleagues (2014) in 52 patients with advanced cancer (various diagnoses) receiving HPN reported significant improvements from baseline in key PS after 1 month (61.6 to 67.3; $p = 0.01$), 2 months (63.2 to 73.2; $p = 0.01$), and 3 months (63.2 to 73.2; $p = 0.01$), irrespective of tumour type.[258] Furthermore, every 1 month of HPN was associated with an increase of in Karnofsky Performance Status (KPS) of 5.8 points ($p < 0.001$).
- Analysis of data from 618 patients with advanced cancer who received HAN (53.9% HPN) in Italy between 1990 and 2012 showed that key PS was related to survival ($p < 0.0001$).[276] One month after starting HAN, KPS remained unchanged in 67% of patients and was increased in 21% of patients, with no significant difference between ETF versus PN. KPS was also significantly increased ($p < 0.05$) in the patients with head and neck cancer.

HPN improves QOL in patients with cancer

- A prospective, longitudinal, observational study reported by Cotogni and colleagues (2017) assessed the QOL (measured using the European Organisation for Research and Treatment of Cancer [EORTC) Core Quality of Life questionnaire [QLQ-C30]) in 111 patients with advanced cancer. All patients had a residual but insufficient oral food intake and required supplemental HPN.[217] Significant improvements were seen in global QOL ($p < 0.001$), physical functioning ($p < 0.001$), role functioning ($p < 0.007$), emotional functioning ($p < 0.001$), appetite ($p = 0.004$) and fatigue (p 0.022) while patients were receiving HPN, even in patients with advanced cancer who were receiving chemotherapy.
- Senesse and colleagues (2015) reported a prospective observational study that evaluated the effect of HPN on QOL and nutritional status in 370 patients with GI cancer, 71% of whom had metastatic disease. Global QOL increased significantly after 28 days of HPN (from 48.9 at inclusion to 50.3, $p = 0.007$).[260]
- Aeberhard and colleagues (2015) reported a multicentre observational benchmarking study of adult HPN in Switzerland.[277] Data on personal characteristics, demographics, and social activities were collected through interviews and QOL data using the MOS SF-36 (version 2). The analysis was based on 33 patients, mostly with cancer, radiation enteritis, or requiring PN following bariatric surgery. Before the disease, 52% of patients were very active whereas 58% were not active at all during the disease but before HPN. Activity levels improved during HPN, with 52% reporting that they were now "a little active". During the 3 month observation period, nearly all patients showed improved mental and physical QOL: physical component scores improved from 34.0 2 to 39.7 and mental component scores improved from 41.91 to 46.35.[277]
- In a prospective observational study by Culine and colleagues (2014) to assess the impact of HPN on QOL in cancer patients ($n = 767$), significant improvement from baseline were seen in QOL (Functional Assessment of Cancer Treatment – General [FACT-G] questionnaire) after 28 days of HPN (from 48.35 ± 5.01 at baseline to 49.95 ± 5.82; improvement of 3.2%; $n = 412$; $p < 0.0001$).[257] Mean physical wellbeing improved by 13% at day 28, and familial/social, emotional and functional wellbeing improved by 3.2, 4.1 and 6.6%, respectively. Overall, QOL was improved in 60% of patients, and 15% had stable QOL, after 28 days of HPN. Furthermore, almost 80% of patients perceived a positive impact of HPN (i.e., >5 on a 0–10 visual analogue scale).
- In a longitudinal study conducted by Vashi and colleagues (2014) in 52 patients with advanced cancer (various diagnoses) receiving HPN, significant improvements from baseline in global QOL (EORTC QLQ-C30) were reported after 2 months (from 37.1 to 49.2; $p = 0.02$), and 3 months (from 30.6 to 54.4; $p = 0.02$), irrespective of tumour type.[258] Every 1 month of HPN was associated with an increase of 6.3 points in global QOL ($p < 0.001$).
- Several older studies provide further evidence that in patients with incurable cancer who survive for more than 3 months, QOL remains stable in those receiving HPN.[278-281]

3.3.4 Clinical benefits of PN

3.3.4.1 MORTALITY AND SURVIVAL

CRITICAL ILLNESS

PN has been shown to reduce mortality versus standard care in malnourished critically ill patients with pancreatitis

- Results of a meta-analysis of seven studies involving 798 patients comparing PN with standard care (conventional oral diet and IV dextrose) by Braunschweig and colleagues (2001) found that, in studies involving a high proportion of malnourished patients, standard care was associated with a significantly higher risk for mortality compared with PN (relative risk (RR) 3.0; 95% CI 10.9–8.56).[282] Although this study was conducted some years ago, it has informed current ASPEN and ESPEN guidelines on PN in the critical care setting, which recommend timely use of PN in the ICU if EN is contraindicated or not tolerated.[90; 283] Given this recommendation, it is unlikely that future studies will be conducted to compare the use of PN versus no PN in critically ill patients who are malnourished or at high nutritional risk.
- Xian-li and colleagues (2004) conducted a randomized study to compare glutamine-supplemented TPN and standard TPN versus no TPN in 64 patients with serious acute pancreatitis receiving traditional therapy.[284] Serum albumin concentrations were low at admission, suggesting poor nutritional status, but increased significantly after 2 weeks of standard or glutamine-supplemented TPN groups compared with no TPN ($p < 0.05$ for both comparisons). Furthermore, mortality was significantly higher in patients who did not receive TPN (43.5%) than in patients who received either glutamine-supplemented TPN (0.0%) or standard TPN (14.3%).

In critically ill patients, higher protein and energy intake is associated with significantly reduced mortality and shorter time to discharge alive, even when patients do not achieve target intake

- A prospective multicentre cohort study by Compher and colleagues showed that greater protein and energy intake is associated with lower mortality and faster time to discharge alive in ICU patients who are at high risk for malnutrition.[138] A total of 2,853 mechanically ventilated patients with ≥4 days' stay in the ICU and a subset of 1,605 patients with ≥12 days' stay were included in the analysis. Most patients had been admitted to an ICU for medical reasons (65%) or emergency surgery (30%). TPN was used in 8.7% of patients and SPN in 13.8%. The results showed that every 10% increase in protein and energy intake relative to goal was associated with a significant decrease in odds of mortality of 6.6% and 7.1%, respectively, for high-risk patients in the ≥4 day group ($p = 0.003$ and $p < 0.001$) and by 10.1% and 11.6%, respectively, ($p = 0.003$ and $p < 0.001$) in the ≥12 day group.[138] Likewise, time to discharge alive was 5.1% and 4.5% shorter ($p = 0.01$ and $p = 0.019$) for each 10% increase in protein and energy intake, respectively, relative to goal in the ≥4 day group, and by 9.2% and 9.1% (both $p = 0.002$) in ≥12 day group.[138] These significant improvements in clinical outcomes occurred even though patients received only 62% and 59% of their goal energy and protein intake.
- A retrospective cohort study by Zusman and colleagues (2016) involving 5,053 critically ill patients who received enteral and/or parenteral feeding and were in the ICU for more than 96 hours showed that increasing protein intake (assessed as g per day and % of requirement, with a target of 1.3 g/kg) was linearly and independently associated with decreased 60 day mortality (HR 0.99, CI 0.98–0.99, $p = 0.02$).

- Nicolo and colleagues (2015) evaluated whether increasing protein delivery reduces mortality and time to discharge alive from the ICU.[285] Data were analysed from the Canadian Improving Nutrition Practices in the Critically Ill International Nutrition Surveys 2013.[285] The sample included 2,828 and 1,584 patients who remained in the ICU for ≥4 and ≥12 days, respectively (65% of patients were admitted to medical ICUs). Patients in the ≥4 day sample received an average of 60.5% and 64.1% of their prescribed protein and energy intake, respectively, while patients in the ≥12 day sample received 66.7% and 70.7%, respectively. The proportion of patients receiving PN or SPN was not reported. The results showed that higher protein intake was associated with reduced mortality in the ≥4 day sample (OR 0.63; 95% CI 0.47–0.84), adjusted model, and for the ≥12 day sample (OR 0.65; 95% CI 0.45–0.94), relative to patients achieving <80% of goal intake. Furthermore, in the ≥12 day sample, time to discharge alive was shorter for patients receiving ≥80% of prescribed protein (hazard ratio [HR] 1.25; 95% CI, 1.04–1.49).
- In a prospective observational cohort study by Allingstrup and colleagues (2012) involving 113 critically ill patients, higher protein provision was associated with improved survival time.[134] The results were confirmed in a Cox regression analysis, which showed that increased protein provision was associated with a significantly lower hazard ratio for death (risk of death vs time was decreased by 2% for each g of protein and amino acids provided; unadjusted HR 0.98; 95% CI 0.96–0.99; $p = 0.01$). The results remained significant after adjusting for baseline patient characteristics. However, provision of energy, resting energy expenditure, and energy and nitrogen balances were not related to the risk of death in these patients.
- Alberda and colleagues (2009) conducted an international, multicentre study (167 ICUs from 21 countries) to investigate how the amount of protein and energy administered affected clinical outcomes.[91] They followed 2,772 mechanically ventilated patients to determine 60 day mortality and number of ventilator-free days; 8.0% or patients received TPN and 17.6% received SPN (ETF + PN). Patients received an average of 1,034 kcal and 47 g of protein per day. Regression analysis showed that an increase of 1,000 kcal per day reduced 60 day mortality [OR 0.76; 95% CI 0.61–0.95; $p = 0.014$] and increased the number of ventilator-free days (OR 3.5; 95% CI 1.2–5.9; $p = 0.003$) for patients with BMI <25 or ≥35 kg/m^2. Likewise, an additional 30 g protein per day reduced 60 day mortality (OR 0.84; 95% CI 0.74–0.96; $p = 0.008$) for patients with a BMI <25 or ≥35. The authors suggest that increasing nutrient provision in the early phase of critical illness to minimize protein–energy deficit may improve clinical outcomes, particularly in patients with a low or high BMI.

(H) Timely high protein intake in the ICU is associated with reduced hospital mortality in mechanically ventilated critically ill patients without sepsis

- Weijs and colleagues (2014) reported out a post-hoc analysis of prospectively collected observational data from a mixed medical/surgical ICU in the Netherlands.[286] Data were from 843 critically ill patients who received prolonged mechanical ventilation (>72 hours). Protein was provided with a target of 1.2–1.5 g/kg pre-admission body weight; 1% of patients received TPN and 26% received SPN (ETF + PN). Higher protein intake was associated with significantly lower mortality in non-septic, non-overfed patients ($n = 419$): 36.8%, 35%, 26.5%, and 19.1% in patients with protein in takes of <0.8, 0.8–<1.0, 1.0–<1.2, and ≥1.2 g/kg, respectively ($p = 0.033$). Hospital mortality was 34.5% for patients with day 4 protein intake <1.2 g/kg compared with 19.1% for patients with protein intake ≥1.2 g/kg ($p = 0.015$).

In patients with severe traumatic brain injury, SPN may provide survival benefits compared with ETF or PN alone

- In a prospective RCT by Fan and colleagues in patients with undergoing surgery for severe traumatic brain injury, the mortality rate was significantly lower in patients receiving SPN (ETF + PN) than in patients receiving either ETF or PN alone (χ^2 = 7.50, 16.37; $p < 0.05$, $p < 0.01$).[245]

INTESTINAL FAILURE

- Guidelines highlight that PN is a life-sustaining therapy for patients with reduced GI function who are unable to absorb sufficient macronutrients and/or water and electrolytes to meet their nutritional needs and therefore does not require evaluation of efficacy in RCTs.[28] Furthermore, the ability of PN to preserve QOL and promote rehabilitation supports its use in the home setting (HPN).[28]

HPN is associated with high probability of survival in patients with benign intestinal failure (IF)

- Pironi and colleagues (2012) conducted a benchmarking exercise to compare the literature on HPN against the results of a prospective European survey that evaluated the appropriateness of the current indications for HPN.[42] Analysis of the published data showed that HPN is associated with a high probability of survival, as evidenced by a decreasing annual mortality rate over time with HPN (>5% during the first 3 years ~5% for years 3–5; <5% for years 5–10). Patients with CD had the best outcome, with a mean survival rate of 88% at 10 years. Furthermore, the best survival outcomes were observed in patients <40–45 years. This study also found that most deaths in adults during HPN were due to the underlying disease, not as a complication of HPN.
- Dibb and colleagues investigated long-term survival in adults who received HPN at a UK national referral centre for IF over a 33 year period.[230] Data from 545 patients who received HPN for more than 3 months between 1978 and 2011 was analysed (2,330 patient-years' HPN). Overall survival rate for patients without malignancy at the time of IF was 93%, 71%, 59%, and 28% at 1, 5, 10, and 20 years, respectively. Multivariate analysis showed that overall survival was better in patients with CD, mesenteric ischaemia, and chronic intestinal pseudo-obstruction than in those with scleroderma or radiation enteritis.

HPN supports long-term survival in paediatric patients with primary IF

- Colomb and colleagues (2007) reported data on the long-term outcomes of 302 children who received HPN at a single centre in France in 1980–1999.[287] Median age at start of HPN was 1.5 years, and median duration of HPN was 1.3 years. By the end of the study, 54% of children had been weaned from HPN and 26% were still receiving HPN. The survival rate at 2, 5, 10, and 15 years were 97%, 89%, 81%, and 72%, respectively, with outcome and survival mainly determined by the underlying disease. The authors concluded that nearly all children with primary digestive disease survive if they are referred early to a specialized centre for nutritional support.
- More recently, Nader and colleagues (2013) reviewed data from 251 children with IF who were discharged on HPN from a single centre during 2000–2013[288] (mean age at HPN initiation, 0.7 ± 0.3 years; mean duration of HPN, 1.9 ± 0.4 years). At the end of the study period, 52% of patients had been weaned off PN, after a mean of 1.9 years, and 34% of children were still receiving HPN. Rate of catheter-related complications was low (mean 1.7 ± 0.5 per 1,000 days of HPN) and decreased from 2012. Twenty-four children died while receiving HPN (10%), the majority from the underlying disease.

CANCER

HPN may be superior to surgical intervention in some cancer patients with IF resulting from chronic radiation enteritis

- ESPEN guidelines highlight that HPN may be a superior to surgical intervention in terms of survival and long-term nutrition autonomy for some patients with chronic radiation enteritis (CRE) based on the results of two studies.[157] The first was a retrospective study by Gavazzi and colleagues (2006) involving 30 patients with mechanical bowel obstruction due to CRE who were divided into two groups based on their initial treatment (HPN or surgery).[173] Overall 5 year survival was significantly longer for patients in the HPN group ($p = 0.0231$). Furthermore, all patients in the HPN group achieved nutritional autonomy, compared with 58.8% of patients in the surgery group ($p = 0.01$). The second study, by Kalaisselvan and colleagues (2014), involved analysis of data on nutritional and survival outcomes in 23 patients with CRE referred to a national IF unit over 1998–2011 (1,994 patient-years).[174] Most patients with IF secondary to CRE required long-term HPN, and surgical intervention was needed infrequently. The 10 year survival of the cohort was 48.2%.

HPN may improve survival in patients with advanced cancer

- ESPEN guidelines on nutrition in cancer patients highlight that for patients expected to survive for several months, artificial nutrition may improve survival in those who are unable to meet their nutritional needs through the oral route.[157] Two studies are cited in support of this statement. Bozzetti and colleagues (2014) prospectively studied the associated between patient or clinical characteristics and survival with HPN in 414 patients with incurable cancer.[172] Mean and median survival were 4.7 and 3.0 months, respectively; and significantly prognostic variables were Karnofsky PS, tumour spread, and Glasgow Prognostic Score. Importantly, 50% of patients on HPN survived longer than typically observed for historic controls (i.e., ≤2 months for hospital patients with out PN support and <2–3 weeks for patients followed at home), with about 25% of patients surviving for ≥6 months. This suggests that HPN may confer a survival benefit for some patients with incurable cancer. The second study was a retrospective study by Fan and colleagues (2007) to identify long-term survivors (alive >1 year after start of HPN); 115 patients with malignant GI tract obstruction were identified who had received HPN as palliative care.[177] Median time from start of PN to death was 6.5 months; 11 patients survived ≥1 year and 2 patients were still alive at almost 4 years.
- Soo and colleagues (2008) conducted a cohort study in 38 patients with advanced cancer enrolled in a HPN program in Canada, to identify patient-related variables associated with survival.[289] Higher Karnofsky PS (>50) at the start of HPN was associated with longer median survival (6 months, vs 3 months in patients with Karnofsky PS <50; $p = 0.001$).
- In the randomized prospective study conducted by Lundholm and colleagues (2004) to investigate the impact of specialized nutrition-focused care (including PN) in 309 cancer patients with progressive cachexia (primarily due to GI tumours), patients receiving PN had longer survival than patients who did not receive nutrition report ($p < 0.01$; survival duration not reported) compared with control patients who did not receive nutrition support.[259]
- Hoda and colleagues (2005) carried out a retrospective analysis of data from 52 adults with incurable cancer to determine whether HPN extends survival. Median time from start of HPN to death was 5 months (range 1–154 months); 16 patients survived for at ≥1 year, suggesting that HPN may be associated with long-term survival in selected patients with incurable cancer.[290]

- Guerra and colleagues (2015) evaluated the impact of PN on survival in 55 patients undergoing active treatment for cancer-related intestinal occlusion, 85% of whom were malnourished.[291] The survival rate was higher in patients who received HPN after hospital discharge than in those who remained in hospital (log-rank 7.090; $p = 0.008$). Furthermore, survival was prolonged in patients who started chemotherapy during or after initiation of PN (log-rank 17.316; $p < 0.001$). Importantly, 51% of patients were able to receive further chemotherapy after starting PN because their PS (European Cooperative Oncology Group; ECOG) had improved.
- Brard and colleagues evaluated the use of TPN in a historical cohort of 55 patients with terminal intestinal obstruction related to ovarian cancer. Patients receiving TPN survived a median of 72 days, compared with 41 days if TPN was not administered ($p = 0.01$),[292] and the mortality rate ratio for TPN versus no TPN was 0.59 (95% CI 0.35–1.00). Sixty-four percent of women receiving TPN were concurrently receiving chemotherapy, compared with 24% of those not receiving TPN, which may reflect patient and physician preference for concurrent TPN and chemotherapy. Stratified analysis showed that patients who received both chemotherapy and TPN after terminal intestinal obstruction had a median survival of 74 days, compared with 42 days for those not receiving concurrent TPN ($p = 0.09$); the mortality rate ratio was 0.54 (95% CI 0.23–1.30).

INFLAMMATORY BOWEL DISEASE

In patients with complicated inflammatory bowel disease (IBD), HPN is a safe alternative to prolonged hospitalization and may delay the need for surgery

- Evans and colleagues (2003) reviewed hospital pharmacy data on all patients with IBD who received HPN between 1996 and 2000,[293] and conducted telephone interviews to assess QOL. The 15 patients included in the study received an average of 75 days' PN (range 7–240). HPN was deemed successful in 80% of patients such that 53% of patients were able to receive planned definitive surgery and 27% did not require surgery because their condition resolved while on HPN. All patients preferred HPN to further hospitalization and reported their QOL at home to be good or excellent.

KIDNEY DISEASE

IDPN improves surrogate markers for survival and improves wellbeing in patients on maintenance haemodialysis (HD)

- In the multicentre open-label Phase 4 RCT conducted by the German IDPN Trial group, IDPN, administered three times weekly for 16 weeks, resulted in a statistically significant and clinically relevant increase (≥15%) in mean serum prealbumin ($p < 0.05$), a surrogate marker for outcome and survival in HD patients with malnutrition,[294] compared with nutritional counselling.[272]
- Analysis of data from a 2 year prospective randomized study comparing IDPN plus ONS with ONS alone in malnourished patients on HD showed that while IDPN did not improve overall 2 year mortality, an increase in prealbumin >30 mg/L within 3 months independently predicted a 54% decrease in 2 year mortality (OR 0.46; 95% CI 0.27–0.79), reduced hospitalizations, and improved general wellbeing (measured by the Karnofsky PS) (*p* values not reported).[294]

3.3.4.2 OTHER CLINICAL OUTCOMES

CRITICAL ILLNESS AND SURGERY

Timely administration of PN in ICU patients with contraindications to early ETF reduced the requirement for mechanical ventilation and number of days with clinically significant coagulation failure compared with standard care

- In a large multicentre single-blind RCT evaluating the nutritional and clinical benefits of early PN (within 24 hours of admission) in critically ill adults with a short-term relative contradiction to early ETF, patients randomized to early PN required fewer days of mechanical ventilation than those receiving standard care (usual clinical practice in individual ICUs) (7.73 vs 7.26 days per 10 patient–ICU days; risk difference 0.47; 95% CI –0.82 to –0.11; $p = 0.01$) and had fewer days with clinically significant coagulation failure (–0.34 days per 10 patient–ICU days; 95% CI –0.57 to –0.08; $p = 0.01$).[132]

Timely initiation of SPN (ETF + PN) may optimize clinical outcomes in critically ill patients

- Heidegger and colleagues (2013) conducted an RCT (the 'Swiss SPN study') to determine whether delivering 100% of energy targets with SPN (ETF + PN) on days 4–8 of ICU stay would optimise clinical outcomes.[130] The study involved 305 medical and surgical ICU patients who received <60% of their energy target on ETF alone on day 3 of ICU admission; patients were randomized to ETF alone or SPN. Initiation of SPN resulted in a reduced risk for hospital-acquired infection (HR 0.65; 95% CI 0.43–0.97; $p = 0.0338$), fewer days of antibiotics ($p = 0.001$), and earlier weaning from mechanical ventilation for patients without hospital-acquired infection ($p = 0.0028$).
- In the prospective RCT carried out by Fan and colleagues comparing the effects of timely SPN (ETF + PN), ETF alone, and PN alone on immune function, nutritional status, complications, and clinical outcomes in patients undergoing surgery for severe traumatic brain injury, SPN was associated with significantly shorter stay in the ICU ($p < 0.05$ and $p < 0.01$), number of patients receiving assisted mechanical ventilation ($p < 0.05$ and P < 0.01) and its duration ($p < 0.05$ and $p < 0.01$) than those receiving ETF or PN alone.

Patients receiving TPN after liver transplantation had improved respiratory muscle function, reducing the need for ventilatory support

- Reilly and colleagues (1990) conducted an RCT to evaluate the impact of perioperative TPN versus no nutritional support on ICU outcomes in malnourished (hypoalbuminemic) patients undergoing liver transplantation. Twenty-eight patients were randomized to no nutrition support ($n = 10$), TPN with standard amino acids ($n = 8$), or TPN with added branched-chain amino acids ($n = 10$) for 7 days post-transplant. Patients who did not receive TPN had significantly longer ICU stay ($p < 0.05$). Furthermore, both TPN groups achieved respiratory independence earlier than the group receiving no nutrition support, although the difference was not statistically significant. Hospital costs were also lower for patients who received TPN.[295] Although conducted some years ago, this study is included in current ASPEN and ESPEN guidelines.[5; 41]

3.3.4.3 COMPLICATIONS

SURGERY

Preoperative PN may reduce surgical complications, particularly in malnourished patients

- The Cochrane Colorectal Group (2012) have evaluated the literature on preoperative nutritional support in patients undergoing GI surgery.[296] Three studies were included that compared preoperative PN with no nutrition support in these patients, most of whom were malnourished. The meta-analysis showed a significant reduction in major post-operative complications from 45% in the control group who received no nutrition support to 28% in the group receiving PN (RR 0.64; 95% CI 0.46–0.87), with low heterogeneity.
- Two RCTs published before Cochrane review but that were not included support this finding. An RCT by Bozzetti and colleagues (2000) that evaluated perioperative TPN in malnourished patients with GI cancer showed that 10 days' preoperative TPN, continued postoperatively, significantly reduced the rate of complications by approximately one-third compared with no preoperative nutrition (37% vs 57%; $p = 0.03$); non-infectious complications accounted for most of this difference (12% vs 34%; $p = 0.02$).[54] In addition an RCT by the Veterans Affairs TPN Study group involving 395 malnourished patients who required laparotomy or non-cardiac thoracotomy found that severely malnourished patients who received perioperative TPN had significantly fewer non-infectious complications than patients who did not receive TPN (5% vs 43%; $p = 0.03$).[53]
- A meta-analysis of seven studies ($n = 798$) by Braunschweig and colleagues (2001) to evaluate the benefits of PN versus standard care (conventional oral diet and IV dextrose) in patients undergoing surgery for cancer of the oesophagus or stomach found that in studies with high percentages of malnutrition, PN was associated with a trend toward a lower risk of infection ((RR 1.17 for standard care vs PN; 1.17, 95% CI 0.88–1.56).[297]
- Similarly, another meta-analysis of randomized studies in patients undergoing surgery for cancer of the oesophagus or stomach reported by Braunschweig et al. (2004) demonstrated a trend for reduced infections and complication rates with PN in studies of malnourished patients (RR 1.17; 95% CI 0.88–1,56 for standard care vs PN) and a reduction in post-operative complications
- Heyland and colleagues (2001) carried out a meta-analysis of 27 randomized trials in surgical patients, to compare use of TPN versus standard care (usual oral diet plus IV dextrose).[57] TPN was associated with significantly fewer major complications (RR 0.81; 95% CI 0.65–1.01), particularly in malnourished patients.
- In the randomized study by Xian-li and colleagues (2004) that compared glutamine-supplemented TPN, standard TPN and no TPN in 64 patients with serious acute pancreatitis receiving traditionally therapy,[284] the incidence of complications (acute respiratory distress syndrome, multi-system organ failure) was significantly higher in patients receiving no TPN (21%) than in those receiving standard TPN (11%; $p < 0.01$) or glutamine-supplemented TPN (4%; $p < 0.01$). Furthermore, length of stay was significantly shorter for patients receiving either standard TPN (28.6 days; $p < 0.05$) or glutamine-supplemented TPN (25.3 days; $p < 0.01$) compared with no TPN (39.1 days).

- Thoracic chyle leakage is a major complication of oesophagectomy. In a prospective study by Weijs and colleagues (2017), consecutive patients with chyle leakage (n = 371) were assigned to a low-fat diet (for leakage <500 mL/day), TPN (for leakage >1,000 mL/day), or a low-fat diet or TPN (for leakage 500–1,000 mL/day) depending on whether the chyle leakage was increasing or decreasing at diagnosis and the patient's condition.[298] Treatment could then be stepped up (e.g., TPN or surgery) based on outcomes with the initial treatment. A low-fat diet was the initial treatment for 61 patients (78%) and was successful in 40 (66%) after a median of 9 days. TPN was subsequently administered to 20 of the 61 patients (33%) who had persistent or increasing leakage and was successful in stopping the leakage in 17 (85%; reoperation was performed in the remaining 3 patients). TPN was the initial treatment in 15 patients (19%) and successfully stopped leakages in 11 (73%) after a median of 5 days (the remaining patients underwent reoperation). Surgical closure was the initial treatment in one patient.
- Jacobson and colleagues (2012) evaluated the impact of preoperative TPN in 15 consecutive patients with moderate-to-severe CD undergoing bowel surgery and primary anastomosis who received preoperative TPN for 18–90 days (mean, 46 days). All patients receiving TPN had clinical remission during the preoperative period, and there was no evidence of significant early postoperative complications (≤30 days), compared with 29 patients in the control group (n = 105) who did not receive TPN (p values not reported).

TRAUMA

Timely ETF combined with PN may reduce the incidence of complications in patients with severe traumatic brain injury

- In the prospective RCT by Fan and colleagues that compared the effects of timely SPN (ETF + PN), ETF alone, and PN alone in patients undergoing surgery for severe traumatic brain injury, SPN was associated with lower rates than ETF alone for aspirated pneumonia (27.5% vs 50.0%; $\chi^2 = 6.39$, $p < 0.05$), hypoproteinemia (17.5% vs 55.0%; $\chi^2 = 18.26$, $p < 0.01$) and diarrhea (20.0% vs 60.0%; $\chi^2 = 20.00$, $p < 0.01$). Rates were lower with SPN than with PN alone for stress ulcer (22.5% vs 47.5%; $\chi^2 = 8.24$, $p<0.01$), intracranial infection (12.5% vs 32.5%; $\chi^2 = 6.88$, $p<0.01$) and pyemia (25.0% vs 47.5%; $\chi^2 = 6.57$, $p < 0.05$).[245]

CANCER

PN or ETF may improve the tolerability of chemotherapy in cancer patients

- Malnutrition is associated with a high risk of early discontinuation of chaemotherapy.[299] Pan and colleagues (2013) conducted a multicentre, cross-sectional study involving 2,248 hospitalized cancer patients in China to understand the impact of malnutrition, nutritional risk, and nutritional support on clinical outcomes.[300] The rate of malnutrition at baseline and reassessment were 19.7% and 26.8%, respectively. Patients who received ETF or TPN had significantly reduced relative risk of chemotherapy-related adverse events than patients who did not receive nutrition support (RR 0.08 [95% CI 0.01–0.62] and 0.56 [0.33–0.96]).

3.3.5 Economic benefits of PN

CRITICAL ILLNESS

Timely use of PN in critically ill patients with contraindications to early ETF or in critically patients who do not achieve nutritional targets with ETF alone may significantly reduce the total costs of hospital care

- Doig and colleagues (2013) conducted a cost-minimization analysis from the perspective of the US acute care hospital system to estimate the cost implications of providing early PN (within 24 hours of ICU admission) to patients with short-term relative indications to early ETF. Clinical outcomes and measures of resource consumption were taken from a multicentre clinical trial involving 1,363 patients, combined with cost distributions obtained from the literature. The analysis showed that early PN significantly and meaningfully reduced the total costs of acute hospital care by US$3,150 per patient (95% CI 1,314–4,990). (Mean costs of ICU care were $58,924 [95% CI 57, 631–60,239) with standard care and $55,772 [95% CI 54,484–57,082[with early PN.) All sensitivity analyses demonstrated significant cost savings with early PN, including use of European cost data.[136]
- Pradelli and colleagues used discrete event simulation and a deterministic simulation model to evaluate the cost-effectiveness of SPN (ETF + PN) administered on days 4–8 of ICU admission compared with continued ETF in patients who did not achieve ≥60% of their targeted energy intake by day 3. Total hospitalization costs were estimated at 112,338 CHF per patient receiving EN and 108,999 CHF per patient receiving SPN, resulting in an estimated net cost reduction with SPN of 3,339 CHF per patient. Each 1,000 kcal decrease in cumulative energy deficit with SPN was associated with a 10% reduction in the risk of nosocomial infection (OR 0.90; 95% CI 0.83–0.99; $p < 0.05$). The 5.3% absolute reduction in nosocomial infection with SPN yielded a number needed to treat to avoid one infection of 19, with a saving of 63,048 CHF per infection avoided. The cost of the intervention was therefore more than offset by the cost saving realized through the reduction in nosocomial infection.[135]
- Not all studies have reported cost savings with early use of PN in the ICU. Vanderheyden and colleagues reported the cost analysis from the 2007–2010 EPaNIC trial[126] Early PN (n = 2,312) was associated with mean costs of €17,973 (SD €18,965), compared with €16,863 (SD €18,190) for late PN (n = 2,328), a difference of €1,110. However, the cost increment with early PN was only €94 per patient in those who did not develop an infection and who did not require prolonged ICU support, who comprised 70.1% of the total population. Furthermore, as discussed in Section 3.3.1.1, the trial on which this analysis is based had several important methodological limitations that are likely to have biased the cost analysis in favour of late PN. For instance, patients in this study remained in the ICU for only a short time (average, 3 4 days in >70% patients), which may not have been long enough to demonstrate a benefit with early PN. Also, 75% of patients had a normal or slightly higher than normal BMI,[137] suggesting that this population may not be representative of the population typically indicated for early PN in the ICU setting. Clinical outcomes in patients who are not malnourished are less likely to be altered by the addition of PN.

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The cost of PN in the hospital setting may compare favourably with other supportive therapies such as dialysis for acute renal failure (ARF)

- Shields and colleagues reported on the long-term cost-effectiveness of in-hospital TPN over 10 years (1983–1993) in 162 patients with acute GI failure (4,997 patient-days; 192 central venous catheters). In patients with non-malignant disease, fed for >21 days (mean 50 days), 10 year survival was 74%, at a cost of £4,723 per year of life saved; in patients with malignant disease, 5 year survival was 27%, at a cost of £8,351 per year of life saved. On the assumption that TPN was life-saving in patients who need long-term TPN, these costs were considered to compare favourably with other technologies such as dialysis for ARF, which has an in-hospital mortality rate of 50% (even with dialysis). Treatment by an expert team improved patient selection and complications rates, and reduced costs.[301] Although this study was published some years ago, and therefore may not reflect current practice, PN is still likely to compare favourably with other supportive technologies used in the ICU, as in-hospital mortality for ARF remains high (up to 60%) and is associated with significant costs.[302]

PN can be delivered in different ways, ranging from bespoke pharmacy-compounded PN to commercial premixed multichamber bags

- Alfonso and colleagues (2016) conducted a systematic literature review of studies comparing MCB and pharmacy-compounded PN from January 1990 to November 2014; 18 published studies (mostly retrospective) met the inclusion criteria. Ten studies (including one prospective randomized trial and multiple retrospective analyses) reported a lower risk of BSI with MCBs compared with other delivery systems. Sixteen studies reported ergonomic and/ or economic outcomes; most reported a potential cost benefit with MCB, with consistent reports of reduced time and labour compared with other systems. The largest cost benefit was seen in studies that evaluated total hospitalization costs (e.g., costs relating to infectious complications and length of stay in the hospital or ICU). The authors noted that methodological factors limited the quality of the evidence.[303] Furthermore, none of the included studies evaluated errors associated with the PN process, which have been shown to be reduced for MCB PN compared with compounded PN preparation.[304]

HPN

The cost of HPN for intestinal failure is comparable for malignant and non-malignant causes

- Naghibi and colleagues conducted a systematic review and meta-analysis of survival, QOL, and cost-effectiveness of HPN in patients with inoperable bowel obstruction, based on 12 studies involving 437 patients. In the base-case analysis, the incremental cost for HPN over no nutritional treatment was £22,197, yielding an incremental cost-effectiveness ratio (ICER) of £176,587 per quality-adjusted life-year (QALY) gained. However, this ICER was highly sensitive to the utility values in the treatment group (–30% to 75%), and to the cost of PN (±26%) and survival of the treatment and non-treatment groups (–24% to +10% and –20% to +7%, respectively), although ICERs remained above £123,000 per QALY gained in all sensitivity analyses. The daily cost for HPN was £240. The authors comment that whilst the costs of HPN are high, they are comparable to those for the "less controversial and accepted practice of HPN for benign disease". Performance status and predicted survival are key factors in deciding on HPN for a patient with malignant bowel obstruction. The authors also note that although cost-effectiveness analysis is the dominant method used in health economics to value health technologies, experts suggest that the willingness to pay threshold (i.e., the maximum amount of money that a healthcare system is prepared to give up to ensure that a health technology is implemented[305]) may be more relevant for the evaluation of interventions in palliative care, as it is typically higher (e.g., up to £70,000 per QALY in the UK) than the ICER threshold.[306] It is also important to note that some health technology assessment agencies (e.g., the National Institute for Health and Care Excellence [NICE] in the UK) apply additional criteria to end-of-life treatments.[307] Treatments that meet these criteria may be recommended at a higher ICER threshold.

HPN is likely to be cost-saving compared with hospital-based PN for many healthcare systems

- HPN has a key role in shortening the hospital stay for patients who are ready to be discharged but who require IV nutrition,[308] which is likely to realize considerable cost savings for many healthcare systems.
- An economic analysis by Marshall and colleagues found that HPN was significantly cost saving compared with hospital PN in Canada. In this study, the cost of home and hospital PN was compared through detailed review of the medical records for all patients managed by an HPN programme between 1996 and 2001 whose PN was initiated in hospital (n = 29). Direct medical costs were estimated for the 2 weeks before hospital discharge and for the first month after discharge home. Common indications were malignancy, IBD, and intestinal ischemia (n = 12, 6, and 4, respectively). Mean daily costs were higher in in the last week of hospitalization than in the first month of discharge ($567 vs $405; $P < 0.0001$). Acute care accounted for <10% of overall costs on HPN. HPN was estimated to realize monthly savings of $4,860 per patient (95% CI 2,700–7,000) compared with provision of PN in hospital, with even greater savings in elderly patients and those with underlying malignancy.[309]
- ESPGHAN–ESPEN guidelines on HPN in children note a paediatric study (age range 0.04–15.83 years at start of hospital TPN) which reported that the number of septic episodes was significantly reduced when children were transferred to HPN (from 1/142 days in hospital [interquartile range 99–290] to 1/567 days at home [251–614); based on 17,562 and 10,348 hospital-days, respectively). The cost of treating an episode of sepsis was estimated at £4,733–6,495. Overall HPN was associated with potential savings of approximately €1 million in a single year.[310]

HPN becomes more cost-effective with duration of use

- A 1996 cost–utility analysis by Richards and Irving, taking the perspective of the UK National Health Service, reported that HPN was 65% more cost-effective than hospital care in patients with IF. This was based on detailed data from 64 patients from a single hospital who received HPN for a median of 6 nights per week (range 2–7) for a median of 4 years (range 0.5–15). HPN accounted for 77% of the total cost in the first year (£34,157 of £44,288, which included costs for equipment that would not be incurred in subsequent years). QALYs gained were 0.516 in year 1, 2.58 in year 5, and 5.16 in year 10, with marginal costs per QALY gained of £85,829, £66,224, and £54,734, respectively. Hospitalization reduces utility, and a patient treated in hospital for the median 4 years would incur costs of £312,595, yielding a cost per QALY of £189,451. HPN is life-saving for many patients. The quality-adjusted survival for younger patients (<44 years) is significantly better than that for older patients (>55 years, which significantly reduces the marginal cost per QALY. Furthermore, the longer a patient survives, the more cost-effective HPN becomes. Weaning from HPN because of intestinal adaptation reduces the cost per QALY even further. The results of this cost–utility analysis support timely initiation of HPN in patients with cancer, that is, when performance status, which is an independent predictor of survival, is higher.

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4

RECOMMENDATIONS FROM KEY GUIDELINES: MEDICAL NUTRITION

Summary

Medical nutrition is increasingly recognised as an integral part of the overall patient management strategy for malnutrition, in hospitals and in the community, based on the evidence that medical nutrition leads to improvements in nutritional intake, body composition, clinical, functional and economic outcomes.

In many countries evidence-based guidelines on the management of malnutrition have been developed by national authorities, government agencies, health departments and professional organisations and in many cases through collaboration and joint working by these stakeholders. The guidance available covers different patient groups in different care settings but they consistently include Medical Nutrition as an integral part of patient care. Some include practical advice for healthcare practitioners on how and when to use different forms of nutritional intervention, (including ONS and ETF), but unambiguous and practical advice should be included more routinely in guidance documents.

Patients with complex and often chronic conditions are highly susceptible to the negative consequences of malnutrition. Professional groups with expertise in nutrition including ESPEN, ASPEN and the Academy of Nutrition and Dietetics have led the field in developing extensive guidance on the management of malnutrition in a variety of patient groups including older people, people with cancer, dementia, gastrointestinal disease, COPD and spinal injury. These evidence-based guidelines describe the circumstances in which medical nutrition should be used as part of a range of strategies to provide optimal nutritional care.

The importance of nutritional care and the role of Medical Nutrition are increasingly recognised by government level organisations such as NICE, SIGN, the National Board of Health in Denmark, the Haute Authorité de Santé, France and organisations specialising in specific conditions such as the Clinical Oncology Society of Australia through their condition-specific guidance for healthcare providers and practitioners. This is a critical step in raising the awareness of the issue of malnutrition with specialist healthcare practitioners who otherwise may miss malnutrition and who are ideally placed to recognise the problem early and instigate appropriate nutritional care.

A key aspect of many guidance documents is the correct targeting of nutritional intervention, including the use of medical nutrition, at patients who have been identified as malnourished or at risk of malnutrition. It is clear that appropriate use of nutritional intervention is part of the wider task of identifying patients at nutritional risk and implementing timely and appropriate care. There is emerging evidence that screening may reduce the prevalence of malnutrition and that screening programmes, that include intervention and care planning, can contribute to improved outcomes.

Conclusion

Many national, international and professional guidelines exist that include medical nutrition as an integral part of patient care. However, continued effort is needed to ensure guidelines are updated to reflect the evidence base, to integrate good nutritional care into guidelines for specific diseases (e.g. nutritional support as part of cancer care guidelines), and to ensure that these guidelines are recognised and established as a credible and essential basis for good patient care. Translation of “academic guidelines” into practical advice for healthcare providers is needed to achieve both improved patient outcomes and to ensure appropriate use of resources.

Recommendations

On the issue of **ONS and ETF as an integrated part of guidelines** the MNI makes the following recommendation:

Action	Issues to consider
Guidance on managing malnourished patients or patients at risk of malnutrition should reflect current evidence and should provide healthcare providers and practitioners with clear and practical advice about how and when to use different forms of nutritional intervention, including ONS and ETF	• Nutrition experts have a key role in collaborating with other groups to ensure that the issue of malnutrition and the opportunity for effective management is included in guidance for patients with specific diseases • Efforts should be made to ensure that the guidance is widely disseminated and adopted

Examples

Evidence-based guidelines for the nutritional management of patients with a variety of conditions are listed. This list is not exhaustive, and other existing and newly developed national and professional guidelines could extend this overview in the future e.g. relating to PN. Guidelines from around the world have been included if available in English or if an English translation could be obtained.

This unique overview is a starting point which it is hoped will encourage a review of key guidelines and prompt the sharing of information.

4.1 Recommendations from international, national and professional guidelines: ONS

Tables 4.1 to 4.5 include the results of efforts made to identify evidence-based national and professional guidelines referring to ONS as an integral part of patient and disease management across the world. Relevant professional and national organisations were contacted or searches of websites were undertaken, including the US Department of Health and Human Sciences National Guideline Clearinghouse (www.guideline.gov), searches of the published literature from 2002 to 2016 were completed, and approaches were made to contacts in relevant areas. Other guidelines may exist but are not included as they were not identified using the above strategies or we were unable to obtain information in the English language for inclusion. We would welcome information about other guidelines that could be included in future editions of this report.

In addition, guidelines for nutrition support exist in the following countries and are to our knowledge based on the guidelines developed by ESPEN:

- China (www.cspen.org);
- Czech Republic

Note: Terminology referring to ONS is not consistent within the various guidelines; therefore, the term [ONS] has been inserted in place of these terms to avoid confusion.

The tables that follow include the recommendations relating to ONS only as they appear in the guidelines or documents from various organisations. Please refer to the full documents for other information relating to nutritional management e.g. screening, assessment and use of other forms of nutritional support.

GENERAL

Table 4.1 **Summary of some examples of evidence-based national and professional guidelines referring to ONS as an integral part of patient and disease management - General** (parts of guidelines relevant to ONS are presented here, standard ONS formulae only)

Country	Body	Patient Group	Title	Recommendation, guideline or standard [grade of evidence, where available]
Denmark	The National Board of Health (2008)	Patients in hospitals	Screening and treatment of patients at nutritional risk. Guidelines for physicians, dietitians, nurses and other HCPs	There is a positive effect of ONS in patients where there is an indication for intensive nutritional therapy according to NRS-2002 ONS recommended for: • Patients who need an energy-dense diet • Patients with low food intake • Patients with chewing and swallowing difficulties, such as patients with dysphagia, patients with painful mouth and throat, patients with paralysis and generally impaired condition because of dementia or amyotrophic lateral sclerosis
Denmark	The Danish Veterinary and Food Administration (2009)	Patients in institutions	Recommendations for Food in Danish Institutions	ONS recommended for: • Patients with chewing and swallowing difficulties, such as patients with dysphagia, patients with painful mouth and throat, patients with paralysis and generally impaired condition because of dementia or amyotrophic lateral sclerosis • Patients with chronic disease, patients with general low energy and protein intake, for recovery after surgery – before considering enteral nutrition
Denmark	– The Danish Veterinary and Food Administration – The National Board of Health – DTU National Food Institute –Danish Diet & Nutrition Association –The Association of Danish Clinical Dietitians	Any patient (not infants)	The National Diet Handbook	ONS recommended for: • Patients with chewing and swallowing difficulties • Patients with chronic disease, patients with general low energy and protein intake, for recovery after surgery • Patients where there is an indication for intensive nutritional therapy according to NRS-2002

Table 4.1 Continued

Country	Body	Patient Group	Title	Recommendation, guideline or standard [grade of evidence, where available]
England and Wales	National Institute for Health and Care Excellence (NICE) (2006)	All patients in hospital and in the community	Nutrition Support for Adults: Oral Nutrition Support, Enteral Tube Feeding and Parenteral Nutrition[1]	Indications for oral nutrition support: • Healthcare professionals should consider oral nutrition support* to improve nutritional intake for people who can swallow safely and are malnourished** or at risk of malnutrition*** [A] • Healthcare professionals should ensure that the overall nutrient intake of oral nutrition support offered contains a balanced mixture of protein, energy, fibre, electrolytes, vitamins and minerals [D (GPP)] • Oral nutrition support should be stopped when the patient is established on adequate oral intake from normal food [D (GPP)] Note: see Table 4.6 for summary of grading of recommendations *NICE has published a Quality Standard on Nutrition Support in Adults which has been developed from this guideline. https://www.nice.org.uk/guidance/qs24*
Finland	National Nutrition Council (2010)	All patients in hospital, community, care/elderly homes and rehabilitation centres	Nutrition treatment recommendation	Intensive nutrition treatment is recommended in case of poor appetite or malnutrition or risk of malnutrition. Intensive nutrition treatment includes, for example, food fortification, snacks, ONS and tube feeds. Protein-rich ONS are recommended in the case of protein-rich intensive nutrition treatment **– This recommendation concerns all diseases (e.g. cancer, renal, ulcerative colitis [UC]) and also elderly patients and children** Modified food diet: • Liquid food – ONS are always recommended • Puréed food – ONS can be recommended depending on the situation
Norway	Norwegian Directorate for Health (2009)	All patients in hospital and in the community	National scientific guidelines for prevention and treatment of malnutrition	Use an appropriate high energy and nutrient-dense diet in combination with ONS for people at risk of malnutrition [A]
Sweden	The National Board of Health and Welfare (2000) SWESPEN	All patients within healthcare	Problems with nutrition within healthcare: prevention and treatment. A small practical handbook to have in the pocket: Nutritional treatment within healthcare	Summary: [ONS] have positive effects when given to patients at risk of or with manifest malnutrition. This applies for some chronic diseases but not all; more studies are needed [ONS] should be given when the need for energy and nutrients is not covered by the usual food

Table 4.1 Continued

Country	Body	Patient Group	Title	Recommendation, guideline or standard [grade of evidence, where available]
The Netherlands	Steering Committee Malnutrition (Stuurgroep Ondervoeding, 2009)	Malnutrition in general, all lines of healthcare) (including children)	Guidelines Malnutrition: screening and treatment	Summary: guidelines for all lines of healthcare about screening with screening tools and how to treat malnourished patients. A table is used to show how to treat malnourished patients with regard to their nutritional intake • When 75–100% of the nutritional requirement is met, use protein and energy-rich food, if necessary combined with ONS • When 50–75% of the nutritional requirement is met, use protein- and energy-rich food and combine with ONS • When < 50% of the nutritional requirement is met, use protein- and energy-rich food, continue ONS if possible, and start tube feeding
UK	Malnutrition Advisory Group of BAPEN (2003)	All	The 'MUST' Report Nutritional screening of adults: a multidisciplinary responsibility[2]	There is substantial evidence of the beneficial clinical effects of [ONS] containing a mixture of macro- and micronutrients in particular groups of patients in hospital and the community, and of greater benefit in individuals with a BMI of < 20 kg/m^2 than > 20 kg/m^2, particularly patients in the community. [A – at least 1 RCT as part of the body of literature of overall good quality and consistency addressing the specific recommendation]
UK	BAPEN (2000)	Patients in the community	Guidelines for the detection and management of malnutrition[3]	• Treatment typically begins with food but may progress to the use of [ONS]. In some patients it may begin with food and [ONS] • If ordinary food is ineffective in improving nutritional status and ineffective in achieving the goals set at the beginning of treatment, [ONS] (mixed micro- and macronutrient supplements in solid or liquid form) can be of value. This is because they are readily available, easy to consume between meals, require little or no preparation, and are largely additive to food intake in undernourished subjects [A – at least 1 RCT as part of the body of literature of overall good quality and consistency addressing the specific recommendation]

Table 4.1 Continued

Country	Body	Patient Group	Title	Recommendation, guideline or standard [grade of evidence, where available]
USA	Council for Nutritional Strategies in Long-Term Care (2000)	With or at risk of malnutrition	Nutritional management in long-term care: development of a clinical guideline	• [ONS] can increase dietary intake and produce weight gain • [ONS] must be given between meals in order not to substitute for calorie intake at meals
USA	American Society for Parenteral & Enteral Nutrition (2010)	Adults	Nutrition Screening, Assessment and Intervention in Adults[4]	• Nutrition support intervention is recommended for patients identified by screening and assessment as at risk for malnutrition or malnourished [C]
Australia	Dietitians Association of Australia Malnutrition Guideline Steering Group (2009)	Malnutrition in adult patients across care settings	Evidence-based practice guidelines for the nutritional management of malnutrition in adult patients across the continuum of care[5]	• [ONS] (high energy and/or protein) may improve outcomes See full guidelines for details of evidence base for outcomes in specific settings (across settings, acute care, rehabilitation, residential aged care and community) Note: See Table 4.7 for summary of grading of recommendations Nutrition goals, intervention, monitoring practice tips: When providing [ONS], consider the following (see full guidelines for individual references): ~ Base individual prescription on gap between oral intake and estimated requirements not met through oral intake alone ~ Continue the nutrition support for an adequate timeframe since this is correlated with improved weight change ~ Avoid administering high energy and protein [ONS] at mealtimes ~ Deliver the [ONS] via the medication round to facilitate adherence ~ Encourage a supportive environment to facilitate adherence ~ Use dietetic assistants to improve adherence to meal plans and [ONS]

*Oral nutrition support includes any of the following methods to improve nutritional intake: fortified food with protein, carbohydrate and/or fat, plus minerals and vitamins; snacks; ONS; altered meal patterns; the provision of dietary advice (DA)
**Malnourished: BMI < 18.5 kg/m^2, unintentional weight loss > 10% within the last 3–6 months, a BMI < 20 kg/m^2 and unintentional weight loss > 5% within the last 3–6 months
***At risk of malnutrition: eaten little or nothing for more than 5 days and/or likely to eat little or nothing for the next 5 days or longer or poor absorptive capacity, and/or high nutrient losses and/or increased nutritional needs from causes such as catabolism

OLDER PEOPLE

Table 4.2 **Summary of examples of evidence-based national and professional guidelines referring to ONS as an integral part of patient and disease management – Older People** (parts of the guidelines relevant to ONS are presented here, standard ONS formulae only)

Country/Region	Body	Title	Recommendation, guideline or standard [grade of evidence]
Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Geriatrics[6]	• In patients who are undernourished or at risk of under-nutrition, use ONS to increase energy, protein and micronutrient intake, maintain or improve nutritional status, and improve survival [A] • In frail elderly, use ONS to improve or maintain nutritional status [A] • In geriatric patients after hip fracture and orthopaedic surgery, use ONS to reduce complications [A] • In early and moderate dementia, consider ONS – and occasionally tube feeding – to ensure adequate energy and nutrient supply and to prevent under-nutrition [C] • ONS, particularly with high protein content, can reduce the risk of developing pressure ulcers [A] • In the case of nutritional risk (e.g. insufficient nutritional intake, unintended weight loss > 5% in 3 months or > 10% in 6 months, BMI < 20 kg/m^2), initiate ONS and/or tube feeding early [B] Note: see Table 4.8 for summary of grading of recommendations
Denmark	The Danish Veterinary and Food Administration (2002)	Elderly with low food intake (patients in institutions and elderly in home care)	ONS recommended for: Dietary management of malnutrition, decreased appetite and weight loss
Denmark	The National Board of Health (2007)	Older people – guidelines for municipalities	ONS recommended for: • Older people with low energy and protein intake to prevent underweight and loss of function and strength because of malnutrition
Finland	National Nutrition Council (2010)	Nutrition recommendation for elderly "Ravitsemussuositukset ikääntyneille" (from free-living elderly to hospitalised patients)	• ONS are recommended for elderly people who have acute disease, hip fracture, too-low body weight (recommendations BMI > 23 kg/m^2) or weight loss > 3 kg/3 months. ONS are also recommended for use after surgery • ONS are often also recommended for cancer, COPD, heart failure and dysphagia patients and patients who have poor appetite

Table 4.2 Continued

Country/Region	Body	Title	Recommendation, guideline or standard [grade of evidence]
France	Haute Autorité de Santé (2011)	Clinical practice guidelines from the French Health High Authority: Nutritional support strategy in protein-energy malnutrition in the elderly[7]	Methods of nutritional support: Oral nutritional support. This comprises nutritional guidance, assistance during eating, provision of enriched food and oral nutritional supplements, some of which are reimbursed **Choice of method of nutritional support:** The choice of a nutritional support strategy is based on the patient's nutritional status and on spontaneous food, energy and protein intake (see Table 4.8). It also takes into account the nature and severity of any underlying disease(s) and associated disabilities as well as their foreseeable outcome (swallowing disorders, for example). Nutritional support strategy must also take into account the opinion of patients and their close relatives as well as ethical considerations. Apart from situations contra-indicating oral feeding, nutritional support should, as a priority, be initiated by providing DA and/or fortified foods, [C] if possible in collaboration with a dietitian. Oral nutritional supplements (ONS) may be given if these supportive measures are ineffective or from the onset in patients with severe malnutrition [C] **Practical measures:** *Oral nutritional support:* Studies on malnourished elderly patients have shown an improvement in body weight and survival and a reduction in the incidence of complications after oral nutritional support [A] **ONS:** High energy and/or high-protein ONS come in different flavours, with or without lactose, and in a variety of forms (liquid, cream, etc.). Several types of products are available, including dairy desserts, soups, complete meals, fruit juices, etc. Preference should be given to high energy (> 1.5 kcal/ml or/g) and/or high-protein products (proteins > 7.0 g/100 ml or 100 g or proteins > 20% of total energy intake) *ONS are prescribed as follows:* • ONS may be eaten as a snack or during meals. When they are provided during meals, they must be eaten in addition to meals and not as a meal replacement. As a snack, they should be given about 2 h before or after a meal in order not to spoil the appetite • The prescription of an ONS should supply an additional food intake of 400 kcal/day and/or 30 g protein/day; this generally requires 2 units per day • Patients should be told that ONS are a treatment for malnutrition to encourage consumption • The taste of the prescribed ONS should be suited to patient preferences in terms of being salty or sweet, creamy or not, and in terms of flavour. A vanilla or plain product may be modified by adding flavours (fruit syrup, caramel, coffee, chocolate powder, etc.). Consumption may be encouraged by varying products and flavours and respecting patient preferences

Table 4.2 Continued

Country/Region	Body	Title	Recommendation, guideline or standard [grade of evidence]
			• ONS should be adapted to any disabilities (difficulties in swallowing or in gripping objects, etc.). The texture of drinks may be modified with a thickening powder (not included on the list of reimbursed products) • ONS intake may be encouraged by serving them at the correct temperature. Sweet products are often preferred cold. ONS that should be served hot may often be heated up in a double boiler or microwave oven. Once opened, the supplement may be kept for 2 h at room temperature and for up to 24 h in the refrigerator • A regular check should be performed to ensure that the prescribed ONS are actually consumed • When patients live at home, the first prescription is made for a maximum period of 1 month. After medical reassessment, subsequent prescriptions may be made for a maximum period of 3 months. Medical reassessment should be based on the following: ~ body weight and nutritional status ~ clinical course of underlying disease(s) ~ estimation of spontaneous food intake ~ tolerability of ONS ~ level of compliance with the ONS prescription

Table 4.2 Continued

Country/Region	Body	Title	Recommendation, guideline or standard [grade of evidence]
USA	Hartford Institute for Geriatric Nursing – Academic Institution (2008)	Nutrition. In: Evidence-based geriatric nursing protocols for best practice	Provide [ONS] [ONS] should not replace meals but rather be provided between meals but not within the hour preceding a meal or at bedtime [Level IV]. See NICE (2006) algorithm for use of [ONS] (see Figure 4.2 in this report)
USA	University of Texas at Austin School of Nursing, Family Nurse Practitioner Program – Academic Institution (2006)	Unintentional weight loss in the elderly	Management/Treatment Non-pharmacological therapy • Increasing nutrition through food should be the first step prior to initiating dietary supplements [ONS]. [Strength of Recommendation: B; Quality of Evidence: Fair] • If the patient's caloric needs cannot be met with 3 meals and 3 snacks per day, high energy and nutritionally-dense [ONS] should be added. [Strength of Recommendation: B; Quality of Evidence: Fair/Poor] • [ONS] are associated with weight gain and reduced fatality. [Strength of Recommendation: A; Quality of Evidence: Good] • [ONS] should be given between meals and not with meals to minimise appetite suppression and compensatory decreased intake of food at mealtimes. [Strength of Recommendation: A; Quality of Evidence: Good] • Get the patients to sample the [ONS] and give them a variety. Presentation of the supplement should also be varied. [Strength of Recommendation: B; Quality of Evidence: Fair/Poor] • A liquid supplement [ONS] in which the energy is supplied by glucose instead of fat is less likely to cause satiation. [Strength of Recommendation: B; Quality of Evidence: Fair]
USA	Academy of Nutrition and Dietetics (2009)	Unintended Weight Loss (UWL) in Older Adults Evidence-based Nutrition Practice Guideline (login required)	**Indications for [ONS]*** The Registered Dietitian (RD) should recommend [ONS] for older adults who are undernourished or at risk of under-nutrition (i.e. those who are frail, those who have infection, impaired wound healing, pressure ulcers, depression, early to moderate dementia and/or after hip fracture and orthopaedic surgery). Studies support [ONS] as a method to provide energy and nutrient intake, promote weight gain and maintain or improve nutritional status or prevent under-nutrition [Strong] *Note that the guidance uses the term 'medical food supplements' but to avoid confusion with vitamin and mineral food supplements, the term ONS has been inserted in its place

CHILDREN

Table 4.3 **Summary of examples of evidence-based national and professional guidelines referring to ONS as an integral part of patient and disease management – Children** (parts of the guidelines relevant to ONS are presented here, standard ONS formulae only)

Country/Region	Body	Title	Recommendation, guideline or standard [grade of evidence]
Europe	European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Committee on Nutrition (2010)	Practical approach to paediatric enteral nutrition: A comment by the ESPGHAN Committee on Nutrition[8]	• [ONS]* should be given only as an addition to other foods when enhancement of oral energy and substrate intake is necessary *Note: The term 'supplement feeds' (sip feeds) is used in the original paper but it has been replaced here with 'ONS' to avoid confusion
Europe	ESPEN-ESPGHAN-ECFS (2016)	ESPEN-ESPGHAN-ECFS guidelines on nutrition care for infants, children, and adults with cystic fibrosis[9]	**Guideline: oral nutritional supplements** • We recommend clinicians consider the use of oral nutritional supplements for treating children and adults who fail to achieve optimal growth rates and nutritional status with oral dietary intake and pancreatic enzyme replacement therapy (PERT) alone. (Grade of evidence: low) • We recommend clinicians regularly review and re-evaluate patients who are taking oral nutritional supplements to determine whether the patient should continue taking them. (Grade of evidence: high)
UK	British Society of Paediatric Gastroenterology Hepatology and Nutrition (BSPGHAN) (2008)	Guidelines for the Management of Inflammatory Bowel Disease (IBD) in Children in the United Kingdom	• Exclusive enteral nutrition (given either orally or enterally) is effective first line therapy for small and large bowel disease, inducing remission in 60–80% of cases (EL +1 -1) • Supplementary therapy may reduce the risk of relapse and may improve growth and nutritional status (EL 2-) • Nutritional support should be considered as adjunctive therapy for any patient with CD or UC who has malnutrition. Nasogastric/gastrostomy tube feeding can be considered • Supplemental enteral feeding or cyclical enteral nutrition for children with CD in remission may improve growth and help to maintain remission

Table 4.3 **Continued**

Country/Region	Body	Title	Recommendation, guideline or standard [grade of evidence]
England	NICE (2014)	Pressure Ulcers: Prevention and Management[10]	Prevention: Nutritional supplements and hydration Do not offer nutritional supplements specifically to prevent a pressure ulcer in neonates, infants, children and young people with adequate nutritional status for their developmental stage and clinical condition. Management: Nutritional supplements and hydration 1.5.4 Offer an age-related nutritional assessment to neonates, infants, children and young people with a pressure ulcer. This should be performed by a paediatric dietitian or other healthcare professional with the necessary skills and competencies. 1.5.5 Discuss with a paediatric dietitian (or other healthcare professional with the necessary skills and competencies) whether to offer nutritional supplements specifically to treat a pressure ulcer in neonates, infants, children and young people whose nutritional intake is adequate. 1.5.6 Offer advice on a diet that provides adequate nutrition for growth and healing in neonates, infants, children and young people with a pressure ulcer. 1.5.7 Discuss with a paediatric dietitian whether to offer nutritional supplements to correct nutritional deficiency in neonates, infants, children and young people with a pressure ulcer. 1.5.8 Assess fluid balance in neonates, infants, children and young people with a pressure ulcer. 1.5.9 Ensure there is adequate hydration for age, growth and healing in neonates, infants, children and young people. If there is any doubt, seek further medical advice.

SPECIFIC DISEASES

Table 4.4 **Summary of examples of evidence-based national and professional guidelines referring to ONS as an integral part of patient and disease management – Specific Diseases and Conditions** (parts of guidelines relevant to ONS are presented here, standard ONS formulae only)

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with hip fracture	Scotland	Scottish Intercollegiate Guidelines Network (SIGN) (2009)	Management of hip fracture in older people	Rehabilitation: supplementing the diet of hip fracture patients in rehabilitation with high [ONS] containing minerals and vitamins should be considered [A] Note: see Table 4.6 for summary of grading of recommendations. (Grade A similar to NICE)
	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Geriatrics[6]	In geriatric patients after hip fracture and orthopaedic surgery, use ONS to reduce complications [A] Note: see Table 4.8 for summary of grading of recommendations
	USA	American Academy of Orthopaedic Surgeons (AAOS) (2014)	American Academy of Orthopaedic Surgeons clinical practice guideline on management of hip fractures in the elderly.	Nutrition Moderate evidence supports that postoperative nutritional supplementation reduces mortality and improves nutritional status in hip fracture patients. (Strength of Recommendation: Moderate ***)
Patients with dementia	Europe	European Society for Clinical Nutrition and Metabolism (2015)	ESPEN Guidelines on Nutrition in Dementia[11]	We recommend the use of ONS to improve nutritional status. (Grade of evidence: High; Strength of recommendation: Strong)

Table 4.4 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with pressure ulcers (pressure injury)	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Geriatrics[6]	• ONS, particularly with high protein content, can reduce the risk of developing pressure ulcers [A] • Based on positive clinical experience, enteral nutrition (by means of ONS or tube feeding) is also recommended in order to improve healing of pressure ulcers [C] Note: see Table 4.8 for summary of grading of recommendations
	International	European Pressure Ulcer Advisory Panel (EPUAP), National Pressure Ulcer Advisory Panel (NPUAP) and Pan Pacific Pressure Injury Alliance (PPPIA) (2014)	Prevention and treatment of pressure ulcers	Energy intake: Offer fortified foods and/or high calorie, high protein oral nutritional supplements between meals if nutritional requirements cannot be achieved by dietary intake. (Strength of Evidence = B; Strength of Recommendation = CC) Consider enteral or parenteral nutritional support when oral intake is inadequate. This must be consistent with the individual's goals. (Strength of Evidence = C; Strength of Recommendation = C) Protein intake: Offer high calorie, high protein nutritional supplements in addition to the usual diet to adults with nutritional risk and pressure ulcer risk, if nutritional requirements cannot be achieved by dietary intake. (Strength of Evidence = A; Strength of Recommendation = C) Supplement with high protein, arginine and micronutrients for adults with a pressure ulcer Category/ Stage III or IV or multiple pressure ulcers when nutritional requirements cannot be met with traditional high calorie and protein supplements. (Strength of Evidence = B; Strength of Recommendation = 👍) The strength of recommendation in this document is indicated by multiples of a thumbs-up symbol
	USA	Academy of Nutrition and Dietetics	Spinal Cord Injury (SCI) Evidence-Based Nutrition Practice Guideline (login required)	**Nutrition Intervention to Prevent Development of Pressure Ulcers** If a patient with SCI is at risk of pressure ulcer development as indicated by biochemical, anthropometric and lifestyle factors, the RD should implement aggressive nutrition support measures. The range of options may include [ONS]* and enteral and parenteral nutrition. Research suggests that improved nutrition intake, body weight and biochemical parameters may be associated with reduced risk of pressure ulcer development [Strong Conditional] **Nutrition Prescription for SCI Patients with Pressure Ulcers** A nutrition prescription should be formulated as part of the nutrition intervention for patients with SCI and pressure ulcers which includes the energy, protein, fluid and micronutrient requirements. Evidence suggests that additional energy and protein is needed for optimal healing of pressure ulcers. Fluid and micronutrient needs will vary depending on the patient's status. See the Assessment of Nutritional Needs for Pressure Ulcers for determining levels of each of these [Consensus Imperative] *Note that the guidance uses the term 'Medical food supplements' but to avoid confusion with vitamin and mineral food supplements, the term ONS has been inserted in its place

Table 4.4 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with Pressure Ulcers (Pressure Injury)	Australia	Trans-Tasman Dietetic Wound Care Group (2011) Endorsed by Dietitians Association of Australia & Dietitians New Zealand	Evidence-based practice guidelines for the dietetic management of adults with pressure injuries	• Nutritional interventions should start with modification of current dietary intake and progress to the use of [ONS] before considering enteral support [III–3; Grade C] Note: see Table 4.7 for summary of grading of recommendations
	England	National Institute for Health and Care Excellence (NICE) (2014)	Pressure Ulcers: Prevention and Management[10]	**Prevention: Nutritional supplements and hydration** 1.1.11 Do not offer nutritional supplements specifically to prevent a pressure ulcer in adults whose nutritional intake is adequate. **Management: Nutritional supplements and hydration** 1.4.4 Offer adults with a pressure ulcer a nutritional assessment by a dietitian or other healthcare professional with the necessary skills and competencies. 1.4.5 Offer nutritional supplements to adults with a pressure ulcer who have a nutritional deficiency. 1.4.6 Provide information and advice to adults with a pressure ulcer and, where appropriate, their family or carers, on how to follow a balanced diet to maintain an adequate nutritional status, taking into account energy, protein and micronutrient requirements. 1.4.7 Do not offer nutritional supplements to treat a pressure ulcer in adults whose nutritional intake is adequate.
	Finland	National Nutrition Council (2010)	Nutrition treatment recommendation "Ravitsemushoito – Suositus sairaaloihin, terveyskeskuksiin, palvelu- ja hoitokoteihin sekä kuntoutuskeskuksiin"	**Pressure ulcers and chronic wounds:** Intensive nutrition treatment and at least 1 protein-rich ONS/day

Table 4.4 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with COPD	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Cardiology and Pulmonology[12]	Frequent small amounts of ONS are preferred to avoid postprandial dyspnoea and satiety and to improve compliance [B] Note: see Table 4.8 for summary of grading of recommendations
	Europe	European Respiratory Society (2014)	Nutritional assessment and therapy in COPD: a European Respiratory Society statement[13]	**Treatment of weight loss in COPD** Oral nutritional supplements (as powders, puddings or liquids) can be used to supplement the diet when nutrient requirements cannot be satisfied through normal food and drink. **Conclusions:** 5) Nutritional intervention is likely to be effective in undernourished patients (based on the Cochrane review) and is probably most effective if combined
	England and Wales	National Institute for Health and Care Excellence (NICE) (2010)	Chronic Obstructive Pulmonary Disease: in over 16s: Diagnosis and Management[14]	If the BMI is low, patients should also be given [ONS] to increase their total calorific intake and be encouraged to take exercise to augment the effects of nutritional supplementation
	International	Global Initiative for Chronic Obstructive Lung Disease (2017)	Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease	Nutritional support: Low-to-moderate quality evidence suggests that nutritional support promotes significant gain in weight and fat-free mass among patients with COPD, especially if malnourished. In addition, significantly greater changes from baseline have been observed in supplemented patients for six-minute walk test, respiratory muscle strength and (only in malnourished patients) overall HRQoL as measured by SGRQ. Positive effects have been observed when nutritional supplementation is proposed alone or as an adjunct to exercise training. The optimal amount and duration of supplementation are not clearly established.

Table 4.4 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with COPD	USA	Academy of Nutrition and Dietetics (2008)	Chronic Obstructive Pulmonary Disease (COPD) Evidence-based Nutrition Practice Guideline (login required)	**Macronutrient Composition of [ONS]*** RDs should advise that the selection of [ONS] for individuals with COPD should be influenced more by patient preference than the percentage of fat or carbohydrate. There is limited evidence to support consumption of a particular macronutrient composition of [ONS] [Fair] **COPD: Frequent Small Amounts of [ONS]** RDs should recommend frequent small amounts of [ONS] for individuals with COPD. Studies report that frequent small amounts of [ONS] are preferred to avoid postprandial dyspnoea and satiety and to improve compliance [Fair] **COPD: [ONS] for Inpatients** For inpatients with COPD who have low BMI (less than 20 kg/m^2), unintentional weight loss, reduced oral intake or who are at nutritional risk, registered dietitians should initiate provision of [ONS]. Studies report that [ONS] for 7–12 days results in increased energy intake in the inpatient setting [Fair] **COPD: [ONS] for Outpatients** For outpatients with COPD who have low BMI (less than 20 kg/m^2), unintentional weight loss, reduced oral intake or who are at nutritional risk, RDs should recommend consumption of [ONS]. In the outpatient setting, studies report that [ONS] results in increased energy intake, with weight gain more likely when combined with exercise [Fair] *Note that the guidance uses the term 'Medical food supplements' but to avoid confusion with vitamin and mineral food supplements, the term ONS has been inserted in its place
Patients with cystic fibrosis	Europe	ESPEN-ESPGHAN-ECFS (2016)	ESPEN-ESPGHAN-ECFS guidelines on nutrition care for infants, children, and adults with cystic fibrosis[9]	**Guideline: oral nutritional supplements** • We recommend clinicians consider the use of oral nutritional supplements for treating children and adults who fail to achieve optimal growth rates and nutritional status with oral dietary intake and pancreatic enzyme replacement therapy (PERT) alone. (Grade of evidence: low) • We recommend clinicians regularly review and re-evaluate patients who are taking oral nutritional supplements to determine whether the patient should continue taking them. (Grade of evidence: high)

Table 4.4 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with acute or chronic pancreatitis	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Pancreas[15]	Acute pancreatitis • Oral feeding (normal food and/or ONS) can be progressively attempted once gastric and outlet obstruction has resolved, provided it does not result in pain, and complications are under control [C] Chronic pancreatitis • 10–15% of all patients require ONS [C] Note: see Table 4.8 for summary of grading of recommendations
Patients with liver disease	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Liver Disease[16]	Alcoholic steatohepatitis • In general, ONS are recommended [B] Liver cirrhosis • If patients are not able to maintain adequate oral intake from normal food, use ONS [C] Note: see Table 4.8 for summary of grading of recommendations

Table 4.4 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with HIV and chronic infectious diseases	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Wasting in HIV and Other Chronic Infectious Diseases[17]	**HIV** • Diarrhoea does not prevent a positive effect of ONS on nutritional status [A] • Nutritional counselling with ONS or counselling alone are equally effective at the beginning of nutritional support and/or for preserving nutritional status [B] • In settings where qualified nutritional counselling cannot be provided, ONS may be indicated in addition to normal food, but this should be limited in time [C] **Chronic infectious diseases** • Nutritional support should be given to patients with under-nutrition resulting from infectious diseases – prefer ONS [B] Note: see Table 4.8 for summary of grading of recommendations
Patients with renal disease	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Adult Renal Failure[18]	**Acute Renal Failure (ARF)** • In uncomplicated ARF, when spontaneous alimentation is insufficient, ONS may be useful to meet estimated requirements [C] **Patients on maintenance haemodialysis (HD) therapy** • Use ONS to improve nutritional status [A] • ONS should be the preferred route in conscious HD patients Note: see Table 4.8 for summary of grading of recommendations
	Canada	Canadian Society of Nephrology (2011)	Clinical practice guidelines and recommendations on peritoneal dialysis adequacy[19]	[ONS] should be considered for patients with mild-to-severe malnutrition [B]. However, certain supplements may be poorly tolerated by individual patients, and thus close monitoring is required [A]
Patients with GI disease	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Gastroenterology[20]	**CD** • In the case of persistent intestinal inflammation (e.g. steroid-dependent patients) use ONS [B] • Use ONS in addition to normal food to improve nutritional status and to eliminate consequences of under-nutrition such as growth retardation [A] • Using ONS, a supplementary intake of up to 600 kcal/day can be achieved in addition to normal food [A] **Short bowel syndrome** • Use ONS or tube feeding if normal nutritional status cannot be maintained by normal food alone [C] Note: see Table 4.8 for summary of grading of recommendations

Table 4.4 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with intestinal failure	Europe	European Society for Clinical Nutrition and Metabolism (2016)	Management of acute intestinal failure: A position paper from the European Society for Clinical Nutrition and Metabolism (ESPEN) Special Interest Group[21]	**Enteral nutrition:** Disease-specific formulae are probably not required; many different standard oral nutritional supplements or enteral feeds may be helpful in intestinal failure, selected according to their energy density and convenience **Oral feeding;** Except in situations where fasting is believed to help promote fistula healing or control (e.g. acute phase, very proximal, high output fistula), patients will be advised to eat ad libitum. Regular meals as well as the use of oral nutritional supplements should be considered. The supervision of an experienced dietician is essential for best results, not least because of the problems with the net secretory state of many of these patients and the consequent need to restrict salt-free fluids.
	Europe	European Society for Clinical Nutrition and Metabolism (2016)	ESPEN guidelines on chronic intestinal failure in adults[22]	**Intestinal rehabilitation strategy - medical** We suggest the addition of oral isotonic nutritional supplements in borderline (i.e. B1 category of clinical classification) Short Bowel Syndrome intestinal failure patients at risk of malnutrition. (Grade of evidence: low)
Surgical patients	Europe	European Society for Clinical Nutrition and Metabolism (2017)	ESPEN Guideline: Clinical Nutrition in Surgery[23]	• Perioperative nutritional therapy is indicated in patients with malnutrition and those at nutritional risk. Perioperative nutritional therapy should also be initiated, if it is anticipated that the patient will be unable to eat for more than five days perioperatively. It is also indicated in patients expected to have low oral intake and who cannot maintain above 50% recommended intake for more than seven days. In these situations, it is recommended to initiate nutritional therapy (preferably by the enteral route - ONS-TF) without delay. (GPP, strong consensus) • When patients do not meet their energy needs from normal food it is recommended to encourage these patients to take oral nutritional supplements during the preoperative period unrelated to their nutritional status. (GPP, consensus) • Preoperatively, oral nutritional supplements shall be given to all malnourished cancer and high-risk patients undergoing major abdominal surgery. A special group of high-risk patients are the elderly people with sarcopenia (A, strong consensus) • Immune modulating oral nutritional supplements including arginine, omega-3 fatty acids and nucleotides can be preferred and administered for five to seven days pre-operatively. (0/GPP, majority agreement)

Table 4.4 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Surgical patients (continued)				• Pre-operative enteral nutrition/oral nutritional supplements should preferably be administered prior to hospital admission to avoid unnecessary hospitalization and to lower the risk of nosocomial infections (GPP, strong, consensus) • Regular reassessment of nutritional status during the stay in hospital and, if necessary, continuation of nutrition therapy including qualified dietary counselling after discharge, is advised for patients who have received nutrition therapy perioperatively and still do not cover appropriately their energy requirements via the oral route (GPP, strong, consensus) Note: see Table 4.10 for summary of grading of recommendations
	Europe	European Society for Clinical Nutrition and Metabolism (2012)	Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations [24]	Postoperative nutritional care • Patients should be screened for nutritional status and, if deemed to be at risk of undernutrition, given active nutritional support. For the standard ERAS patient, preoperative fasting should be minimised and postoperatively patients should be encouraged to take normal food as soon as possible after surgery. ONS can be used to supplement total intake. See also Guidelines for perioperative care in elective rectal/pelvic surgery[25] and Guidelines for perioperative care for pancreaticoduodenectomy[26]
	England and Wales	National Institute for Health and Care Excellence (NICE) (2006)	Nutrition Support for Adults: Oral Nutrition Support, Enteral Tube Feeding and Parenteral Nutrition[1]	Oral nutrition support for surgical patients • Patients should be encouraged to commence oral food intake 4 hours after surgery. can swallow safely and are malnourished [B] Note: see Table 4.6 for summary of grading of recommendations

Table 4.4 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Surgical Patients (continued)	The Netherlands	Quality Institute for Healthcare (CBO, 2007)	Perioperative Feeding Guidelines	Summary: guidelines on how to screen for and treat malnutrition before, during and after surgery (general) • It is recommended to screen for malnutrition and treat malnutrition before surgery. The best way to treat serious malnutrition is to start immediately with artificial supplements or tube feeding. Start 7–10 days before surgery [D] • If malnutrition is diagnosed, [ONS] must be used instead of trying to improve the nutritional status with DA [A1] • [ONS] are preferred over parenteral feeding when treating malnutrition prior to surgery [C] Grading of recommendations: A1) Systematic reviews of at least some A2-level clinical trials that have shown consistent results A2) Randomised comparative clinical trials of good quality (randomised double-blind controlled trials), good sample size and consistency B) Randomised clinical trials of poor quality, insufficient sample size or other comparative trials (non-randomised, comparative, cohort research, patient-controlled research) C) Non-comparative research D) Expert opinion, for example, from committee members
Patients with SCI	USA	Academy of Nutrition and Dietetics (2009)	Spinal Cord Injury (SCI) Evidence-based Nutrition Practice Guideline (login required)	**Nutrition Intervention to Prevent Development of Pressure Ulcers** If a patient with spinal cord injury is at risk of pressure ulcer development as indicated by biochemical, anthropometric and lifestyle factors, the RD should implement aggressive nutrition support measures. The range of options may include [ONS]* and enteral and parenteral nutrition. Research suggests that improved nutrition intake, body weight and biochemical parameters may be associated with reduced risk of pressure ulcer development [Strong Conditional] **Nutrition Prescription for SCI Patients with Pressure Ulcers** A nutrition prescription should be formulated as part of the nutrition intervention for patients with SCI and pressure ulcers which includes the energy, protein, fluid and micronutrient requirements. Evidence suggests that additional energy and protein is needed for optimal healing of pressure ulcers. Fluid and micronutrient needs will vary depending on the person's status. See the Assessment of Nutritional Needs for Pressure Ulcers for determining levels of each of these [Consensus Imperative]

Table 4.4 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Stroke patients	England and Wales	National Institute for Health & Care Excellence (NICE) (2008)	Stroke: National Clinical Guideline for Diagnosis and Initial Management of Acute Stroke and Transient Ischaemic Attack (TIA)[27]	Nutritional support should be initiated for people with stroke who are at risk of malnutrition. This may include ONS, specialist DA and/or tube feeding
	Scotland	Scottish Intercollegiate Guidelines Network (SIGN) (2010)	Management of Patients with Stroke: identification and management of dysphagia Management of patients with stroke: Rehabilitation, prevention and management of complications, and discharge planning	Following nutritional screening, those identified as undernourished and those at risk of becoming undernourished should be referred to a dietitian and considered for prescription of [ONS] as part of their overall nutritional care plan [C] Note: see Table 4.6 for summary of grading of recommendations (Grade C similar to NICE)
	Australia	Stroke Association	Clinical Guidelines for Stroke Management 2017	For stroke patients whose nutrition status is poor or deteriorating, nutrition supplementation should be offered.

ONCOLOGY

Table 4.5 **Summary of examples of evidence-based national and professional guidelines referring to ONS as an integral part of patient and disease management in Oncology** (parts of guidelines relevant to ONS are presented here)

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with cancer	Europe	European Society for Clinical Nutrition and Metabolism. Officially endorsed by the European Society of Surgical Oncology (ESSO), the European Association for Palliative care (EAPC) and the Chinese Society of Clinical Oncology (CSCO) (2016)	ESPEN guidelines on nutrition in cancer patients[28]	**Nutrition interventions:** **Efficacy of nutritional intervention:** We recommend nutritional intervention to increase oral intake in cancer patients who are able to eat but are malnourished or at risk of malnutrition. This includes dietary advice, the treatment of symptoms and derangements impairing food intake (nutrition impact symptoms), and offering oral nutritional supplements. (Strength of recommendation STRONG; Level of evidence Moderate)
Patients under-going anti-cancer therapy	Australia	Dietitians Association of Australia (2013)	Updated evidence-based Practice Guidelines for the Nutritional Management of Patients Receiving Radiation Therapy and/or Chemotherapy[29]	In chemotherapy patients, simple nutrition intervention (simple dietary counselling and/or supplements without medical nutrition therapy) is effective at improving dietary intake and weight but does not improve patient-centred outcomes. [Grade A]

Table 4.5 **Continued**

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients undergoing anti-cancer therapy	Australia	Clinical Oncology Society of Australia (2011, last modified June 2014)	Evidence-based practice guidelines for the nutritional management of adult patients with head and neck cancer	**Surgery** Preoperative nutrition intervention in malnourished patients may lead to improved outcomes, such as quality of life, and reduce adverse related consequences of malnutrition [Recommendation Grade: B] Peri-operative *n*-3 fatty acid enriched nutrition support may improve nutritional outcomes such as weight, lean body mass and fat mass.[Grade C] **Radiotherapy and chemotherapy** Nutrition intervention (dietary counselling and/or [ONS] and/or tube feeding) improves/ maintains nutritional status [Recommendation Grade: A] Nutrition intervention (dietary counselling and/or [ONS] and/or tube feeding) improves patient-centred outcomes (QOL, physical function, and patient satisfaction) [Recommendation Grade: B] **Post treatment** Nutrition intervention (dietary counselling and/or [ONS]) for 3 months post treatment improves/maintains nutritional status [Recommendation Grade: A] Nutrition intervention (dietary counselling and/or [ONS]) for 3 months post treatment improves/maintains QOL [Recommendation Grade: A] Note: See Table 6.6 for summary of grading of recommendations
Patients with head and neck cancer	Scotland	Scottish Intercollegiate Guidelines Network (SIGN) (2011, revised 2016)	Diagnosis and Management of Colorectal Cancer	**Nutrition and weight loss** Patients and families understandably focus on what patients are able to eat. Although there is no evidence that nutritional supplements, parenteral or enteral feeding are of benefit in preventing cancer cachexia when the disease is advanced, evidence is emerging that it may be of value at an earlier stage. Referral to a specialist state registered dietitian or advice from a nutrition support team should be sought where appropriate. As anorexia and weight loss are so distressing for the patient and their family, the issue of nutrition must be addressed.

Table 4.5 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with head and neck cancer	Spain	(2008)	Consensus document on Nutrition in Cancer (Nutr Hosp Suplementos. 2008;1(1):13)	• Nutritional care should be provided early and it should be part of the overall treatment plan for oncology patients • The cancer patient's diet should be in line with healthy nutrition guidelines (balanced, varied, desirable and sufficient to meet needs) • When DA is not enough, nutritional support should be given • Symptoms such as anorexia, nausea and vomiting as a result of the cancer or its treatment make it difficult for patients to meet their nutritional needs • Cancer patients may need artificial nutrition (same indications as non-cancer patients) with an appropriate formula to meet their particular needs • The effectiveness of nutritional support must be balanced with the risk of its use (Summary in English of section on Nutritional Intervention Criteria: goals, directions and evidence)
	USA	Academy of Nutrition and Dietetics (2013)	Oncology evidence-based nutrition practice guideline	**ONC: Nutrition Intervention of Adult Oncology Patients with Cancer Cachexia** In adult oncology patients who have been identified to have pre-cachexia or cancer cachexia, prompt and aggressive intervention to address nutrition impact symptoms and preserve or prevent loss of lean body mass (LBM) and weight should be initiated by the RDN. Early rather than later intervention to prevent weight loss in this population is more likely to be effective. The metabolic derangements in cancer cachexia that promote wasting can lead to loss of weight and LBM and poor outcomes. [Consensus]. **ONC: [ONS] Containing Fish Oil for the Adult Oncology Patient** If sub-optimal symptom control or inadequate dietary intake has been addressed and the adult oncology patient is still experiencing loss of weight and LBM, the RDN may consider use of a [ONS] containing EPA as a component of nutrition intervention. Research indicates that [ONS] containing fish oil (actual consumption, 1.1 g to 2.2 g of EPA per day) resulted in significant weight stabilization or weight gain and preservation or improvement of LBM in adult oncology patients with weight loss. [Grade I and II]

Table 4.5 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with head and neck cancer	USA	Academy of Nutrition and Dietetics (2013)	Oncology Evidence-based Nutrition Practice Guideline	Head and neck cancer: [ONS]* and radiation Dietitians should consider use of [ONS] to improve protein and calorie intake for patients with head and neck cancer undergoing radiation therapy. Use of [ONS] may be associated with fewer treatment interruptions and a reduction of mucosal damage, and it may minimise weight loss.
Patients with lung cancer	USA	American College of Chest Physicians (ACCO) (2013)	Complementary Therapies and Integrative Medicine in Lung Cancer - Evidence-Based Clinical Practice Guidelines	• In patients undergoing treatment of lung cancer who have experienced weight loss, the addition of high calorie and protein supplements (1.5 kcal/mL) as a nutritional adjunct is suggested to achieve weight stabilization (Grade 2C) • In patients with lung cancer who have sarcopenia, oral nutritional supplementation with n-3 fatty acids is suggested in order to improve the nutritional status (Grade 2C)

Table 4.6 **NICE Guidelines: Grading of recommendations** (adapted from NICE 2006)[1]

Grade	Evidence
A	• At least one meta-analysis, systematic review or RCT rated as 1++ (i.e. high-quality meta-analyses, systematic reviews of RCTs or RCTs with a very low risk of bias), directly applicable to the target population, or • A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+ (i.e. well-conducted meta-analyses, systematic reviews of RCTs or RCTs with a low risk of bias), directly applicable to the target population and demonstrating overall consistency of results, or • Evidence drawn from a NICE technology appraisal
B	• A body of evidence including studies rated as 2++ (i.e. high-quality systematic reviews of case-control or cohort studies, high-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal), directly applicable to the target population and demonstrating overall consistency of results, or • Extrapolated evidence from studies rated as 1++ or 1+
C	• A body of evidence including studies rated as 2+ (i.e. well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal), directly applicable to the target population and demonstrating overall consistency of results, or • Extrapolated evidence from studies rated as 2++
D	• Evidence level 3 (i.e. non-analytic studies, e.g. case reports, case series) or 4 (i.e. expert opinion), or • Extrapolated evidence from studies rated as 2+, or • Formal consensus
D (GPP)	• A good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group

Table 4.7 **Dietitians Association of Australia Guidelines: Grading of recommendations**

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

*Full details of level of evidence according to type of research question available from NHMRC[30]

Table 4.8 **ESPEN Guidelines: Levels of evidence used in guidelines pre- 2015**
(adapted from Schutz 2006)[31]

Grade	Level of evidence	Requirement
A	Ia Ib	• Meta-analysis of randomised controlled trials (RCTs) • At least one RCT
B	IIa IIb III	• At least one well-designed controlled trial without randomisation • At least one other type of well-designed quasi-experimental study • Well-designed non-experimental descriptive studies such as comparative studies, correlation studies, case-control studies
C	IV	• Expert opinions and/or clinical experience of respected authorities

Table 4.9 **ESPEN Guidelines: Levels of evidence used in guidelines from 2015 onwards**
(adapted from Bischoff et al. 2015)[32]

Levels of evidence	
1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort or studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is casual
2+	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is casual
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is casual
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

According to the Scottish Intercollegiate Guidelines Network (SIGN) grading system. Source: SIGN 50; A guideline developer's handbook. Quick reference guide October 2014

Table 4.10 **ESPEN Guidelines: Grades of evidence used in guidelines from 2015 onwards**
(adapted from Bischoff et al. 2015)[32]

Grades of recommendation	
A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population; or A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+
O	Evidence level 3 or 4; or extrapolated evidence from studies rated as 2++ or 2+
GPP	Good practice points/expert consensus: Recommended best practice based on the clinical experience of the guideline development group

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Table 4.11 Signposts for evidence grading of other international organisations

Recommending body	Signpost for evidence grading
National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel and Pan Pacific Pressure Injury Alliance	http://www.internationalguideline.com/static/pdfs/NPUAP-EPUAP-PPPIA-PUGuideline-MethodAddendum-2014.pdf
Academy of Nutrition and Dietetics	https://www.andeal.org/recommendation-ratings
ASPEN	http://pen.sagepub.com/content/36/1/77.full.pdf+html
Clinical Oncology Society of Australia	http://wiki.cancer.org.au/australia/COSA:Head_and_neck_cancer_nutrition_guidelines/Introduction#Literature_critique
NASPGHAN	http://www.cebm.net/
Surviving Sepsis Campaign	http://www.sccm.org/Documents/SSC-Guidelines.pdf
ESPGHAN	http://www.espghan.org/fileadmin/user_upload/guidelines_pdf/Guidelines_2404/Management_of_Pediatric_Ulcerative_Colitis___Joint.24.pdf
ESPEN	http://www.espen.org/files/ESPEN-Guidelines/0__Standard_operating_procedures_for_ESPEN_guidelines_and_consensus_papers_2.pdf

4.1.2 Guidelines: From theory to practice for enhanced patient care

Practical guidance for healthcare professionals about when to use ONS is essential and should be a key component of many guidelines

- The method of nutrition support included in these practical guides should be carefully considered and should take account of the evidence base, condition of the patient (both clinical and nutritional), their prognosis and preferences. Although not based on robust evidence, food fortification is often recommended as the first line approach with ONS reserved for if/when this strategy is not successful. Care must be taken to review patients on a regular basis and to quickly identify if nutritional goals are not being met so that an alternative strategy can be used e.g. ONS. NICE (2006) highlight that oral nutrition support strategies are not exclusive and can be used in combination.[1]
- Practical advice on the use of ONS in clinical practice has been formulated by Stratton and Elia (2007) in a review of reviews on the evidence base for ONS across different patient groups (Figure 4.1).[33]
- Other examples include an Oral Nutrition Support Algorithm in the UK NICE guideline (Figure 4.2), a table with information about grade of risk of malnutrition, and contribution of spontaneous food intake in the Haute Autorité de Santé recommendations in France (Table 4.12).
- In 2012 the National Health Service National Prescribing Centre in the UK published 'Prescribing of adult Oral Nutritional Supplements (ONS): Guiding principles for improving the systems and processes for ONS use' (Table 4.13) with the aim of helping organisations ensure that patients can obtain ONS when clinically appropriate and that the systems and processes are in place to:
  - ~ monitor on-going requirements for ONS;
  - ~ monitor concordance (compliance or adherence) and;
  - ~ monitor patients' clinical condition after a decision is made to discontinue ONS when it appears it is no longer clinically indicated.
- 'Managing Adult Malnutrition in the Community', a practical guide based on clinical evidence and best practice, has been developed in the UK by a multi-professional consensus panel. It has been endorsed by 10 key healthcare professional associations and has been designed to support GPs and other community healthcare professionals to identify and manage individuals at risk of disease-related malnutrition. Amongst other relevant topics it includes:
  - ~ information about managing malnutrition according to risk category, including practical tips to aid clinical judgement
  - ~ a pathway for using ONS in the management of malnutrition (see Figure 4.3);
  - ~ information on optimising oral intake, providing an overview of the practical elements and evidence for dietary advice and ONS
- These practical guides allow healthcare professionals to make decisions about the appropriate use of ONS.

- Identify malnutrition or risk of malnutrition using routine screening across healthcare settings with a valid, evidence-based tool such as 'MUST'. Implement appropriate nutritional treatment as part of a care plan for malnutrition as soon as possible.
- Consider ONS as part of the care plan for the treatment of malnutrition*:
  - ~ ONS can be used if improvements in energy, protein and micronutrient intakes are required. ONS tend not to suppress appetite or voluntary food intake. ONS can be particularly effective at improving total nutritional intake in acutely ill, elderly and post-surgical patients
  - ~ For patients requiring longer-term oral nutritional support, often in the community, it is likely that a variety of types of ONS (e.g. flavours, textures, consistencies) and encouragement to comply with ONS would be beneficial to maintain improvements in nutritional intake
  - ~ ONS can be used to attenuate weight loss in the acutely ill patient or aid weight gain in chronically ill patients. Improvements in weight (> 2 kg), especially in the underweight, are associated with improvements in function in the chronically ill
  - ~ ONS (~250-600 kcal/d) can be used to help improve clinical outcome in hospitalised patients, acutely ill elderly, patients undergoing GI surgery and in hip fracture patients
  - ~ Consider high protein ONS to reduce the risk of development of pressure ulcers in high-risk groups (frail elderly, hip fracture, poor mobility) and to help improve outcome in hip fracture patients
- When providing ONS, consider patients needs for energy, protein and micronutrients. Any specific identifiable nutrient deficiencies (trace elements, minerals, vitamins) should be corrected where possible.
- The goal(s) of treatment with ONS should be identified for an individual patient at the start of treatment. Thereafter, regular and frequent monitoring of patients receiving ONS should be undertaken to:
  - ~ Assess ONS acceptability
  - ~ Monitor ONS effectiveness by monitoring the patients' progress towards the treatment goal(s). These could include measures of energy and nutritional intake, appetite, nutritional status, functional measures, clinically relevant outcomes (pressure ulcer size, infection, quality of life)
  - ~ Encourage compliance with ONS where appropriate
  - ~ Assess whether ONS are still required or if other forms of nutritional support (e.g. tube feeding) are warranted
  - ~ Monitor changes in clinical and nutritional status

*The care plan, including when to refer to a dietitian or nutrition support team, should be devised by a multidisciplinary team according to local policy and resources

Figure 4.1 **Recommendations for use of ONS in clinical practice** (adapted from Stratton and Elia. 2007)[33]

Table 4.12 **Example of a nutritional management strategy detailing when to use ONS for older people** (adapted from Haute Autorité de Santé 2011)[34]

Spontaneous dietary intake	Nutritional Status: Normal	Nutritional Status: Malnutrition	Nutritional Status: Severe Malnutrition
Normal	• Monitoring	• Dietary advice • Fortified diet • Reassessed* at 1 month	• Dietary advice • Fortified diet & **ONS** • Reassessed* at 15 days
Reduced, but more than half of usual intake	• Dietary advice • Fortified diet • Reassessed* at 1 month	• Dietary advice • Fortified diet • Reassessed* at 15 days and if failure: **ONS**	• Dietary advice • Fortified diet and **ONS** • Reassessed* at 1 week, if failure: Enteral Nutrition
Very reduced and less than 50% of normal intake	• Dietary advice • Fortified diet • Reassessed* at 1 week, and if failure: **ONS**	• Dietary advice • Fortified diet and **ONS** • Reassessed* at 1 week, and if failure: Enteral Nutrition	• Dietary advice • Fortified diet and Enteral Nutrition from outset • Reassessed* at 1 week

*Reassessment should include: Weight and nutritional status, clinical condition and prognosis, estimation of spontaneous food intake, tolerance and compliance with treatment

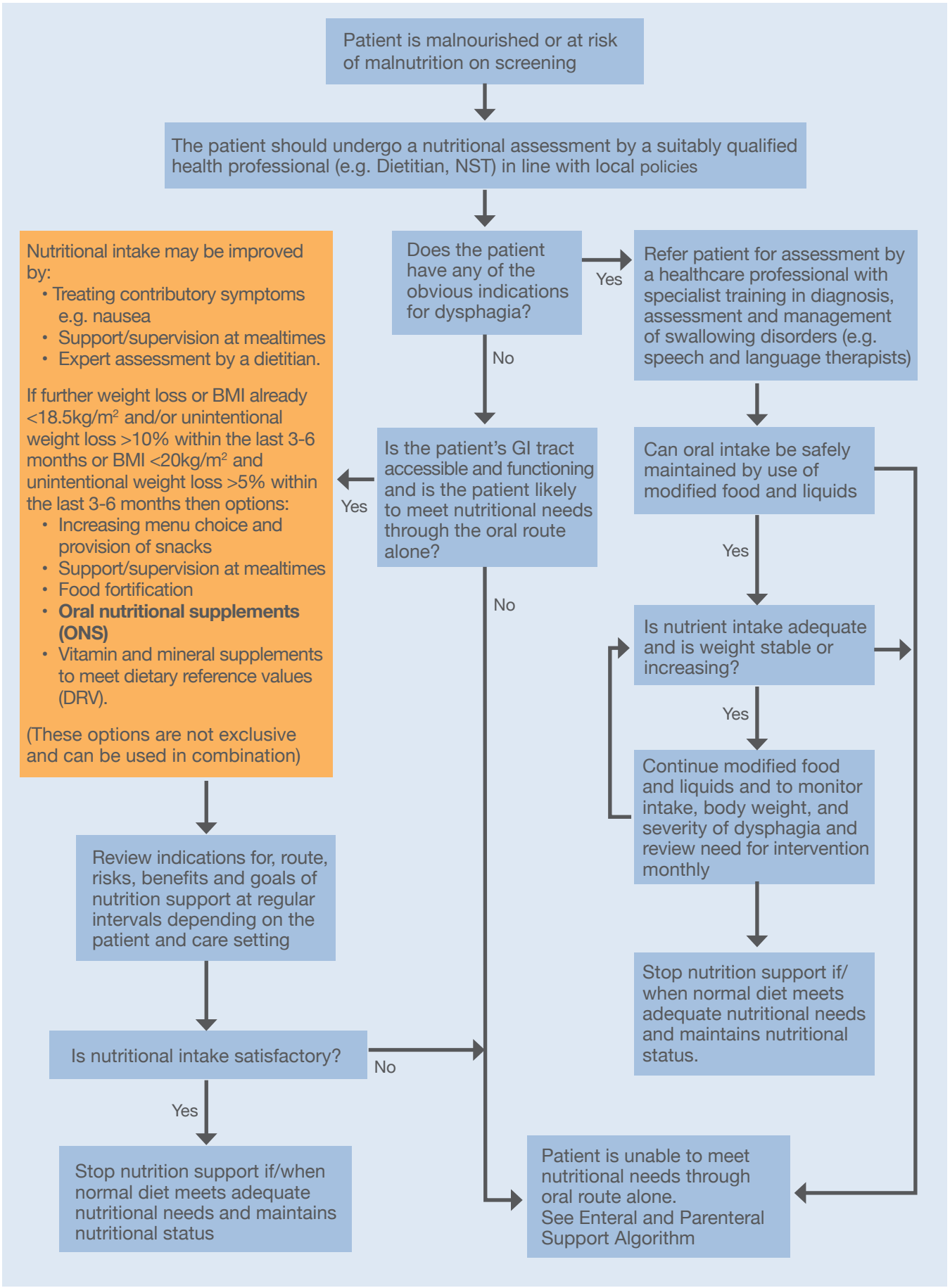

Figure 4.2 **Oral Nutrition Support Algorithm** (adapted from NICE, 2006)[1]

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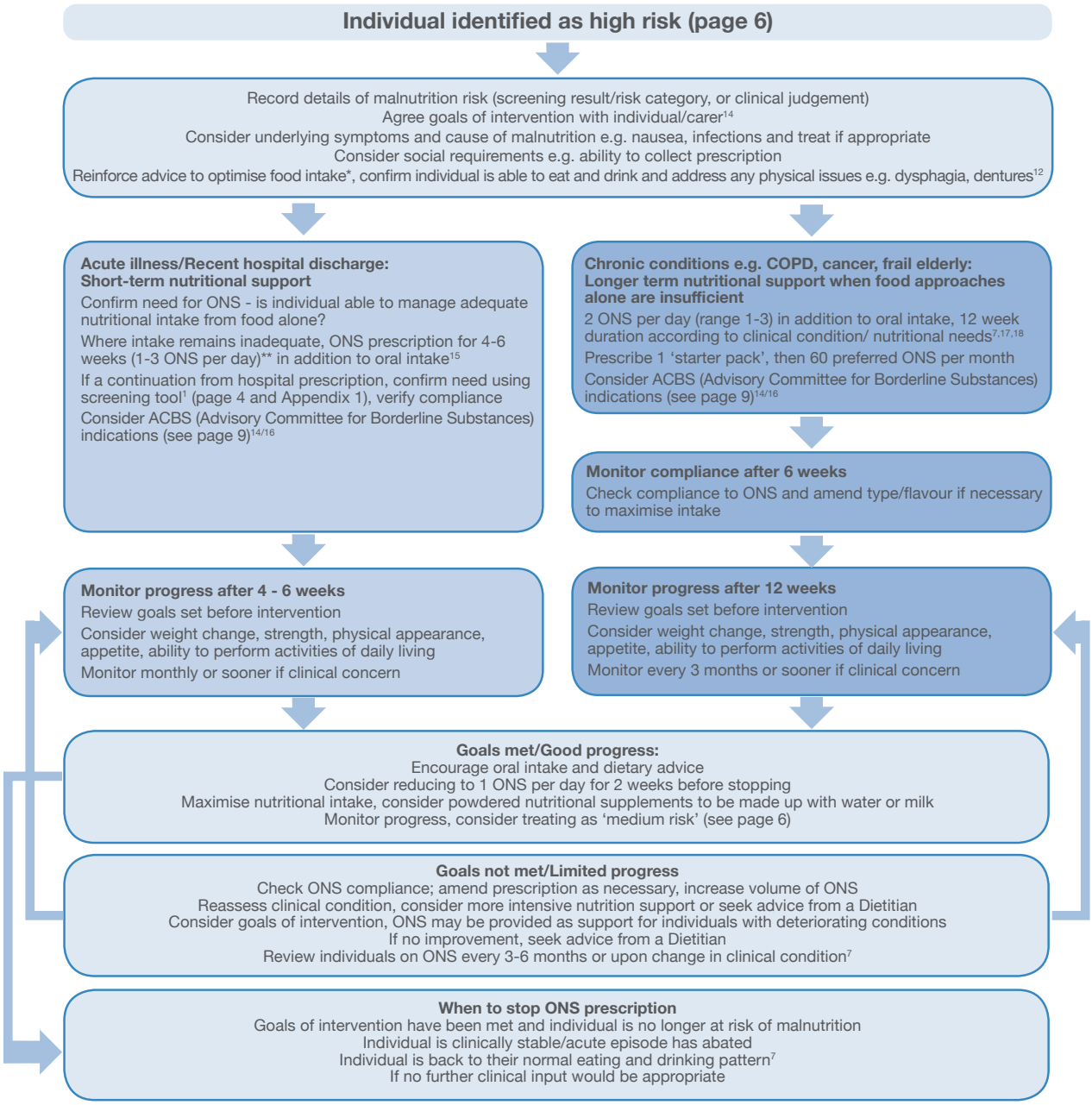
Table 4.13 **Ten Guiding Principles for improving the systems and processes for ONS use**
(adapted from NHS National Prescribing Centre [NPC]: Prescribing of adult ONS, 2012)*

1	Local health economies should understand their local clinical need for adult oral nutrition support and map this against local work force expertise.
2	Local health economies should understand their local procurement arrangements for adult ONS in primary, secondary and social care.
3	Commissioners should review prescribing arrangements for adult ONS.
4	Local health economies should ensure that a validated screening tool such as the 'Malnutrition Universal Screening Tool' ('MUST') is embedded into everyday care so that the results of screening are linked to a care plan.
5	Local health economies should develop standard templates for care plans to be used with 'at risk' adult patients across primary, secondary and social care. Goals should be set and the care plan monitored and reviewed so that oral nutritional supplements are used appropriately.
6	Local health economies should work with care home commissioners and providers to ensure high standards of nutritional screening, education and assessment for oral nutritional support is embedded in the care home environment.
7	Local health economies should assess local training needs for all health and social care staff for the identification and treatment of adult undernutrition and implement an education programme for all appropriate front line staff, carers and patients. Competencies for basic skills should be developed.
8	Local health economies should develop measurements for assessing the quality of the provision of adult ONS.
9	Commissioners should consider incentives to improve adult oral nutrition support and prescribing practice.
10	Local health economies should consider setting up local fora to oversee nutrition issues in primary, secondary and social care with an emphasis on the interface.

*In April 2011 the NPC integrated into the National Institute for Health and Clinical Excellence (NICE). However, the guiding principles do not constitute formal guidance of the National Institute for Health and Clinical Excellence. More information available at https://www.webarchive.org.uk/wayback/archive/20130426203534/http://www.npc.nhs.uk/quality/ONS/resources/borderline_substances_final.pdf

Pathway for using Oral Nutritional Supplements (ONS) in the Management of Malnutrition



ONS – oral nutritional supplements/sip feeds/nutrition drinks (BNF section 9.4.2)[16] (see pages 8-9)

Advice on ONS prescription according to consensus clinical opinion. ONS prescription-units to prescribe per day e.g. 2 ONS = 2 bottles/units of ONS per day
** For more detailed support or complex conditions seek advice from a Dietitian*
***Some individuals may require more than 3 ONS per day – seek dietetic advice*
***NOTE:** ONS requirement will vary depending on nutritional requirements, patient condition and ability to consume adequate nutrients, ONS dose and duration should be considered*

This pathway has been taken from 'Managing Adult Malnutrition in the Community' – for more information and references please go to www.malnutritionpathway.co.uk

Figure 4.3 **Pathway for using Oral Nutritional Supplements (ONS) in the Management of Malnutrition**

Reproduced with kind permission from Anne Holdoway, Panel Chair. For details of references cited within this table and further information please refer to the original document available at http://malnutritionpathway.co.uk/

4.1.3 Guideline implementation: Benefits for patients and healthcare systems

Published guidelines demonstrate that ONS are recognised as a key component of care across a wide variety of patient groups. The implementation of guidelines that include the use of ONS in practice have been shown to positively influence clinical practice and patient outcome, for example, in the prevention and management of pressure ulcers, in surgical patients and in patients with hip fracture as documented in the examples below.

Screening and use of ONS is more frequent in patients with pressure ulcers (hospital and community)

- A cross-sectional survey of 363 institutions and home-care settings in the Netherlands, Germany and the UK (hospitals 46.9%, nursing homes 25.8% and home care 21.6%) showed that 66.1% of organisations had implemented the European Pressure Ulcer Advisory Panel Guidelines for Pressure Ulcer Prevention and Treatment:[35]
  - ~ nutritional screening in pressure ulcer care was conducted significantly more frequently in organisations where the nutritional guideline was used compared with institutions and organisations not using the guidelines (18.3% 'never' performed screening vs 3.0%; $p = 0.001$);[35]
  - ~ ONS were used more frequently in organisations using the guidelines, whereas tube feeding was used equally in the 2 groups. PN was given less frequently in the group using the guidelines.[35]

Better energy intake and reduced pressure ulcers in patients with hip fracture (hospital)

- A pre- and post-test comparison group study of patients with hip fracture ($n = 100$, mean age 81 years) showed that the use of nutritional guidelines (including preoperative carbohydrate loading and postoperative ONS) compared with standard hospital food and regular nutrition support according to doctors' and nurses' knowledge and goodwill significantly increased energy intake ($p < 0.001$). In addition, 5 days postoperatively, fewer patients in the intervention group developed pressure ulcers (18%) compared with the control group (36%) ($p = 0.043$).[36]

Improved clinical outcomes in surgical patients (hospital)

- Clinical benefits were observed in a study of older patients ($n = 117$, median age 67 years, range 60–85) who received a multidisciplinary protocol of perioperative care established by the ACERTO project ($n = 75$) (included early instead of delayed postoperative feeding and preoperative nutrition support for malnourished patients) compared with patients who received traditional care ($n = 42$). The number of hours of preoperative fasting decreased, and patients were fed 1 day earlier after the introduction of the new protocol:[37]
  - ~ surgical site infection was significantly reduced (9/42; 28.1% vs 2/75; 2.6%; OR 9.9, 95% CI 2.0–48.6; $p < 0.01$);
  - ~ overall postoperative morbidity diminished (16/42; 38.1% vs 16/75; 21.3%; OR 2.2, 95% CI 0.98–5.2; $p = 0.05$);
  - ~ both total length of stay (10 [2–44]) vs 4 [2–140] days) and postoperative stay (6 [1–43] vs 2 [1–99] days, $p < 0.01$) reduced.

Screening guidelines: benefits of implementation

A key aspect of many of the guidelines listed in Table 4.1 to Table 4.5 is the correct targeting of nutritional support, including the use of ONS, at patients who have been identified as malnourished or at risk of malnutrition. It is clear that appropriate use of nutritional support is a key part of the wider task of identifying patients at nutritional risk and implementing timely and appropriate care plans to address their needs. Nutritional screening has become mandatory in some countries (for example Scotland, the Netherlands and Denmark), although this is not yet widespread across Europe. Documentation of nutritional status as part of clinical examination and treatment is included in legislation in Norway. Evidence is emerging that screening may reduce the prevalence of malnutrition (see country example The Netherlands) and that the use of screening programmes that include intervention and care planning can contribute to improved outcomes, although more work is needed in this area.

Implementation of screening guidelines in the hospital setting

- In a study investigating the prevalence of under-nutrition in Swiss hospitals, the proportion of patients found to be at risk of under-nutrition remained constant (1 in 5); however, the proportion of nutritional interventions increased from 63% (in year 1) to 72% (in year 2) to 78% (in year 3) (p <0.05 by analysis of variance), providing a promising indication that participating hospitals became more aware over the course of the study.[38]
- In a study of hospital in-patients undergoing orthopaedic surgery (n = 98), weekly screening by nurses using the NRS-2002 tool was used to help to implement a preventative nutrition policy (patients with an NRS score ≥ 3 were referred to the Clinical Nutrition Unit for nutritional assessment and intervention). Data was collected at 3 time points: Group A = baseline, Group B = 6 months after implementation of NRS-2002, Group C = at 3 years:[39]
  - ~ proportion of patients with weight loss > 5% reduced significantly (58% vs 33% vs 29%, p <0.05);
  - ~ proportion of patients referred to the Clinical Nutrition Unit significantly increased (16% vs 63% vs 82%, p <0.05);
  - ~ hospital length of stay was reduced in Group C (50±47 days) compared with Group A (72±52) (p <0.05).
- In a group pre- and post-test study in patients aged > 65 years admitted to sub-acute geriatric and rehabilitation wards, the use of nutritional screening and an early intervention programme (referral to a dietitian, nutritional assessment and nutrition care plan) led to significantly increased energy (p = 0.0001) and protein intake (p = 0.01) and improvements in health-related QOL (p <0.05).[40]
- Implementation of nutrition guidelines improved nutrition screening performance (p = 0.012 from 1st to 8th point in prevalence survey) in a Norwegian University hospital but not the fraction of patients treated (p = 0.66).[41]
- Implementation of nutrition standards (defined by the Danish Health Quality Programme) improved records for screening (NRS-2002) (56% to 77%; p <0.001), nutrition plans (21% to 56%; p <0.0001) and monitoring (29% to 58%; p <0.0001), with an improvement in energy intake (> 75% of energy requirements) from 52% to 68% (p <0.007) and protein intake (33% vs 52%; p <0.001).[42]

Implementation of screening guidelines in the community setting

- A study of the implementation of a written food and meal policy, systematic screening (using the MNA-SF) and nutrition care planning (including energy and protein drinks, small meals and snacks) in nursing home residents (n = 20, time series design, i.e. residents used as their own controls, quarterly measurements from December 2004 to December 2005) showed:[43]
  - ~ a significant increase in the proportion of weight-stable residents over the study (52.6% at baseline vs 87.7% at the end of the study, p <0.01);
  - ~ a significant reduction in the proportion of residents losing weight (42% to 13.3%, p <0.01).
- Implementation of screening using 'MUST' in line with NICE guidelines in 6 care homes in the UK (n = 208 residents, median age 86 (37–105) years, data collected on the same residents before and after implementation for 3 months) showed:[44]
  - ~ a significant increase in documentation of nutritional information (height 43–100%, weight 75–100%, and proportion screened using 'MUST' 57–100% [p <0.001]);
  - ~ a 32% increase in the use of nutritional care plans;
  - ~ a 31% reduction in hospital admissions (13% vs 9%) (27% reduction in emergency admissions, 11% vs 8%), although this was not significant;
  - ~ a significant reduction in length of hospital stay (58%, mean length of stay reduced from 2.67 days ±11.48 to 1.13 days ±4.74, p <0.005) and hospital costs (mean saving €674[i] [£599] per resident over 3 months).

Nutritional screening as part of a programme of nutritional care

A review of the evidence for the impact of improving nutritional care on nutritional and clinical outcomes and cost suggested that screening alone may be insufficient to achieve beneficial effects with the following implications for practice:[45]

- Consensus on screening suggests that adequately validated and reliable screening tools are a useful way of identifying patients at risk of malnutrition.
- Nutritional screening together with appropriate intervention may confer benefits on patients in terms of outcome. Nutritional screening alone is unlikely to result in measurable benefits.
- Provision of optimal nutritional care encompasses not only screening and assessment, but also food service provision, eating environment, feeding assistance, recognition of individual needs and preferences, monitoring and documentation.
- Such improvements are likely to benefit from a multidisciplinary approach, with input from senior managers and clinicians.

[i]Calculated based on an exchange rate of 1 GBP = 1.1245 EUR (Source: Interbank 12/07/2017)

Implementation in practice: A national example – Scotland

- Nutritional screening is mandatory in Scottish hospitals. Under the terms of the Scotland Act 1998, the devolved administration in Scotland has the power to pass laws on a range of issues including health.
- Figure 4.4 provides an overview of some of the key milestones in the evolution of strategies to improve nutritional care in NHS Scotland.
- The introduction of mandatory government standards for Food, Fluid and Nutritional Care in Hospitals in Scotland in 2003 ensured that under-nutrition was highlighted as a key issue at NHS Board level in every locality (see Table 4.14 for a summary of the standards).

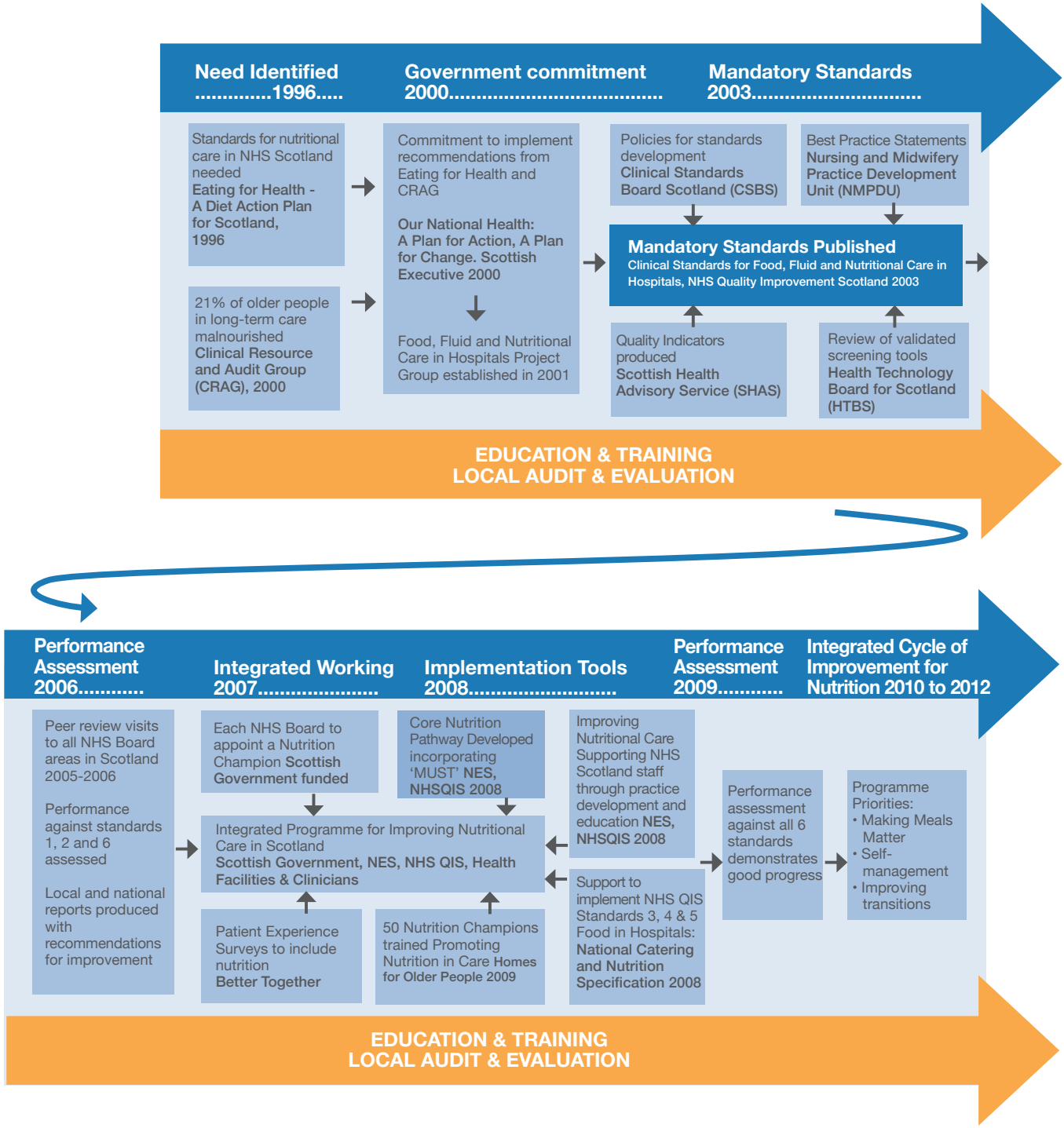


Figure 4.4 **Overview of some key milestones in the evolution of strategies to improve nutritional care in Scotland**

Table 4.14 **Summary of Clinical Standards for Food, Fluid and Nutritional Care in Hospitals, NHS Quality Improvement Scotland 2003**

Standard	Standard statement
1. Policy and Strategy	Each NHS Board has a policy, and a strategic and co-ordinated approach, to ensure that all patients in hospitals have food and fluid delivered effectively and receive a high quality of nutritional care.
2. Assessment, Screening and Care Planning	When a person is admitted to hospital, an assessment is carried out. Screening for risk of undernutrition is undertaken, both on admission and on an ongoing basis. A care plan is developed, implemented and evaluated.
3. Planning and Delivery of Food and Fluid to Patients	There are formalised structures and processes in place to plan the provision and delivery of food and fluid.
4. Provision of Food and Fluid to Patients	Food and fluid are provided in a way that is acceptable to patients.
5. Patient Information and Communication	Patients have the opportunity to discuss, and are given information about, their nutritional care, food and fluid. Patient views are sought and inform decisions made about the nutritional care, food and fluid provided.
6. Education and Training for Staff	Staff are given appropriate education and training about nutritional care, food and fluid.

- Performance assessments of standards 1, 2 and 6 in 2005–2006 revealed that work had begun, with many NHS Boards having made progress with implementing screening. Work was still needed, especially education and training.
- A range of innovative strategies was subsequently developed to help NHS Boards to implement the guidelines. A multi-agency Integrated Programme for Improving Nutritional Care in Scotland was established, funding for Nutrition Champions was made available by the Scottish Government, and a Core Nutrition Pathway (Figure 4.5) and an Education Framework for Nutritional Care were developed. Patients' views were also sought.
- In 2009, each NHS Board undertook a local self-assessment followed by an external peer review visit to assess performance against standards 1, 2 and 6 and a full report against standards 3, 4 and 5. The national overview and local reports are available **here**. The national overview report also includes examples of good practice.
- After the first review, 5 challenges were set for NHS Boards, and progress against these, as described in the national report, is listed below:
  - ~ implementing nutritional assessment, screening and care planning by 2009: this has been achieved by almost every NHS Board in Scotland;
  - ~ planning and implementing improved care for patients with complex nutritional needs: this has been achieved by most NHS Boards, although some organisations find it challenging to formalise access to all key members of the complex nutritional care team;

~ including nutritional care in job/personal development plans (as appropriate): this has been achieved across Scotland;

~ demonstrating leadership commitment and reporting to the Board: this has been achieved in every NHS Board;

~ ensuring budgets and resources are allocated to underpin improvement: nutritional care is clearly funded across NHS Scotland. However, while it is relatively straightforward to budget for catering and supplement requirements, it is less easy to define and cost clinical requirements.

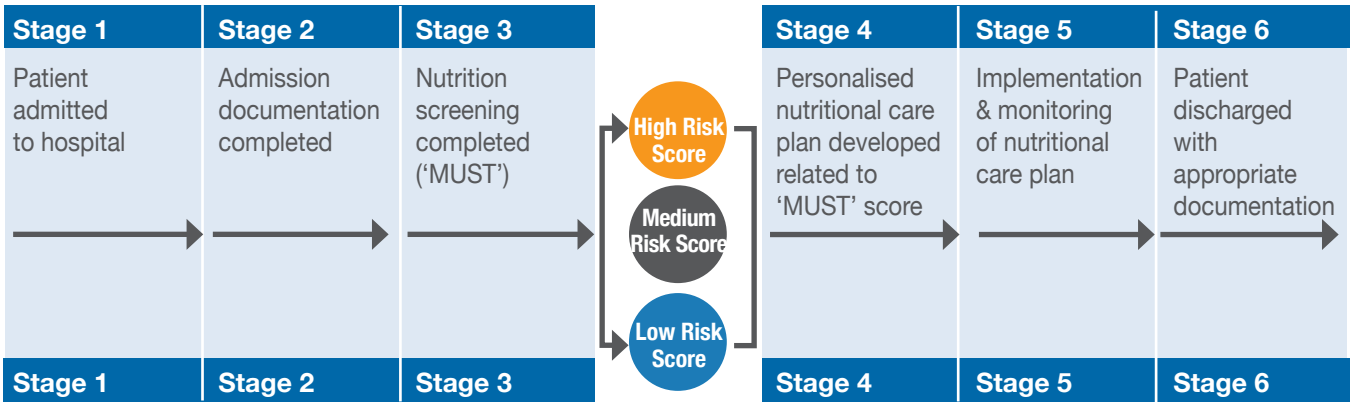


Figure 4.5 **The Core Nutrition Pathway** (adapted from NHS Education for Scotland, NHS Quality Improvement Scotland 2008)

- The Improving Nutritional Care Programme is under the remit of the Healthcare Improvement Scotland Patient Safety Programme. It is the second phase of the Integrated Programme for Improving Nutritional Care. It builds on progress to date by undertaking targeted improvement activities to improve nutritional care for people at risk of malnutrition in identified priority areas as outlined in Figure 4.6.
- The Nutrition Champions have a key leading role; learning sessions have been delivered to build capacity and capability, and a series of initiatives have been put in place to gather and share experience. Full details including resources are available at http://www.knowledge.scot.nhs.uk/improvingnutritionalcare.aspx

Making Meals Matter	• Improving meal time processes • Training and introducing volunteers at meal times
Self Management (long term conditions)	• Helping people with long term conditions to self-manage their nutritional care
Improving Transitions	• Improving communication of nutritional care in the transition between care home and hospital

Figure 4.6 **The Improving Nutritional Care Programme priority areas** (adapted from Health Improvement Scotland, 'Improving Nutrition... Improving Care' March 2012)

Implementation in practice: A national example – The Netherlands

- In the Netherlands, screening for malnutrition is mandatory in hospital (including children) and in nursing and residential homes. Figure 4.7 illustrates the events that led to this change.

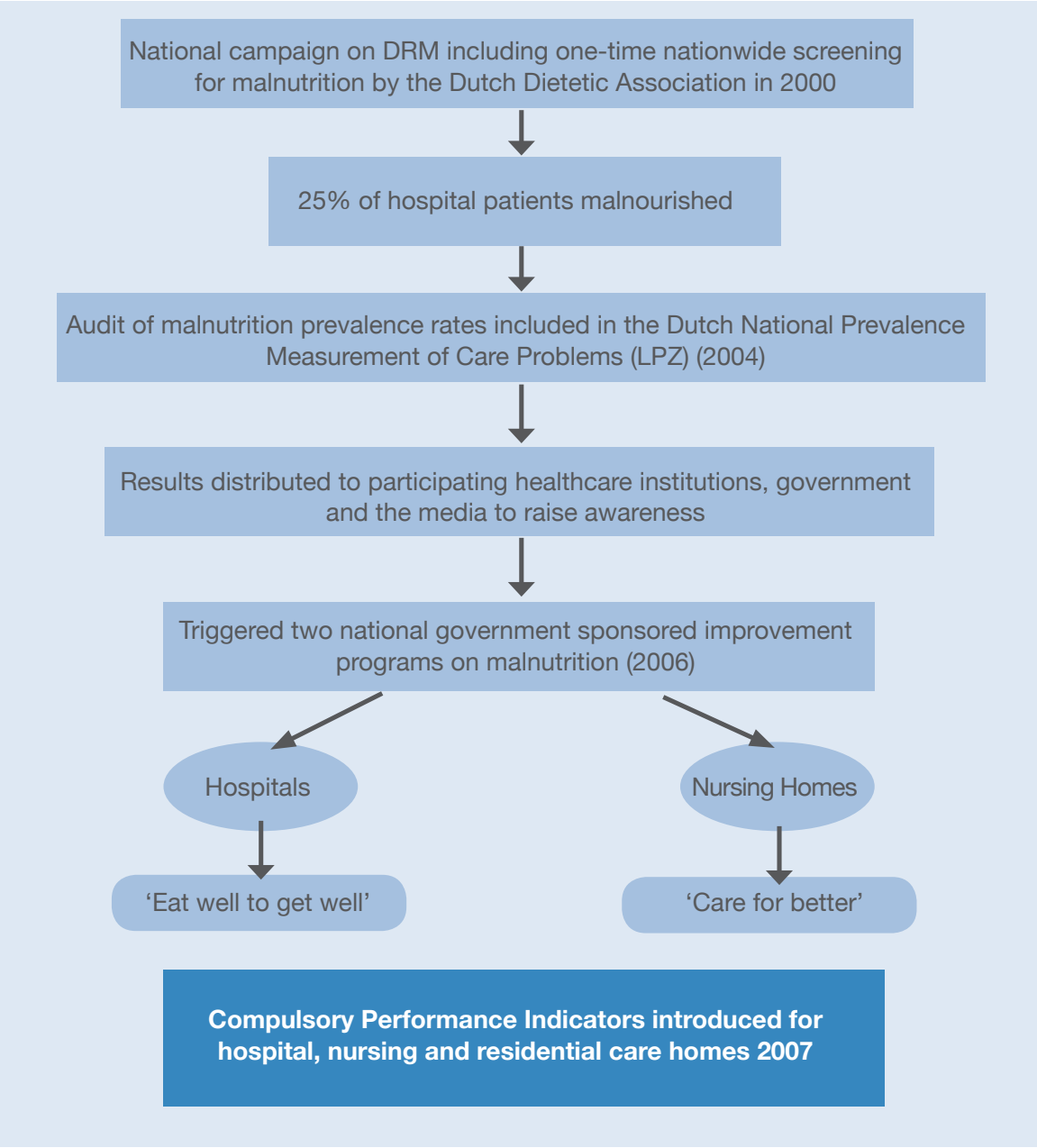


Figure 4.7 **Evolution of strategies to tackle malnutrition in the Netherlands**[46]
(LPZ: Landelijke Prevalentiemeting Zorgproblemen)

- An analysis of the results from national audits conducted in The Netherlands from 2004 to 2010 shows that the prevalence of malnutrition decreased (Figure 4.8). Furthermore, the more often hospitals and home care organisations participated in the annual audits, the lower the prevalence of malnutrition (p <0.001). Participation in the national improvement programmes also resulted in lower prevalence rates (p = 0.027), suggesting that increasing awareness and actively working towards improvement could be important in lowering the rate of malnutrition.[46]

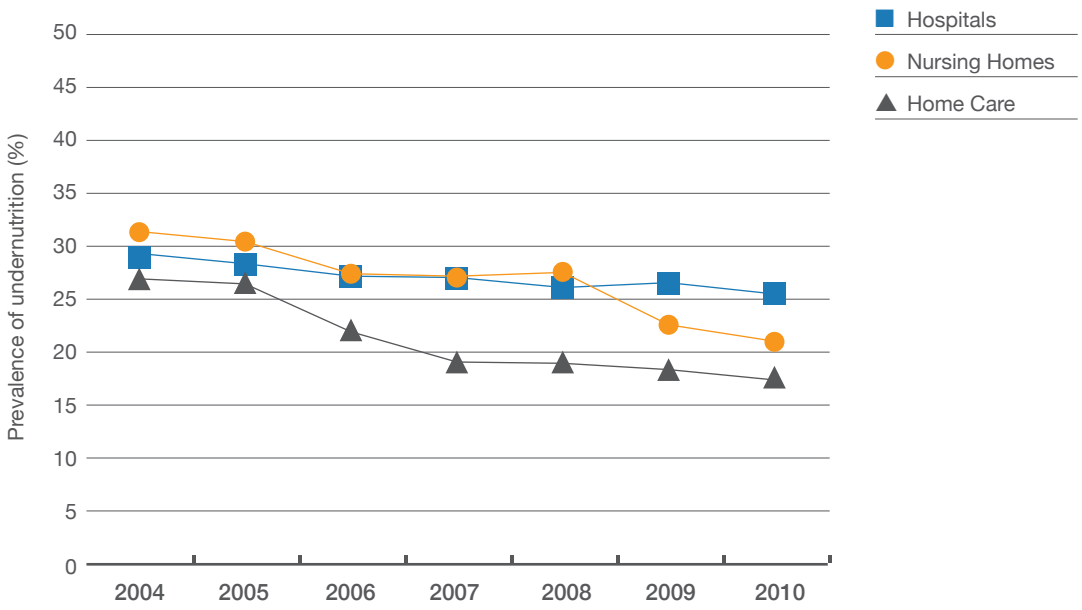


Figure 4.8 **Malnutrition prevalence rates from 2004 to 2010.** LPZ

- Extensive information about the Dutch approach, including details of methodology, implementation strategies and toolkits, is available on the Fight Malnutrition website at http://www.fightmalnutrition.eu/. The following 10 steps summarise the Dutch approach:
  - ~ a multidisciplinary steering group with national key people;
  - ~ up-to-date prevalence data to create and sustain awareness;
  - ~ quick and easy screening tools with treatment plans;
  - ~ screening as a mandatory quality indicator;
  - ~ evidence-based validated tools and cost-effectiveness research;
  - ~ Ministry of Health as a key stakeholder;
  - ~ implementation of projects in all care settings;
  - ~ toolkit with free accessible half fabricates and best practices;
  - ~ multidisciplinary project teams in all institutions;
  - ~ training programmes and workshops.

4.1.4

Nutritional Care: Good Practice Examples - ONS

Summary

Evidence based guidelines can only improve patient care if implemented successfully in practice.

Good practice in nutritional care at professional, political and societal level should focus on ensuring that there is awareness of the issue. It should also include action by government and professional organisations to put in place policies and mechanisms to ensure that health and social care providers implement safe, cost-effective, sustainable and practical nutritional quality improvement programmes to enhance patient care. Many good examples of such work exist. The Medical Nutrition International Industry (MNI) is committed to supporting this work through an annual grant for the most innovative national initiative to fight malnutrition and increase the awareness of malnutrition.

Good practice in nutritional care in social and health care settings should incorporate a range of strategies and activities designed to ensure that each patient receives the most appropriate individually tailored and timely nutrition intervention to optimise nutritional intake and status with a view to improving outcome. A search of the literature and for unpublished work revealed some examples that demonstrate benefits in patient care:

- Implementation of screening using 'MUST' improved nutritional care, improved appropriate use of care plans and reduced hospital stay and costs;
- Use of dietetic assistants to provide intensive feeding support, including ONS (as recommended by the Welsh Assembly Government guidelines), in older women with hip fracture significantly increased energy intake and reduced mortality both in the acute trauma ward and at 4-month follow-up;
- Implementation of a nutritional care protocol for patients with cancer in a Spanish hospital led to attenuation of weight loss in 60% of patients and weight gain in 17% of patients;
- Implementation of a nutritional care programme for older people in a Belgian hospital led to a significant reduction in length of hospital stay.

Most likely other examples exist but are not available in the public domain; efforts need to focus on encouraging the sharing of experience and good practice. Examples of such initiatives include the NICE implementation programme and 33rd ESPEN Congress theme 'Nutrition in translation – bridging science and practice'.

"Translating evidence and guidelines into best practice is a key to ensuring that people who require nutrition support receive the right intervention at the right time in the course of their illness, irrespective of the healthcare setting."

Professor Olle Ljungqvist (2007)[ii]

[ii]Clin Nutr 2007;2(Suppl 1)1-2

Conclusion

There are some good examples of where implementation of nutritional guidelines can have positive effects for patients and healthcare providers. However, it is often difficult to identify examples either because gaps still exist between guidelines that are in place but are not yet fully implemented or because good practice has not been documented and shared. Healthcare professionals need the time, the right skills and resources, and the right forum in which to share good practice. Consideration should be given to innovative ways to facilitate the sharing of good practice at local, national and international level.

Recommendations

On the issue of **Nutritional care: good practice examples** the MNI makes the following recommendation:

Action	Issues to consider
Examples of good practice should be shared widely to facilitate the implementation of nutritional guidelines and ensure best use of resources	• There is potential for more effective use of limited resources if examples of good practice are shared more widely. Healthcare providers and practitioners can share experience of what has been found to be effective and what does not work in practice. Locally developed resources can often be used in other areas saving time and duplication of effort • Sharing good practice should be embedded as a routine part of professional practice and delivery of good patient care

Table 4.15 Summary of the main output of a selection of MNI grant submissions*

Country (year of submission)	Organisation	Project Title	Main actions/outcomes/achievements
Belgium (2011)	Members of Société Belge de Nutrition Clinique and Vlaamse Vereniging voor Klinische Voeding en Metabolisme	"Interactions between experts in clinical nutrition and Public Health Authorities"	• Recommendations for malnutrition screening tools in various settings • National Quality Charter • Action for promoting implementation of nutrition teams in hospital settings • Participation in Nutrition Day survey • Awareness campaign during the week of Nutrition Day
Denmark (2009) (Award winner 2009)	Danish Society for Clinical Nutrition and Metabolism (DAPEN) and The Danish National Board of Health	"Fighting Malnutrition with a Multi-modal Strategic Approach: The Danish Experience 2007-9"	National guidelines and accreditation within nutrition in all Danish hospitals achieved by a multi-modal approach including: • Cooperation between DAPEN, National Board of Health, Danish Veterinary and Food Administration and politicians, industry and local forces • Systematic evidence-based approach to development of nutritional pathway led by experts in the field • Awareness raised through education, tools and media contact • A basis for an implementation procedure established • National fund created for projects in clinical nutrition • Follow-up studies undertaken to insure goals achieved
Greece (Award winner 2012)	Greek Society for Clinical Nutrition and Metabolism (GRESPEN)	Fighting mal-nutrition in Greece: from idleness to mobilization – key actions to achieve awareness and new legislation	• Increase awareness of malnutrition ~ To provide Greek caregivers (doctors, dieticians, nurses, pharmacists) with educational material (e.g. guidelines, modules) in Greek, in a user-friendly and cost-free way • Change in legislation ~ To persuade politicians to incorporate changes in the Greek legislation regarding Clinical Nutrition issues, and make them mandatory in every public hospital.
Republic of Ireland (Award winner 2013)	Irish Society for Clinical Nutrition and Metabolism (IrSPEN)	Fighting the malnutrition battle: The power of partnerships	• Strong evidence base (e.g. developed robust prevalence data, published 'Cost of Malnutrition in Ireland' report, first report on malnutrition in Ireland) • Increased awareness (TV, radio and press response to 2013 conference and successfully changed nutrition agenda) • Nutrition training for key SpR groups now mandatory
Spain (2010) (Award winner 2011)	Spanish Society for Parenteral and Enteral Nutrition (SENPE)	"Fighting hospital malnutrition in Spain: From awareness to action"	• Current burden of hospital malnutrition was assessed at a national level with the PREDyCES study:[iii] ~ 24% of hospitalised patients malnourished in Spain ~ associated with an additional cost of €5,829 per patient • Main findings of the study where used to define the action plan to fight against hospital malnutrition in Spain – malnutrition coding, nutrition screening recommendations, quality indicators for nutrition units • Development of a Multidisciplinary consensus on hospital malnutrition in Spain led by SENPE and involving 22 medical societies, presented to the Spanish Ministry of Health (2011 grant submission)

Table 4.15 Continued

Country (year of submission)	Organisation	Project Title	Main actions/outcomes/achievements
Switzerland (Award winner 2014)	Swiss Society for Clinical Nutrition (GESKES/ SSNC)	A step forward in the fight against malnutrition: Improving home nutritional therapy in Switzerland	Successfully achieved a change in legislation for reimbursement for ONS through key activities: • Development of evidence base • Multi-disciplinary engagement • Economic analysis • Literature review • Request for evidence change
The Netherlands (2010) (Award winner 2010)	Dutch Society on Parenteral and Enteral Nutrition (NESPEN)	"Top-down and bottom-up approach of malnutrition leads to a decrease in prevalence rates in all health care settings in The Netherlands"	• Ongoing collection and feedback of malnutrition data • Mandatory screening and treatment • Annual audit and feedback • Malnutrition in main list of quality indicators in Dutch health care • Protein and energy goals for malnourished patients defined • Recognition of malnutrition as a healthcare problem as important as overweight • Malnutrition defined as 1 of the 4 topics in the National Safety Management system for all Dutch hospitals • Malnutrition (risk of) has become an official indication for reimbursement of medical nutrition in the basic health insurance
Turkey (Award winner 2016)	Society of Clinical Enteral Parenteral Nutrition Turkey (KEPAN)	Seeding a fertile land: a little effort before graduation can open a big window to awareness of malnutrition	KEPAN conducted the first Clinical Nutrition Congress for Students, which was held between 18-19 March, 2016 in Ankara, Turkey, to promote the awareness of malnutrition and the importance of nutritional support. Knowledge and awareness was assessed before and after and the rate of incorrect answers to nutrition related questions reduced by 60% in all students and by 73% in medical students.
UK (2011) (Award winner 2008)	British Association for Parenteral and Enteral Nutrition (BAPEN)	"Patients to Parliament - A quality improvement strategy for optimising nutritional care"	• BAPEN toolkit to meet quality standards in nutritional care • BAPEN's OFNOSH and 'Digesting OFNOSH' (Organisation of Food and Nutrition Support in Hospitals) promoted in national improvement programme to support teams to organise for good nutritional care • BAPEN 'MUST' e-learning modules for hospitals and community • BAPEN Nutrition Screening Week 2007 to 2011: establishing the risk of malnutrition on admission to hospital and care settings and indicating prevalence in the community • Implementation of BAPEN's 4 tenets of good nutritional care • Quality improvement methodology with local tests of change • Working across organisational boundaries to develop nutritional care pathways • Delivery of exemplar practice • BAPEN invited to write opinion papers targeted at executive level managers

[iii]Full details available at http://www.nutricionhospitalaria.com/pdf/5986.pdf
*Further details and a full list of all submissions available at medicalnutritionindustry.com/mni-grant/

Examples of initiatives to encourage implementation of good practice

- In the UK, NICE has developed an extensive implementation programme to support the NHS, local authorities and the private and voluntary sector to implement NICE guidance. The programme includes implementation tools such as costing tools, slide sets, educational tools and audit support materials. NICE has developed Good Practice Awards, a Shared Learning initiative (either submit or search for good practice or innovations) and a team of Implementation Consultants (more information available at https://www.nice.org.uk/about/what-we-do/into-practice/implementing-nice-guidance). To help to support the implementation of the NICE Nutrition Support Guidelines for Adults, BAPEN has joined with NICE in its Shared Learning initiative by inviting applicants to submit their example of good practice for discussion at the BAPEN Annual Conference and for publication on the BAPEN and NICE websites.
- In 2011, the 33rd ESPEN Congress theme was 'Nutrition in translation – bridging science and practice', with a key focus on translating science into clinical practice. Speakers discussed the theory and challenges surrounding the task of guideline implementation, knowledge translation, implementation strategies and models. This is a good example of how international professional societies can help to disseminate both the results of clinical research and help practitioners to use the results in day-to-day practice to enhance patient care.
- The unique contribution of patient and carers should not be forgotten; the views of patients, carers and patient/carer organisations should be sought and considered at policy and practice level. Action should be taken to make practical information available to patients and carers to help them recognise the issue of disease-related malnutrition and take appropriate steps to help towards their own good nutritional care. An innovative example in this area is the online resource for patients and carers developed by Carers UK and Nutricia Advanced Medical Nutrition 'Care about nutrition. Care with Nutrition.' (see http://nutricia.co.uk/carewithnutrition/).

Examples of good practice

Table 4.16 **Effectiveness of implementing 'MUST' in care homes within Peterborough Primary Care Trust, England** (adapted from Cawood 2009)[44]

Country: UK	**Setting:** Care homes	**Patient Group:** Care home residents

Guideline:
National Institute for Health and Clinical Excellence (NICE) Nutrition Support in Adults Clinical Guideline 32 (2006)[1]

Aim:
- To investigate the effect of implementation of nutritional screening using 'MUST' in care homes on nutritional care and hospital admissions

Method/Intervention:
- The implementation programme included education on malnutrition and management, practical training sessions using 'MUST', standardised care plans, and ongoing follow-up support
- The programme was implemented in 6 care homes (*n* = 208 residents; median age 86 years [range 37–105 years]; 75% female)
- Staff satisfaction was assessed using a questionnaire
- The effectiveness of the programme was assessed by collecting information on the same residents for 3 months before and after the implementation. Documentation on nutritional information (e.g. weight, height), use of screening and nutrition care plans, and number and duration of hospital admissions was collected

Results:
Implementation of the nutritional screening programme resulted in:

- A significant increase in documentation on nutritional information (height 43–100%, weight 75–100%, and proportion screened using 'MUST' 57–100% [p <0.001])
- A 32% increase in the use of nutritional care plans
- A 31% reduction in hospital admissions (13% vs 9%) (27% reduction in emergency admissions, 11% vs 8%), although this was not significant
- A significant reduction in length of hospital stay (58%, mean LOS reduced from 2.67 days ± 11.48 to 1.13 days ± 4.74, p <0.005) and hospital costs (mean saving £599 per resident over 3 months)
- Overall satisfaction with the programme was high (mean 100%)

Conclusion:
- 'In accordance with national guidelines, implementing 'MUST' in care homes improved appropriate use of nutritional care plans, significantly reduced hospital stay and costs, and significantly improved nutritional care'

Further information:

- The implementation programme followed an earlier cross-sectional study of nutritional care in 19 care homes (*n* = 703 residents) in the Peterborough Primary Care Trust, which showed that 32% of residents were at risk of malnutrition (13% medium risk, 19% high risk). In that survey, 64% of residents at high risk of malnutrition were not receiving any form of nutritional support, whereas 9% of residents at low risk were receiving nutritional intervention such as ONS, dietetic care or food fortification[47]
- This project has been included in the NICE Shared Learning Database accessible at www.nice.org.uk (go to the Shared Learning Implementing NICE Guidance, search examples of implementation)
- This project has been included in 'Appropriate Use of Oral Nutritional Supplements in Older People: Good Practice Examples and Recommendations for Practical Implementation' compiled by an expert panel and endorsed by key healthcare professional organisations in the UK (access at http://manage.nutricia.com/uploads/documents/ONS_Guide.pdf). Includes summary details of the nutrition care plan for risk categories including guidance on use of ONS

Table 4.17 **Using dietetic assistants to improve the outcome of hip fracture: a randomised controlled trial of nutritional support in an acute trauma ward**[48]

Country: UK	**Setting:** Hospital	**Patient Group:** Hip fracture

Guideline:
Welsh Assembly Government. National Service Framework for Older People in Wales (2006) (recommends that all hip fracture patients receive ONS)

Aim:
- To assess the effect of intensive feeding support provided by dietetic assistants on postoperative clinical outcome in hospitalised older women with hip fracture (with or without cognitive impairment)

Method/Intervention:
- Subjects randomised to receive either conventional care (usual nurse and dietitian-led care with ONS for all patients) or conventional care plus the personal attention of the dietetic assistant
- The role of the dietetic assistant was to ensure that patients received appropriate help in meeting their nutritional needs, including:
  - ~ Checking food preferences
  - ~ Co-ordinating appropriate meal orders with catering
  - ~ Ordering ONS
  - ~ Provision of feeding aids
  - ~ Assistance with food choice, portion size and positioning at mealtimes
  - ~ Providing encouragement or assistance with feeding for the frailest of patients
  - ~ Collecting data to assist the dietitian with nutritional assessment
- Primary outcome measure: postoperative mortality in the acute trauma unit
  Secondary outcome measures: postoperative mortality at 4 months after hip fracture, length of hospital stay, energy intake and nutritional status.

Results:
- Patients who received the care of a dietetic assistant had significantly reduced postoperative mortality both on the acute ward (4.1% vs 10.1%, $p = 0.048$) and at 4 months (13.1% vs 22.9%, $p = 0.036$) compared with the patients who received conventional care
- Mean daily energy intake was significantly better in dietetic assistant-supported patients (1105 kcal/d vs 756 kcal/d, 95% CI 259–440 kcal/d, $p < 0.001$)
- There was no significant difference in energy intake from conventional food between the two groups; however, the dietetic assistant-supported patients consumed significantly more energy from ONS compared with the patients who received conventional care (123 kcal/d vs 409 kcal/d, 95% CI 232–339, $p < 0.001$)
- A significantly smaller reduction in MAC was observed in dietetic assistant-supported patients (0.39 cm, $p = 0.002$), but no other significant differences were observed in nutritional status between the 2 groups

Conclusion:
- The use of dietetic assistants to deliver intensive feeding support including ONS significantly reduced mortality in the acute trauma ward, and this effect persisted at 4-month follow-up

Further information:

- This project has been included in 'Appropriate Use of Oral Nutritional Supplements in Older People: Good Practice Examples and Recommendations for Practical Implementation' compiled by an expert panel and endorsed by key healthcare professional organisations in the UK (access at http://manage.nutricia.com/uploads/documents/ONS_Guide.pdf). Includes summary details of the nutrition care plan for risk categories, including guidance on use of ONS
- Winner of the 2006 British Dietetic Association Rose Simmonds Award for published scientific work

Table 4.18 **Overview of a nutritional care programme for patients with cancer in Spain** (adapted from Caro 2008)[49]

Country: Spain	**Setting:** Outpatients	**Patient Group:** Cancer

Supported by:
Sociedad Espanola de Nutricion Basica y Aplicada (SENBA)

Aim:
- To develop strategies to improve the quality of nutritional intervention in cancer patients

Method/Intervention:
- A multidisciplinary group developed a protocol describing nutritional assessment and intervention in the form of algorithms based on literature and personal experience. Patients were classified in a 3-step process:
  - ~ type of cancer treatment (curative or palliative);
  - ~ nutritional risk associated with the anti-cancer treatment (low, medium or high risk);
  - ~ nutritional risk assessed by a patient-generated SGA.
- Patients were classified as having:
  - ~ adequate nutritional state;
  - ~ malnutrition or risk of malnutrition;
  - ~ severe malnutrition.
- The protocol was used over a 1-year period in 226 randomly selected patients aged >18 years of age

Results:
- 64% of patients were suffering from malnutrition, increasing to 81% in patients undergoing palliative treatment. Most patients were treated curatively (83%), received oncology treatment, and had moderate or high nutritional risk (69%). 68% of patients were affected by some feeding difficulty
- Mean percentage weight loss was 6.64% (± 0.87, range 0–33%). More than half of the patients required nutritional counselling to control symptoms which made food intake difficult. One-third of patients needed ONS
- Following the nutritional intervention, weight maintenance was observed in about 60% of patients and weight gain was seen in one-sixth of patients

Conclusions:
- The application of the protocol was useful and easy, and it helped in the detection of malnutrition in patients with cancer
- It provided the opportunity to select patients who could benefit from a specific nutritional intervention
- Nutrition support proved effective for most patients

Recommendation:
- The application of the protocol should be started immediately after diagnosis of cancer

Table 4.19 **Overview of a nutritional care programme for older people in hospital in Belgium** (adapted from Pepersack 2005)[50]

Country: Belgium	**Setting:** Hospital	**Patient Group:** Older people

Supported by:
Belgian Ministry of Social Affairs, Public Health and the Environment

Aims:

- To assess the quality of care concerning nutrition among Belgian geriatric units
- To include more routine nutritional assessments and interventions in comprehensive geriatric assessment
- To assess the impact of nutritional recommendations on nutritional status and on length of hospitalisation

Method/Intervention:

- A prospective observational and interventional 6-month trial. For the first 3 months, the nutritional status of patients was assessed (MNA and serum prealbumin [PAB]) on admission and discharge without particular recommendations for nutritional intervention (observational study – phase 1)
- A standardised nutritional intervention was implemented for the last 3 months (intervention study – phase 2)
- Nutritional intervention was started when MNA was <23.5 and/or PAB, 0.2 g/l. Treatable causes of malnutrition were identified using the 'meals on wheels' approach (see Figure 4.9), and caloric supplementation commenced in line with the algorithm in Figure 4.10

Results:

- 1,139 consecutive patients were admitted during the study, mean age 82.9 ± 7.3 years, 70% of the patients were women. MNA was measurable in 73% of cases with a median value of 18.5 points (range 9–29), mean admission PAB concentration was 18.5 ± 7.6 mg/100 ml, and C-reactive protein (CRP) was 5.3 ± 7.5 mg/100 ml
- The proportion of patients receiving caloric supplementation significantly increased during the interventional period (20% vs 25% of patients; p <0.01)
- Length of hospital stay was significantly shorter during phase 2 than during phase 1 (21.7 ± 15.1 days vs 27.1 ± 21.9 days, p <0.001)

Conclusions:

- Nutritional assessment should be part of routine clinical practice in older hospitalised patients

Recommendation:

- The experience from this project should be extended to other hospital wards as malnutrition is common in patient groups other than older people

Medications
Emotional problems (depression)
Anorexia nervosa (tardive) and abnormal attitudes to food
Late-life paranoia
Swallowing problems

Oral problems
No money

Wandering and other dementia behaviours
Hyperthyroidism, hyperparathyroidism
Entry problems (malabsorption)
Eating problems (physical and cognitive)
Low salt, low cholesterol diets
Shopping (food availability)

Figure 4.9 **The 'meals on wheels' approach to diagnosing treatable causes of malnutrition used in the nutritional care programme in geriatric units in Belgium**
(adapted from Pepersack 2005)[50]

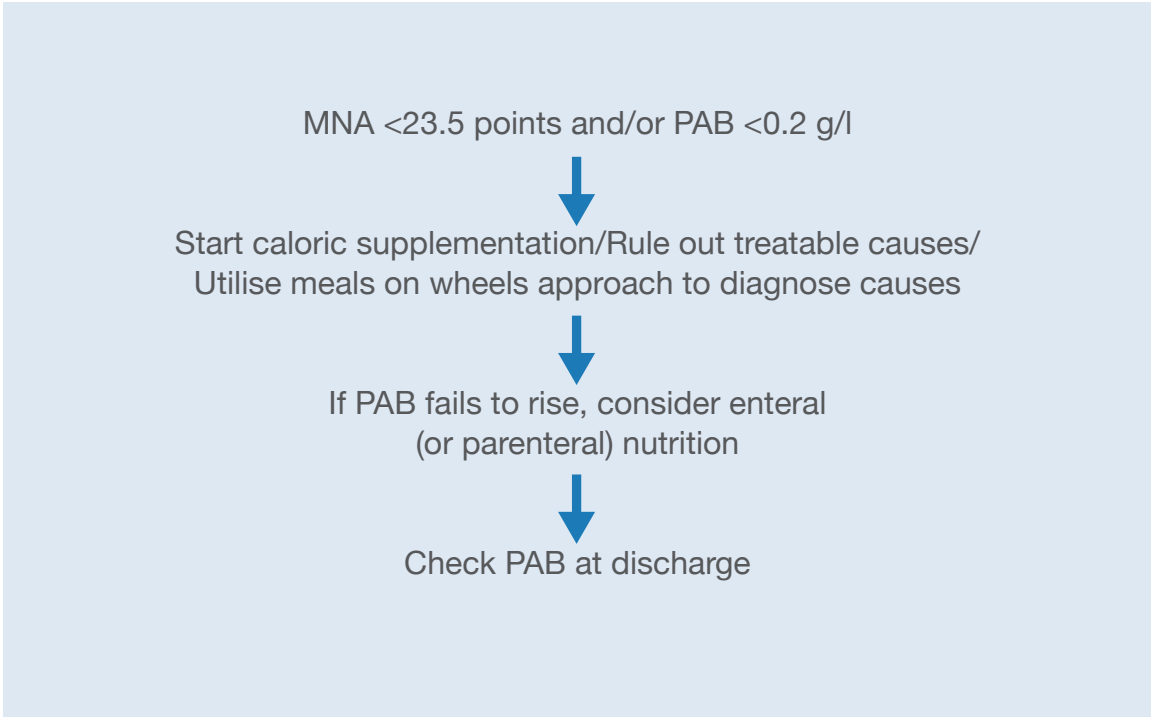


Figure 4.10 **Flowchart suggesting a rational approach to the management of malnutrition used in the nutritional care programme in geriatric units in Belgium**
(adapted from Pepersack 2005)[50]

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4

RECOMMENDATIONS FROM INTERNATIONAL AND INTERNATIONALLY RECOGNISED PROFESSIONAL GUIDELINES:

4.2 Enteral Tube Feeding (ETF)

Tables 4.11 to 4.14 include the results of efforts made to identify evidence-based international and internationally recognised guidelines referring to enteral tube feeding (ETF) as an integral part of patient and disease management across the world. Searches of websites of relevant professional organisations were conducted in addition to a comprehensive search of the US Department of Health and Human Sciences National Guideline Clearinghouse (www.guideline.gov). Guidelines which focus on the practicalities of enteral tube feeding once the decision to initiate feeding has been made have been excluded from this section but are listed in Section 4.2.2 (Guidelines: Theory to practice for enhanced patient care) Table 4.21. Other guidelines may exist but are not included as they were not identified using the above strategies or we were unable to obtain information in the English language for inclusion in the dossier. We would welcome information about other international guidelines that could be included in future editions of the dossier.

Note: The tables that follow include the recommendations relating to ETF only as they appear in the guidelines or documents from various organisations. Please refer to the full documents for other information relating to nutritional management e.g. screening, assessment and use of other forms of nutritional support. Terminology referring to enteral nutrition (EN) is not consistent within the various guidelines; therefore, the definition used within specific guidelines has been noted and summarised in Table 4.20.

GENERAL

Table 4.11 **Summary of some examples of evidence-based international and internationally recognised guidelines referring to enteral tube feeding (ETF) as an integral part of patient and disease management - General** (parts of guidelines relevant to ETF[i] presented here, standard formulas only)

Country	Body	Patient Group	Title	Recommendation, guideline or standard [grade of evidence, where available]
Australia	Dietitians Association of Australia (2015)	Adults in hospital	Nutrition and Hydration Policy Support Handbook For Acute Adult Inpatient Setting[1]	Artificial nutrition support should be considered when patients cannot adequately or safely meet their nutrition requirements orally • Artificial nutrition support should be considered for patients who have had nil nutritional intake for >5 days • EN should be prescribed to patients with a functioning gastrointestinal tract.
England and Wales	National Institute for Health and Care Excellence (NICE) (2006)	All patients in hospital and in the community	Nutrition support in adults Oral nutrition support, enteral tube feeding and parenteral nutrition[2]	• **Indications for enteral tube feeding:** Enteral tube feeding should not be given to people unless they are malnourished or at risk of malnutrition and have; in adequate or unsafe oral intake and a functional, accessible gastrointestinal tract, or they are taking part in a clinical trial. [A]
US	American Society for Parenteral and Enteral Nutrition (2011)	All patients in hospital and community	Nutrition Screening, Assessment, and Intervention in Adults[3]	Nutrition support intervention is recommended for patients identified by screening and assessment as at risk for malnutrition or malnourished: Grade C (intervention is described as "some intervention such as change in diet, enteral or parenteral nutrition, or further medical assessment")
US	American Society for Parenteral and Enteral Nutrition (2014)	All patients in home care environments and alternate care sites*	A.S.P.E.N. Standards for Nutrition Support: Home and Alternate Site Care[4]	The route selected to provide nutrition support therapy shall be appropriate to the patient's medical problems, safety, efficacy, and patient preference. • When functional, the GI tract is the preferred route for nutrition support therapy and should be used to administer nutrition support therapy
US	American Society for Parenteral and Enteral Nutrition (2010)	Adults in hospital	Standards for Nutrition Support: Adult Hospitalized Patients[5]	The route selected to provide nutrition support therapy shall be appropriate to the patient's medical condition and should periodically be assessed for continued appropriateness as well as for its adequacy in meeting goals of the nutrition care plan (see Figure 2 in original guideline)

[i]The definition of Enteral Nutrition varies depending on the recommending body see Table 4.20 for more details. SNS Specialised nutrition support; HSNS Home specialised nutrition support. *Home care is defined as being provided in the traditional home as well as a group home, intermediate care facility, or assisted living facility. Alternate site care facilities can include skilled nursing facilities (SNF), long-term acute care hospitals (LTACHs), or rehabilitation hospitals.

OLDER PEOPLE

Table 4.12 **Summary of some examples of evidence-based international and internationally recognised guidelines referring to enteral tube feeding (ETF) as an integral part of patient and disease management - Older People** (parts of guidelines relevant to ETF presented here, standard formulas only)

Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Australia and New Zealand	Australian and New Zealand Society for Geriatric Medicine (2010)	Position Statement 12. Dysphagia and Aspiration in Older People[6]	• Tube feeding may be useful in temporarily providing nutritional support to patients with a non-progressive cause of aspiration such as stroke. However, its place for the majority of progressive causes is questionable. • Tube feeding (nasogastric or percutaneous) cannot prevent aspiration and neither method is entirely safe when used in patients at risk of aspiration.
Australia and New Zealand	Australian and New Zealand Society for Geriatric Medicine (2015)	Position Statement No. 6. Undernutrition and the Older Person[7]	• Percutaneous Endoscopic Gastrostomy (PEG) feeding in advanced dementia has not been shown to prolong survival, improve nutrition, maintain skin integrity, prevent aspiration or improve quality of life.
England and Wales	National Institute for Health and Care Excellence (NICE) (updated 2006, updated 2016)	Dementia: supporting people with dementia and their carers in health and social care. Clinical Guideline 42[8]	• Nutritional support, including artificial (tube) feeding, should be considered if dysphagia is thought to be a transient phenomenon, but artificial feeding should not generally be used in people with severe dementia for whom dysphagia or disinclination to eat is a manifestation of disease severity. Ethical and legal principles should be applied when making decisions about withholding or withdrawing nutritional support.
Europe	European Society for Clinical Nutrition and Metabolism (2015)	ESPEN Guidelines on Nutrition in Dementia[9]	• We suggest tube feeding for a limited period of time in patients with mild or moderate dementia, to overcome a crisis situation with markedly insufficient oral intake, if low nutritional intake is predominantly caused by a potentially reversible condition.(Grade of evidence: very low; strength of recommendation: weak) • We recommend against the initiation of tube feeding in patients with severe dementia. [Grade of evidence: high; strength of recommendation: strong]
Europe	European Society for Clinical Nutrition and Metabolism (Volkert 2006)	ESPEN Guidelines on Enteral Nutrition: Geriatrics[10]	• Frail elderly may benefit from TF as long as their general condition is stable (not in terminal phases of illness). [Grade B] • In demented patients ONS or tube feeding (TF) may lead to an improvement of nutritional status. • In early and moderate dementia consider ONS—and occasionally TF—to ensure adequate energy and nutrient supply and to prevent undernutrition. [Grade C] • In patients with terminal dementia, tube feeding is not recommended [Grade C] • In case of nutritional risk (e.g. insufficient nutritional intake, unintended weight loss >5% in 3 months or >10% in 6 months, body-mass index (BMI) <20 kg/m^2) initiate oral nutritional supplementation and/or TF early.

Table 4.12 Continued

Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
US	Academy of Nutrition and Dietetics (2009)	Unintended weight loss in older adults guideline[11]	• **Indications for Enteral Nutrition** • The Registered Dietitian (RD) should recommend consideration of enteral nutrition for older adults who are undernourished or at risk of undernutrition; it is clearly indicated in patients with severe dysphagia. Studies support enteral nutrition as a method to provide energy and nutrient intake, promote weight gain and maintain or improve nutritional status or prevent undernutrition. [**Strong Imperative**] • **Contraindications for Enteral Nutrition** • Enteral nutrition may not be appropriate for terminally ill older adults with advanced disease states, such as terminal dementia, and should be in accordance with advance directives. The development of clinical and ethical criteria for the nutrition and hydration of persons through the life span should be established by members of the health care team, including the Registered Dietitian (RD). [**Consensus, Conditional**] • **Initiation of Enteral Nutrition** • To improve energy and nutrient intake in older adults at nutritional risk, enteral nutrition should be initiated as early as possible after confirming tube placement. Studies support that enteral nutrition can be initiated 3 hours after a percutaneous endoscopic gastrostomy (PEG) tube is placed, and placement is confirmed. [**Strong, Imperative**].

Table 4.12 **Children:**

Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
England and Wales	National Institute for Health and Care Excellence (NICE) (2015)	Gastro-oesophageal reflux disease in children and young people: diagnosis and management[12]	Only consider enteral tube feeding to promote weight gain in infants and children with overt regurgitation and faltering growth if: • other explanations for poor weight gain have been explored and/or • recommended feeding and medical management of overt regurgitation is unsuccessful
Europe	European Society for Paediatric Gastroenterology, Hepatology and Nutrition (2010)	Practical Approach to Paediatric Enteral Nutrition: A Comment by the ESPGHAN Committee on Nutrition[13]	• EN is indicated in the patient with at least a partially functional gut and insufficient normal oral intake. To meet nutritional targets in some clinical settings combined PN and EN are necessary, even in the presence of a functional gut.
Europe	European Society for Clinical Nutrition and Metabolism, European Society for Paediatric Gastroenterology, Hepatology and Nutrition and European Cystic Fibrosis Society (2016)	ESPEN-ESPGHAN-ECFS Guidelines on Nutrition Care for Infants, Children, and Adults with Cystic Fibrosis[14]	• We recommend a progressive approach to intensification of nutrition interventions as needs increase: preventive nutritional counselling, dietary modification and/or oral nutrition supplements, and enteral tube feeding. [Grade of evidence: low]
International	Surviving Sepsis Campaign (2012)	Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012[15]	• Enteral nutrition should be used in children who can tolerate it, parenteral feeding in those who cannot [Grade 2C].
US	American Society for Parenteral and Enteral Nutrition (2009)	Nutrition Support of Children with Human Immunodeficiency Virus Infection[16]	[….} or enteral tube feedings may improve weight and growth in children who are HIV+ with growth failure. [Grade C]
US	American Society for Parenteral and Enteral Nutrition (2009)	Nutrition Support of the Critically Ill Child[17]	• In critically ill children with a functioning gastrointestinal tract, enteral nutrition (EN) should be the preferred mode of nutrient pro vision, if tolerated. [Grade C] • A variety of barriers to EN exist in the pediatric intensive care unit (PICU) Clinicians must identify and prevent avoidable interruptions to EN in critically ill children. [Grade D]

Table 4.12 Continued

Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
US	American Society for Parenteral and Enteral Nutrition (2013)	Standards for Nutrition Support: Pediatric Hospitalized Patients[18]	The route selected to provide nutrition support therapy shall be appropriate to the patient's medical condition and should be reassessed periodically for continued appropriateness, as well as its adequacy in meeting goals of the nutrition care plan. • Enteral nutrition (EN) should be used in preference to parenteral nutrition (PN) to the greatest extent possible.
US	North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (2006)	Nutrition Support for Neurologically Impaired Children: A Clinical Report of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition[19]	• Enteral tube feedings can be initiated early in children who are unable to feed orally or who cannot achieve sufficient oral intake to maintain adequate nutritional or hydration status.
US	North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (2012)	Use of Enteral Nutrition for the Control of Intestinal Inflammation in Pediatric Crohn's Disease[20]	• EEN is an effective induction therapy in newly diagnosed [level 1a, grade A] and active CD [level 2b, grade C]. • EEN has an improved adverse-effect profile over corticosteroids [level 1a, grade A]. • EEN has been shown to promote mucosal healing [level 1b, grade A] and has beneficial effect on linear growth [level 2b, grade A]

EEN exclusive enteral nutrition (can be administered orally or via a nasogastric tube)

SPECIFIC DISEASES

Table 4.13 **Summary of some examples of evidence-based international and internationally recognised guidelines referring to enteral tube feeding (ETF) as an integral part of patient and disease management - Specific Diseases and conditions** (parts of guidelines relevant to ETF presented here, standard formulas only)

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with pressure ulcers	US, Europe, Australia, New Zealand, Hong Kong and Singapore	National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel and Pan Pacific Pressure Injury Alliance (2014)	Prevention and treatment of pressure ulcers[21]	• Consider enteral or parenteral nutritional support when oral intake is inadequate. This must be consistent with the individual's goals. [Strength of Evidence = C; Strength of Recommendation = 👍] • If oral intake is inadequate, enteral or parenteral nutrition may be recommended if consistent with the individual's wishes. Enteral (tube) feeding is the preferred route if the gastrointestinal tract is functioning.
Critical illness	US	Society of Critical Care Medicine (SCCM) and the American Society for Parenteral and Enteral Nutrition (ASPEN) (2016)	Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient[22] (Specific patient populations addressed in these expanded and updated guidelines include organ failure (pulmonary, renal, and liver), acute pancreatitis, surgical subsets (trauma, traumatic brain injury [TBI], open abdomen [OA], and burns), sepsis, postoperative major surgery, chronic critically ill, and critically ill obese)	• We recommend that nutrition support therapy in the form of early EN be initiated within 24–48 hours in the critically ill patient who is unable to maintain volitional intake [Quality of evidence: very low] • We suggest the use of EN over PN in critically ill patients who require nutrition support therapy. [Quality of Evidence: Low to Very Low] • Based on expert consensus, we suggest that patients who are at low nutrition risk with normal baseline nutrition status and low disease severity [e.g. NRS 2002 ≤3 or NUTRIC score ≤5] who cannot maintain volitional intake do not require specialized nutrition therapy over the first week of hospitalization in the ICU.
	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Intensive Care[23]	• All patients who are not expected to be on a full oral diet within 3 days should receive enteral nutrition (EN[ii]) [Grade C] • Haemodynamically stable, critically ill patients who have a functioning gastrointestinal tract should be fed early (<24 h) using an appropriate amount of feed. [Grade C] • Use EN in patients who can be fed via the enteral route. [Grade C]

[ii] Note on terminology: see table 4.20

Table 4.13 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Critical illness	International	Surviving Sepsis Campaign (2012)	Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012[15]	Nutrition: • We suggest administering oral or enteral (if necessary) feedings, as tolerated, rather than either complete fasting or provision of only intravenous glucose within the first 48 hrs after a diagnosis of severe sepsis/septic shock [grade 2C]. • We suggest using intravenous glucose and enteral nutrition rather than total parenteral nutrition (TPN) alone or parenteral nutrition in conjunction with enteral feeding in the first 7 days after a diagnosis of severe sepsis/septic shock [grade 2B].
	US	Academy of Nutrition and Dietetics (2012)	Critical Illness (CI) Guideline 2012[24]	**Enteral vs. Parenteral Nutrition** • If enteral nutrition (EN) is not contraindicated (e.g., by hemodynamic instability, bowel obstruction, high output fistula, or severe ileus) then the Registered Dietitian (RD) should recommend EN over parenteral nutrition (PN) for the critically ill adult patient. Research shows less septic morbidity, fewer infectious complications and significant cost savings in critically ill adult patients who received EN vs. PN. There is limited evidence that EN vs. PN affects hospital length of stay (LOS), but an impact on mortality has not been demonstrated. [Rating: Strong, Conditional] **Initiation of Enteral Nutrition** • If enteral nutrition (EN) is not contraindicated (e.g., by hemodynamic instability, bowel obstruction, high output fistula, or severe ileus), then the Registered Dietitian (RD) should recommend that EN be started within 24 to 48 hours following injury or admission to the intensive care unit (ICU) (early EN). Research indicates that EEN is associated with a reduction in infectious complications in critically ill, adult patients. The impact of EEN on mortality and length of stay (LOS) is unclear [Rating: Strong, Conditional]

Table 4.13 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with Renal Failure	US	American Society for Parenteral and Enteral Nutrition (2010)	Nutrition Support in Adult Acute and Chronic Renal Failure[25]	• Patients with renal failure who require nutrition support therapy should receive enteral nutrition if intestinal function permits. [Grade E]
	US	National Kidney Foundation (2000)	Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines for Nutrition in Chronic Renal Failure	If oral nutrition (including nutritional supplements) is inadequate, tube feeding should be offered if medically appropriate. • If tube feedings are not used, intradialytic parenteral nutrition (IDPN; for hemodialysis) or intraperitoneal amino acids (IPAA; for peritoneal dialysis) should be considered if either approach in conjunction with existing oral intake meets the protein and energy requirements. • If the combination of oral intake and IDPN or IPAA does not meet protein and energy requirements, daily total or partial parenteral nutrition should be considered.
	Europe	European Renal Association – European Dialysis and Transplant Association (2007)	EBPG Guideline on Nutrition[26]	Enteral tube [naso-gastric or percutaneous entero-gastrostomy (PEG)] feeding using disease specific formulas for dialysis patients should be prescribed if attempts to increase dietary intake with oral supplements fail and nutritional status does not improve [Evidence level IV].
	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Adult Renal Failure[27]	Acute renal failure (ARF): • In uncomplicated ARF use tube feeding (TF) if normal nutrition and oral nutritional supplements (ONS) are not sufficient to meet estimated requirements. [Grade C] • In severe ARF, the recommendations for TF are the same as for other ICU patients. If possible initiate EN within 24h. Conservatively treated chronic renal failure (CRF): • Use TF when adequate oral intake is not possible despite nutritional counselling and ONS. [Grade C] • In CRF patients in whom adequate oral intake cannot be achieved, consider overnight TF in order to optimize nutrient intake. Patients on maintenance haemodialysis therapy (HD): • Use TF if nutritional counselling and ONS are unsuccessful. [Grade C] • In HD patients in whom adequate oral intake cannot be achieved, consider TF to optimize nutrient intake. In unconscious patients on HD, e.g. in neurology, patients in nursing homes in need of EN, administer TF adapted to the metabolic changes associated with HD. [Grade C]

Table 4.13 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Chronic heart failure	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Cardiology and Pulmonology[28]	• EN is recommended in cardiac cachexia to stop or reverse weight loss on the basis of physiological plausibility. [Grade C] • There is no indication for enteral nutrition (EN) in the prophylaxis of cardiac cachexia. [Grade C] See Table 4.20 for definition of EN.
COPD	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Cardiology and Pulmonology[28]	• There is limited evidence that COPD patients profit from EN per se. [Grade B] • EN in combination with exercise and anabolic pharmacotherapy has the potential to improve nutritional status and function [Grade B] See Table 4.20 for definition of EN
Patients with GI disease	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Gastroenterology[29]	Crohn's disease: • Use tube feeding (and/or oral nutritional supplements) in addition to normal food to improve nutritional status and to eliminate consequences of undernutrition such as growth retardation. [Grade A] • Use tube feeding if a higher intake (>600kcals/day) is necessary [Grade C] Short bowel syndrome: • Adaption phase: Use continuous tube feeding-in limited amounts depending on the enteral fluid loss to improve intestinal adaptation. (Grade C) • Use oral nutritional supplements or tube feeding if normal nutritional status can not be maintained by normal food alone. [Grade C]
Patients with liver disease	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Liver Disease[30]	Alcoholic steatohepatitis: • Use tube feeding if patients are not able to maintain adequate oral intake (even when oesophageal varices are present). [Grade A] Liver cirrhosis: • If patients are not able to maintain adequate oral intake from normal food, use o Oral nutritional supplements or [Grade C] o Tube feeding (even in the presence of oesophageal varices) [Grade A]

Table 4.13 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with HIV and chronic infectious diseases	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Wasting in HIV and other chronic infectious diseases[31]	HIV: • Diarrhoea does not prevent a positive effect of TF on nutritional status [Grade A] • If oral intake is possible, nutritional intervention should be implemented according the following scheme [Grade C]. o nutritional counselling o oral nutritional supplements o tube feeding (TF) o PN • In patients with dysphagia or if oral nutritional supplements are not effective: If normal food intake and optimal use of oral nutritional supplements cannot achieve sufficient energy supply, TF is indicated. [Grade C]
Patients with burns	Europe	European Society for Clinical Nutrition and Metabolism (2013) Note: these recommendations are ESPEN endorsed	ESPEN endorsed recommendations: Nutritional therapy in major burns[32]	• Nutritional therapy should be initiated early within 12 h of injury, preferentially by the enteral route. [Grade: B; Agreement: Strong] • We recommend to give priority to the enteral route[iii], parenteral administration being rarely indicated [Grade: C; Agreement: Strong]

[iii] Note the term "enteral route" has been assumed to refer to tube feeding in this guideline, as no definition is given in the text.

Table 4.13 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with acute or chronic pancreatitis	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Pancreas[33]	Mild acute pancreatitis: • Give tube feeding, if oral nutrition is not possible due to consistent pain for more than 5 days. [Grade C] Severe necrotising pancreatitis: • In severe acute pancreatitis with complications (fistulas, ascites, pseudocysts) tube feeding can be performed successfully. Acute pancreatitis: • Tube feeding is possible in the majority of patients but may need to be supplemented by the parenteral route. [Grade A] Chronic pancreatitis: • Tube feeding is indicated in approximately 5% of patients with chronic pancreatitis. [Grade C]
	US	American College of Gastroenterology (2013)	Management of Acute Pancreatitis[34]	• Nasogastric delivery and nasojejunal delivery of enteral feeding appear comparable in efficacy and safety [strong recommendation, moderate quality of evidence]. • Nasogastric delivery and nasojejunal delivery of enteral feeding appear comparable in efficacy and safety [strong recommendation, moderate quality of evidence].
Patients with cystic fibrosis	Europe	European Society for Clinical Nutrition and Metabolism, European Society for Paediatric Gastroenterology, Hepatology and Nutrition and European Cystic Fibrosis Society (2016)	ESPEN-ESPGHAN-ECFS Guidelines on Nutrition Care for Infants, Children, and Adults with Cystic Fibrosis[14]	• We recommend a progressive approach to intensification of nutrition interventions as needs increase: preventive nutritional counselling, dietary modification and/or oral nutrition supplements, and enteral tube feeding. [Grade of evidence: low]

Table 4.13 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Surgical patients	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Surgery Including Organ Transplantation[35]	Post-operative: • Apply tube feeding in patients in whom early oral nutrition cannot be initiated, with special regard to those o undergoing major head and neck or gastrointestinal surgery for cancer. [Grade A] o with severe trauma. [Grade A] o with obvious undernutrition at the time of surgery. [Grade A] o in whom oral intake will be inadequate (<60%) for more than 10 days. [Grade C] • Initiate tube feeding for patients in need within 24 h after surgery. [Grade A] Organ transplantation: • Before transplantation: In undernutrition, use additional ONS or even TF. [Grade C]
	England and Wales	National Institute for Health and Care Excellence (NICE) (2006)	Nutrition support in adults Oral nutrition support, enteral tube feeding and parenteral nutrition[2]	• **Enteral nutrition support for surgical patients:** Surgical patients who are: malnourished and have; inadequate or unsafe oral intake and a functional, accessible gastrointestinal tract and are due to undergo major abdominal procedures, should be considered for pre-operative enteral tube feeding. [B] General surgical patients should not have enteral tube feeding within 48 hours post-surgery unless they are malnourished or at risk of malnutrition and have; inadequate or unsafe oral intake and a functional, accessible gastrointestinal tract. [A]
	European and International	Enhanced Recovery after Surgery Society (2013) ERAS® Society, the European Society for Clinical Nutrition and Metabolism and the International Association for Surgical Nutrition and Metabolism	Guidelines for Perioperative Care in Elective Colonic Surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations[36]	• Postoperative early enteral feeding, safety: High

Table 4.13 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with Intestinal Failure	Europe	European Society for Clinical Nutrition and Metabolism (2016)	Management of acute intestinal failure: A position paper from the European Society for Clinical Nutrition and Metabolism (ESPEN) Special Interest Group[37]	• Even if parenteral nutrition will be the nutritional support of choice, feeding via the enteral route should always be considered.
	Europe	European Society for Clinical Nutrition and Metabolism (2016)	ESPEN guidelines on chronic intestinal failure in adults[38]	• We suggest the use of enteral tube feeding in combination with oral feeding in patients with CIF with a low-level of HPN dependence (i.e. B1 category of clinical classification) and in whom the expected gain with tube feeding could allow them to wean off HPN. [Grade of evidence: low; strength of recommendation: weak]
Patients with Dysphagia	England and Wales	National Institute for Health and Care Excellence (NICE) (2006)	Nutrition support in adults Oral nutrition support, enteral tube feeding and parenteral nutrition[2]	• People with dysphagia: In the acute setting, for example following stroke, people unable to swallow safely or take sufficient energy and nutrients orally should have an initial 2–4 week trial of nasogastric enteral tube feeding. Healthcare professionals with relevant skills and training in the diagnosis, assessment and management of swallowing disorders should assess the prognosis and options for future nutrition support. [A]
	Europe	European Academy of Neurology (2011)	Late (complicated) Parkinson's disease[iv]	Dysphagia: • Enteral feeding options may need to be considered (short-term nasogastric tube feeding or longer-term feeding systems [percutaneous endoscopic gastrostomy]) [GPP]

[iv] Oertel WH, Berardelli A, Bloem BR, Bonuccelli U, Burn D, Deuschl G, Dietrichs E, Fabbrini G, Ferreira JJ, Friedman A, Kanovsky P, Kostic V, Nieuwboer A, Odin P, Poewe W,Rascol O, Sampaio C , Schupbach M, Tolosa E, Trenkwalder C . Late (complicated) Parkinson's disease. In: Gilhus NE, Barnes MP, Brainin M, editor(s). European handbook ofneurological management. 2nd ed. Vol. 1. Oxford (UK): Wiley-Blackwell; 2011. p. 237-67 (accesed via the National Guideline Clearinghouse https://www.guideline.gov/ 30.05.17).

Table 4.13 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with Stroke	England and Wales	National Institute for Health and Care Excellence (NICE) (2008)	Stroke and transient ischaemic attack in over 16s: diagnosis and initial management. Clinical Guideline 68[39]	• People with acute stroke who are unable to take adequate nutrition and fluids orally should: o receive tube feeding with a nasogastric tube within 24 hours of admission • Nutrition support should be initiated for people with stroke who are at risk of malnutrition. This may include oral nutritional supplements, specialist dietary advice and/or tube feeding.
	Germany	German Society for Clinical Nutrition (DGEM) (2013)	Guideline clinical nutrition in patients with stroke[40]	• Patients with prolonged severe dysphagia anticipated to last for more than 7 days should receive tube feeding [CCP]. • Patients with a decreased level of consciousness and mechanical ventilation often require enteral nutrition for a longer period of time and tube feeding can therefore start early [C]. • Severe swallowing difficulties that do not allow sufficient oral food intake and are anticipated to persist for more than 1 week require early enteral nutrition via feeding tube (at least within 72 hours) [C]. • If a sufficient oral food intake is not possible during the acute phase of stroke, enteral nutrition shall be preferably given via a nasogastric tube [A]. • If enteral feeding is likely for a longer period of time (> 28 days), a PEG should be chosen and shall be placed in a stable clinical phase (after 14 – 28 days) [A]. • Mechanically ventilated stroke patients should receive a PEG at an early stage [B]. • If a nasogastric tube is repeatedly removed accidentally by the patient and if artificial nutrition will probably be necessary for more than 14 days, early placement of a PEG should be considered [B]. A nasal loop (bridle) is an effective alternative in this situation [B].

Abbreviations: CIF Chronic intestinal failure GPP Good practice point, CCP Clinical Consensus Point

CANCER

Table 4.14 **Summary of some examples of evidence-based international and internationally recognised guidelines referring to enteral tube feeding (ETF) as an integral part of patient and disease management in Oncology** (parts of guidelines relevant to ETF presented here, standard formulas only)

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with cancer	Europe	European Society for Clinical Nutrition and Metabolism. Officially endorsed by the European Society of Surgical Oncology (ESSO), the European Association for Palliative care (EAPC) and the Chinese Society of Clinical Oncology (CSCO) (2017)	ESPEN guidelines on nutrition in cancer patients[41]	Modes of nutrition: when to escalate: • If a decision has been made to feed a patient, we recommend enteral nutrition if oral nutrition remains inadequate despite nutritional interventions (counselling, ONS), and parenteral nutrition if enteral nutrition is not sufficient or feasible. [Strength of recommendation STRONG; Level of evidence Moderate] Radiotherapy: • We recommend enteral feeding using naso-gastric or percutaneous tubes (e.g. PEG) in radiation-induced severe mucositis or in obstructive tumors of the head-neck or thorax. [Strength of recommendation STRONG, level of evidence: low]. Medical oncology: Curative or palliative anticancer drug treatment: • In a patient undergoing curative anticancer drug treatment, if oral food intake is inadequate despite counselling and oral nutritional supplements (ONS), we recommend supplemental enteral or, if this is not sufficient or possible, parenteral nutrition. [Strength of recommendation STRONG, level of evidence: very low] High-dose chemotherapy and hematopoietic stem cell transplantation (HCT): • During intensive chemotherapy and after stem cell transplantation we recommend to maintain physical activity and to ensure an adequate nutritional intake. This may require enteral and/or parenteral nutrition. [Strength of recommendation STRONG, level of evidence: very low] • If oral nutrition is inadequate we suggest preferring enteral tube feeding to parenteral nutrition, unless there is severe mucositis, intractable vomiting, ileus, severe malabsorption, protracted diarrhea or symptomatic gastrointestinal graft versus host disease (GvHD). [Strength of recommendation WEAK, level of evidence: low] Home artificial nutrition: • In patients with chronic insufficient dietary intake and/or uncontrollable malabsorption, we recommend home artificial nutrition (either enteral or parenteral) in suitable patients [Strength of recommendation STRONG; Level of evidence Low]

Table 4.14 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with cancer	US	Academy of Nutrition and Dietetics (2013)	Oncology (ONC) Guideline[42]	• In adult oncology patients who have been identified to have pre-cachexia or cancer cachexia, prompt and aggressive intervention to address nutrition impact symptoms and preserve or prevent loss of lean body mass (LBM) and weight should be initiated by the registered dietitian nutritionist (RDN). Early rather than later intervention to prevent weight loss in this population is more likely to be effective. The metabolic derangements in cancer cachexia that promote wasting can lead to loss of weight and LBM and poor outcomes **Medical Nutrition Therapy (MNT) in Adult Oncology Patients Undergoing Chemotherapy or Radiation Treatment:** • If an adult oncology patient is undergoing chemotherapy or radiation treatment, the registered dietitian nutritionist (RDN) should provide medical nutrition therapy (MNT). MNT has been shown to be effective in improving multiple treatment outcomes in patients undergoing chemotherapy, radiation or chemoradiotherapy in ambulatory or outpatient and inpatient oncology settings See Table 4.20 for definition of MNT
Adult cancer patients undergoing anti-cancer treatment and Hematopoietic Cell Transplantation	US	American Society for Parenteral and Enteral Nutrition (2009)	Nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation[43]	Anti-cancer treatment • Nutrition support therapy is appropriate in patients receiving active anticancer treatment who are malnourished and who are anticipated to be unable to ingest and/or absorb adequate nutrients for a prolonged period of time. [Grade: B] Hematopoietic cell transplantation: • Enteral nutrition should be used in patients with a functioning gastrointestinal tract in whom oral intake is inadequate to meet nutrition requirements. [Grade C]
Non-surgical cancer patients	Europe	European Society for Clinical Nutrition and Metabolism (2006)	ESPEN Guidelines on Enteral Nutrition: Non-surgical oncology[44]	During stem cell transplantation: • If oral intake is decreased parenteral nutrition may be preferred to tube feeding in certain situations (i.e. increased risk of haemorrhage and infections associated with enteral tube placement in immune-compromised and thrombocytopenic patients). [Grade C] • Use tube feeding if an obstructing head or neck or oesophageal cancer interferes with swallowing or if severe local mucositis is expected. [Grade C] During radio- or radio-chemotherapy: • Tube feeding can either be delivered via transnasal or percutaneous routes.

Table 4.14 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with cancer of the aerodigestive tract	England and Wales	National Institute for Health and Care Excellence (NICE) (2016)	Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over[45]	• Assess people's need for enteral nutrition at diagnosis, including prophylactic tube placement
	Europe	ESMO (European Society for medical oncology)	Oesophageal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up[46]	• Nutritional support according to the ESPEN guidelines is an integral part of the medical care for patients with oesophageal cancer in the curative and in the palliative setting [II, A] Management of local/locoregional disease: • Nutritional status matters and should be corrected. Endoscopic stenting should not be used in locoregional disease in operable patients and alternative routes of feeding, e.g. with needle catheter jejunostomy, should be preferred [II, A]

Table 4.14 Continued

Patient Group	Country	Body	Title	Recommendation, guideline or standard [grade of evidence]
Patients with head and neck cancers	Australia and New Zealand	Clinical Oncology Society of Australia	Evidence-based practice guidelines for the nutritional management of adult patients with head and neck cancer (2014)[47]	**Quality nutrition care - Nutrition intervention:** • Tube feeding using standard formula can be used to minimise weight loss in the acute post-operative period [Grade C] • Nutrition intervention (dietary counselling and/or supplements and/or tube feeding) improves/maintains nutritional status [Grade A] • Nutrition intervention (dietary counselling and/or supplements and/or tube feeding) improves patient-centred outcomes (quality of life, physical function and patient satisfaction) [Grade B] • Tube feeding can improve protein and energy intake when oral intake is inadequate [Grade B] • Tube feeding may reduce unplanned hospital admissions and reduced disruptions to treatment compared to oral intake alone [Grade C] **Nutrition implementation - Pre treatment:** • Prophylactic enteral feeding should be considered to improve nutritional status, cost and patient outcomes for patients who have T4 or hypopharyngeal tumours undergoing concurrent chemoradiotherapy [Grade C] **Nutrition implementation - Surgery** • Post-operative tube feeding should commence within 24 hours in patients in whom oral feeding cannot be established, with individual consideration to patients depending on surgical procedures in collaboration with the multidisciplinary team [Grade A]. **Nutrition implementation - Radiotherapy and chemotherapy** • Prophylactic tube feeding compared to oral intake alone or intervention tube feeding may reduce unplanned hospital admissions [Grade C] • For patients not tolerating adequate intake orally, tube feeding should be used to help minimize weight loss [Grade B] • Prophylactic tube feeding compared to oral intake alone or intervention tube feeding demonstrates improved nutrition outcomes with less weight loss [Grade B] • Prophylactic tube feeding compared to oral intake alone or intervention tube feeding may improve quality of life during and post treatment [Grade B].

Table 4.15 **NICE Guidelines: Grading of recommendations** (adapted from NICE 2006)[2]

Grade	Evidence
A	• At least one meta-analysis, systematic review, or RCT rated as 1++ (i.e. high quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias), and directly applicable to the target population, or • A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+ (i.e. well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias), directly applicable to the target population, and demonstrating overall consistency of results • Evidence drawn from a NICE technology appraisal
B	• A body of evidence including studies rated as 2++ (i.e. high quality systematic reviews of case-control or cohort studies, high-quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal) directly applicable to the target population, and demonstrating overall consistency of results, or • Extrapolated evidence from studies rated as 1++ or 1+
C	• A body of evidence including studies rated as 2+ (i.e. well-conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal), directly applicable to the target population and demonstrating overall consistency of results, or • Extrapolated evidence from studies rated as 2++
D	• Evidence level 3 (i.e. non-analytic studies e.g. case reports, case series) or 4 (i.e. expert opinion), or • Extrapolated evidence from studies rated as 2+, or • Formal consensus
D (GPP)	• A good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group

Table 4.16 **Academy of Nutrition and Dietetics recommendation ratings**

Academy Evidence-Based Nutrition Practice Guidelines published on the Evidence Analysis Library (EAL) are assigned a rating of: **strong, fair, weak, consensus, or insufficient evidence** based on the following criteria.

Criteria for Recommendation Ratings

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

Recommendations are categorized in terms of either **imperative** or **conditional** statements.

- **Imperative** statements are broadly applicable to the target population and do not impose restraints on their pertinence. Imperative recommendations may include terms such as “should” or “may” and do not contain conditional text that would limit their applicability to specified circumstances.
- **Conditional** statements clearly define a specific situation or population. Conditional recommendations are often presented in an if/then format, such that **if CONDITION than ACTION(S) because REASONS(S)**

Fulfillment of the condition triggers one or more guideline-specified actions.

Adapted by the Academy of Nutrition and Dietetics from the American Academy of Pediatrics, Classifying Recommendations for Clinical Practice Guidelines, Pediatrics.2004;114;874-877s

Table 4.17 **ESPEN Guidelines: Grading of recommendations** (adapted from Schutz 2006)[48]

Grade	Level of evidence	Requirement
A	Ia Ib	• Meta-analysis of randomized controlled trials • At least one randomized controlled trial
B	IIa IIb III	• At least one well-designed controlled trial without randomization • At least one other type of well-designed, quasi-experimental study • Well-designed non-experimental descriptive studies such as comparative studies, correlation studies, case-control studies
C	IV	• Expert opinions and/or clinical experience of respected authorities

Table 4.18 **ASPEN Grading of Guidelines and Levels of Evidence**[v]

Grading of Guidelines	
A	Supported by at least two level I investigations
B	Supported by one level I investigation
C	Supported by at least one level II investigation
D	Supported by at least one level III investigation
E	Supported by level IV or V evidence
Levels of Evidence	
I	Large randomized trials with clear-cut results; low risk of false-positive (alpha) and/or false-negative (beta) error
II	Small, randomized trials with uncertain results; moderate-to-high risk of false-positive (alpha) and/or false-negative (beta) error
III	Nonrandomized cohort with contemporaneous controls
IV	Nonrandomized cohort with historical controls
V	Case series, uncontrolled studies, and expert opinion

[v]From 2012 ASPEN have adopted a revised method of evidence grading based on the GRADE methodology (Druyan 2012) see Table 4.19

Table 4.19 Signposts for evidence grading of other international organisations

Recommending body	Signpost for evidence grading
National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel and Pan Pacific Pressure Injury Alliance	http://www.internationalguideline.com/static/pdfs/NPUAP-EPUAP-PPPIA-PUGuideline-MethodAddendum-2014.pdf
Academy of Nutrition and Dietetics	https://www.andeal.org/recommendation-ratings
ASPEN	http://pen.sagepub.com/content/36/1/77.full.pdf+html
Clinical Oncology Society of Australia	http://wiki.cancer.org.au/australia/COSA:Head_and_neck_cancer_nutrition_guidelines/Introduction#Literature_critique
NASPGHAN	http://www.cebm.net/
Surviving Sepsis Campaign	http://www.sccm.org/Documents/SSC-Guidelines.pdf
ESPGHAN	http://www.espghan.org/fileadmin/user_upload/guidelines_pdf/Guidelines_2404/Management_of_Pediatric_Ulcerative_Colitis___Joint.24.pdf
ESPEN	http://www.espen.org/files/ESPEN-Guidelines/0__Standard_operating_procedures_for_ESPEN_guidelines_and_consensus_papers_2.pdf

Table 4.20 **Definitions of Enteral Nutrition according to recommending body**

Organisation	Term	Definition
Academy of Nutrition and Dietetics	Medical Nutrition Therapy (MNT)	Medical nutrition therapy (MNT) is an evidence-based application of the Nutrition Care Process. The provision of MNT (to a patient/client) may include one or more of the following: nutrition assessment/re -assessment, nutrition diagnosis, nutrition intervention and nutrition monitoring and evaluation that typically results in the prevention, delay or management of diseases and/or conditions.
ASPEN[49]	Enteral Nutrition	"Nutrition provided through the gastrointestinal tract via a tube, catheter, or stoma that delivers nutrients distal to the oral cavity."
ESPEN[50]	Enteral Nutrition	"The term EN is used to comprise all forms of nutritional support that imply the use of "dietary foods for special medical purposes" as defined in the European legal regulation of the commission directive 1999/21/EC of 25 March 1991[vi] independent of the route of application. It includes oral nutritional supplements (ONS) as well as tube feeding via nasogastric, nasoenteral or percutaneous tubes"
ESPEN[23]	Enteral Nutrition	"As oral intake is almost always impossible in these patients, in this chapter the term "EN" is confined to tube feeding exclusively without regard to any kind of oral nutritional supplement".
ESPEN[41]	Artificial Nutrition	Artificial nutrition is the non-volitional application of nutrients via enteral tubes (enteral nutrition) or parenteral infusions (parenteral nutrition).
NASPGHAN[20]	Exclusive Enteral Nutrition (EEN)	EEN can be administered orally or via a nasogastric tube
ESPGHAN[13]	Enteral Nutrition	"EN encompasses the use of dietary foods for special medical purposes as defined in the European legal regulation of the Commission Directive 1999/21/EC,[8] irrespective of the route of delivery."

[vi]Note that the legislation for FSMPs has been updated since publication of these guidelines. See Defintions of Terms at the beginning of this dossier for up to date details of relevant legislation.

4.2.2 Guidelines: Theory to practice for enhanced patient care

Practical guidance for healthcare professionals about how to manage enteral tube feeding both in hospitals and in the community, including the transition from one to the other is essential and should be a key component of many guidelines. Enteral tube feeding should be viewed as an integral part of the nutrition care process and the decision to initiate, the organisation and planning of ETF should be managed within this context.

The decision to initiate and the implementation of ETF is often a complex, multidisciplinary and multi-agency process. Initiating enteral tube feeding may also involve ethical decisions particularly in vulnerable patient groups such as in older people, in paediatrics and in patients without capacity to participate in the decision making process. Whilst these issues need to be considered on a patient level the practicalities and management of the feeding process itself are easier to document. As a result, some internationally recognised organisations have produced practical guidance for healthcare providers to facilitate this process. Some of these key guidance documents are summarised in Table 4.21.

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Table 4.21 Overview of key publications focusing on the practical implementation of enteral tube feeding

Country/ region	Organisation	Ages	Title	Content
US	American Society for Parenteral and Enteral Nutrition	All ages and practice settings	Enteral Nutrition Practice Recommendations (2009)[49]	Focuses on the practice of enteral feeding and not the decision to initiate. Includes the following headings: • Ordering and labelling of enteral nutrition • Enteral formula (medical foods) and infant formula regulation • Water and enteral formula safety and stability • Enteral access • Enteral nutrition administration • Medication administration • Monitoring enteral nutrition administration
US	American Society for Parenteral and Enteral Nutrition	Paediatric and adult patients	A.S.P.E.N. Standards for Nutrition Support: Home and Alternate Site Care (2014)[4]	Provides practice-based standards which are intended for use by healthcare professionals charged with the care of patients receiving nutrition support therapies in the home or alternate site care settings. Covers all aspects of the nutritional care process.
UK	National Institute for Health and Care Excellence (NICE)	All patients in hospital and community	Nutrition Support Quality Standard 24 (2012)[51]	Statement 4. People managing their own artificial nutrition support and/or their carers are trained to manage their nutrition delivery system and monitor their wellbeing. Statement 5. People receiving nutrition support are offered a review of the indications, route, risks, benefits and goals of nutrition support at planned intervals.
Europe	European Society for paediatric gastroenterology, hepatology and nutrition (ESPGHAN)	Paediatrics	Practical Approach to Paediatric Enteral Nutrition: A Comment by the ESPGHAN Committee on Nutrition (2010)[13]	Provides a clinical practice guide to enteral nutrition support (ENS) in paediatric patients.
Europe	European Society for paediatric gastroenterology, hepatology and nutrition (ESPGHAN)	Paediatrics	ESPGHAN Position Paper on Management of Percutaneous Endoscopic Gastrostomy in Children and Adolescents (2015)[52]	Provides a comprehensive guide for health care providers to manage percutaneous endoscopic gastrostomy tubes in a safe, effective, and appropriate way.

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4.2 REFERENCE LIST

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4

RECOMMENDATIONS FROM INTERNATIONAL AND INTERNATIONALLY RECOGNISED PROFESSIONAL GUIDELINES:

4.3 Parenteral nutrition (PN)

Tables 4.1 to Table 4.5 summarize the evidence-based international and internationally recognised guidelines on parenteral nutrition (PN) identified from searches of the websites of the relevant professional organizations and the US Department of Health and Human Sciences National Guideline Clearinghouse (www.guideline.gov). The grading systems used in the guidelines are provided in Table 4.6 to Table 4.15. Links to relevant websites providing further information on the grading of evidence on medical nutrition in clinical guidelines are provided in Table 4.16.

Guidelines focusing on the practical or ethical aspects of administering PN have not been included but are listed in Section 4.4 (Guidelines: Theory to practice for enhanced patient care, Table 4.18. Other guidelines that were not identified using the above strategies may exist. In addition, we have only included guidelines in the English language. We would welcome information about other international guidelines that could be included in future editions of the dossier.

Note: The tables that follow include the recommendations relating to PN only, as they appear in the guidelines or documents, from various organizations, covering use of standard formula only. The full documents should be referred to for other information relating to nutritional management, such as screening, assessment, and use of other forms of nutritional support. Terminology relating to PN used within specific guidelines is presented in Table 4.17.

GENERAL

Table 4.1 **Summary of some examples of evidence-based international and internationally recognised guidelines referring to parenteral nutrition (PN) as an integral part of patient and disease management – General (parts of guidelines relevant to PN, standard formulas only)**

Country	Body	Title	Patient group	Recommendation, guidance or standard [grade of evidence, where available]
Australia	Dietitians Association of Australia (2015)	Nutrition And Hydration Policy Support Handbook For Acute Adult Inpatient Setting[1]	Adults in hospital	• Artificial nutrition support should be considered when patients cannot adequately or safely meet their nutrition requirements orally. • PN can be used for patients who are unable to tolerate or absorb adequate nutrition support via oral and enteral routes.
England and Wales	National Institute for Health and Care Excellence (NICE) (2006)	Nutrition support in adults: oral nutrition support, enteral tube feeding and parenteral nutrition[2]	All patients in the hospital and community	Indications for PN: • Healthcare professionals should consider PN in people who are malnourished or at risk of malnutrition and meet either of the following criteria: - inadequate or unsafe oral and/or EN intake - a non-functional, inaccessible, or perforated (leaking) GI tract [D(GPP)]. • PN should be introduced progressively and closely monitored, usually starting at no more than 50% of estimated needs for the first 24–48 hours. PN can be withdrawn once adequate oral nutrition or EN is tolerated and nutritional status is stable. Withdrawal should be planned and stepwise, with a daily review of the patient's progress [D(GPP)]. • PN should be stopped when the patient is established on adequate oral and/or enteral support. There is no minimum duration for PN [D(GPP)].

Table 4.1 Continued

Country	Body	Title	Patient group	Recommendation, guidance or standard [grade of evidence, where available]
US	ASPEN (2017)	ASPEN Consensus recommendation. When is parenteral nutrition appropriate?[3]	Adult patients	Do not use PN based on medical diagnosis or disease state. • Before starting PN, fully evaluate the feasibility of EN; reserve PN for clinical situations in which adequate EN is not an option. Circumstances where PN is the preferred method of nutrition: • Use PN in patients who are malnourished or at risk for malnutrition when a contraindication to EN exists or the patient does not tolerate adequate EN or lacks sufficient bowel function to maintain or restore nutrition status. Determining when EN is not feasible: • Evaluate clinical factors derived from history, physical examination, and diagnostic evaluations. Time frame for initiating PN: • After 7 days for well-nourished, stable adult patients who have been unable to receive significant (≥ 50% of estimated requirements) oral or enteral nutrients • Within 3–5 days in those who are nutritionally-at-risk and unlikely to achieve desired oral intake or EN • As soon as is feasible for patients with baseline moderate or severe malnutrition in whom oral intake or EN is not possible or sufficient • Delay in a patient with severe metabolic instability until their condition has improved. HPN[a]: • Consider for patients with intestinal failure who are clinically stable and able to receive therapy outside an acute care setting. • Perform a thorough evaluation of medical and psychosocial factors that influence suitability for HPN. • Address financial considerations/insurance coverage and patient responsibilities with patient and caregiver. Initiating HPN: • Establish organizational policies that delineate circumstances in which initiation of PN can take place outside the acute care setting. • Delineate patient-centered eligibility criteria for safely initiating HPN. • Develop strict protocols and procedures for initiating HPN, monitoring response to therapy, and documenting outcomes. • Conduct a comprehensive medical, clinical, and psychosocial assessment of HPN candidates to assess risk factors for adverse events related to initiating PN. • Consider initiating PN at home only when assessment confirms that the benefits greatly outweigh the risks.

Table 4.1 Continued

Country	Body	Title	Patient group	Recommendation, guidance or standard [grade of evidence, where available]
US	ASPEN (2011)	Nutrition screening assessment, and intervention in adults[4]	All patients in hospital and community	Nutrition support intervention is recommended for patients identified by screening and assessment as at risk for malnutrition or malnourished: Grade C (intervention described as "some intervention such as change in diet, EN, PN, or further medical assessment").
US	ASPEN (2014)	Standards for nutrition support: home and alternate site care[5]	All patients in homecare environments and alternate care sites*	The route selected to provide nutrition support shall be appropriate to the patient's medical problems, safety, efficacy, and preference. • When functional, the GI tract is the preferred route for nutrition support therapy.
US	ASPEN (2010)	Standards for nutrition support: adult hospitalized patients[6]	Adults in hospital	The route selected to provide nutrition support shall be appropriate to the patient's medical condition and should be assessed periodically for continued appropriateness as well as for its adequacy in meeting goals of the nutrition care plan (see Figure 2 in original guideline).

[a]Home care is defined as being provided in the traditional home as well as a group home, intermediate care facility, or assisted living facility. Alternate site care facilities can include skilled nursing facilities long-term acute care hospitals, or rehabilitation hospitals.
EN, enteral nutrition; GI, gastrointestinal; GPP, general practice point; HPN, home parenteral nutrition.

OLDER PEOPLE

Table 4.2 **Summary of some examples of evidence-based international and internationally recognised guidelines referring to parenteral nutrition (PN) as an integral part of patient and disease management – Older People (parts of guidelines relevant to PN, standard formulas only)**

Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Europe	ESPEN (2009)	Guidelines on parenteral nutrition: geriatrics[7]	• PN is a safe and effective therapeutic procedure, provided that it is provided by an experienced team. Age *per se* is not a reason to exclude patients from PN [Grade C]. • PN is indicated and may allow adequate nutrition in patients who cannot meet their nutritional requirements via the enteral route, and should be limited to situations when EN is contraindicated or poorly tolerated [Grade C]. • PN support should be instituted in the older person facing a period of starvation of more than 3 days when oral nutrition or EN is impossible, or has been or is likely to be insufficient for more than 7–10 days [Grade C]. • PN is a useful method of nutritional support in older malnourished patients but is less often justified in geriatric patients than EN or oral nutritional supplements [Grade B]. • Indications for PN are similar in younger and older adults in the hospital and at home and are limited to situations when EN is contraindicated or poorly tolerated [Grade B].
Europe	ESPEN (2015)	Guidelines on nutrition in dementia (2015)[8]	• We suggest parenteral fluids for a limited duration in periods of insufficient fluid in take to overcome a crisis situation [Grade of evidence: very low]. • We recommend against the use of artificial nutrition (EN, PN and parenteral fluids) in the terminal phase of life [grade of evidence: very low].

[a]The grading system for recommendations is summarized in Table 4.7 (before 2015) and Table 4.8 (2015 onwards).
EN, enteral nutrition; ESPEN, European Society for Parenteral and Enteral Nutrition; PN, parenteral nutrition.

CHILDREN

Table 4.3 **Summary of some examples of evidence-based international and internationally recognised guidelines referring to parenteral nutrition (PN) as an integral part of patient and disease management – Children (parts of guidelines relevant to PN, standard formulas only)**

Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Europe	European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and ESPEN, supported by the European Society of Paediatric Research	Guidelines on paediatric parenteral nutrition (2005)[9]	• Timing for initiation of PN depends on individual circumstances and the age and size of the infant or child. • In small preterm infants, starvation for just 1 day may be detrimental; thus, PN must be instituted shortly after birth if it is clear that enteral feeds will not be tolerated soon. • In older children and adolescents, longer periods of inadequate nutrition (up to about 7 days) may be tolerated, depending on age, nutritional status, and the disease, surgery, or medical intervention.
Europe	ESPEN, ESPGHAN, and European Cystic Fibrosis Society (ECFS) (2016)	Guidelines on nutrition care for infants, children, and adults with cystic fibrosis[10]	• PN should be reserved for exceptional cases when enteral feeding is not possible (grade of evidence: low).
International	Surviving Sepsis Campaign (2012)	International guidelines for management of severe sepsis and septic shock[11]	• EN should be used in children who can tolerate it; PN in those who cannot [Grade 2C].

Table 4.3 Continued

Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
US	ASPEN (2017)	Consensus recommendation. When is parenteral nutrition appropriate?[3]	Use of PN is based on medical diagnosis or disease state: • Neonatal: Consider PN in the critical care setting, regardless of diagnosis, when EN is unable to meet energy requirements for energy expenditure and growth. • Pediatric: Use PN when the GI tract is not functional or cannot be accessed or when nutrient needs for growth are greater than can be provided through oral intake or EN support alone. Circumstances where PN is the preferred method of nutrition (neonatal and pediatric): • Initiate PN for total or supplemental nutrient provision if EN is not feasible or is not sufficient to meet total nutrient needs. Determining when EN is not feasible (neonatal and pediatric): • Initiate PN and withhold EN when a clear contraindication to EN exists, such as intestinal injury and perforation. • Assess intestinal function, perfusion, and overall hemodynamic stability when evaluating readiness for EN rather than relying on strict adherence to a list of contraindications, such as the presence of umbilical catheters or use of vasoactive medications. Time frame for initiating PN: • Neonatal: begin PN promptly after birth in very low birth weight infants (< 1500 g); there are insufficient data to suggest a specific time frame for initiation of PN in more mature preterm infants or critically ill term neonates. • Pediatric: For the infant, child, or adolescent with a self-limited illness, it is reason able to delay starting PN for 1 week. However, initiate PN within 1–3 days in infants and within 4–5 days in older children and adolescents when it is evident that they will not tolerate full oral intake or EN for an extended period. HPN (pediatric) • Consider HPN for carefully selected, clinically stable pediatric patients who are expected to require PN for an extended period. • Discharge patients to the care of a pediatric homecare team and infusion provider with pediatric experience. • Do not initiate PN in the home setting; patients should be admitted to hospital for initiation of PN.

Table 4.3 Continued

Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
US	Society of Critical Care Medicine (SCCM) and ASPEN (2017)	Guidelines for the provision and assessment of nutrition support therapy in the pediatric critically ill patient[12]	Guidelines relate to critically ill pediatric patients (aged > 1 month and < 18 years) expected to spend > 2–3 days in a PICU admitting medical, surgical, and cardiac patients. Indication for and optimal timing of PN in critically ill children: • On the basis of a single RCT, we do not recommend the initiation of PN within 24 h of PICU admission [quality of evidence: moderate; GRADE recommendation: strong]. Role of PN as a supplement to inadequate EN: • For children tolerating EN, we suggest stepwise advancement of nutrient delivery via the enteral route and delaying PN. Based on current evidence, the role of SPN to reach a specific goal for energy delivery is not known. • The time when PN should be initiated to supplement insufficient EN is unknown. The threshold for and timing of PN initiation should be individualized. Based on a single RCT, SPN should be delayed until 1 week after PICU admission for patients with normal baseline nutrition state and low risk of nutrition deterioration. • On the basis of expert consensus, we suggest PN supplementation for children who are unable to receive any EN during the first week in the PICU. For patients who are severely malnourished or at risk of nutrition deterioration, PN may be supplemented in the first week if they are unable to advance past low volumes of EN [Quality of evidence: low; GRADE recommendation: weak].
US	ASPEN	Nutrition support of the critically ill child (2009)[13]	• In critically ill children with a functioning GI tract, EN should be the preferred mode of nutrient provision, if tolerated [Grade C].
US	ASPEN	Standards for nutrition support: pediatric hospitalized patients (2013)[14]	• PN should be used when the GI tract is not functional or cannot be accessed, or the patient's nutrient needs are greater than can be met through the GI tract.

ASPEN, American Society for Parenteral and Enteral Nutrition, ECSF, European Cystic Fibrosis Society; EN, enteral nutrition; GI, gastrointestinal; HPN, home parenteral nutrition; PICU, pediatric intensive care unit; PN, parenteral nutrition; RCT, randomized controlled trial; SPN, supplemental parenteral nutrition

SPECIFIC DISEASES

Table 4.4 **Summary of some examples of evidence-based international and internationally recognised guidelines referring to parenteral nutrition (PN) as an integral part of patient and disease management – Specific Diseases and Conditions (parts of guidelines relevant to PN presented here, standard formulas only)**

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Critical illness	Canada	Canadian Critical Care Society (CCCS) and Canadian Critical Care Trials Group (CCCTG) (2015)[15]	Canadian Critical Care Nutrition Clinical Practice Guidelines	Use of EN vs PN: • When considering nutrition support for critically ill patients, we recommend EN over PN in patients with an intact gastrointestinal tract. Combination PN and EN (as per 2013 guideline recommendations): • For critically ill patients starting on EN, we recommend that PN is not started at the same time as EN. In the patient who is not tolerating adequate EN, there are insufficient data to put forward a recommendation about when PN should be initiated: Practitioners will have to weigh the safety and benefits of initiating PN on a case-by-case basis. We recommend that PN is not started in critically ill patients until all strategies to maximize EN delivery (such as small bowel feeding tubes, motility agents) have been attempted. Early vs delayed SPN (as per 2013 guideline recommendations): • We strongly recommend that early SPN and high IV glucose are not used in unselected critically ill patients (i.e. low risk patients with short stay in ICU). In the patient who is not tolerating adequate EN, there are insufficient data to put forward a recommendation about when PN should be initiated; practitioners will have to weigh the safety and benefits of initiating PN in patients on a case-by-case basis. PN vs standard care: • We recommend that PN is not used routinely in critically ill patients with an intact gastrointestinal tract; early PN should be considered in nutritionally high-risk patients with a relative contraindication to early EN.
	Europe	ESPEN (2009)	Guidelines on parenteral nutrition: intensive care (2009)[16]	• All patients who are not expected to be on normal nutrition within 3 days should receive PN within 24–48 h if EN is contraindicated or if they can not tolerate EN [Grade C]. • All patients receiving less than their targeted enteral feeding after 2 days should be considered for SPN [Grade C].

Table 4.4 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Critical illness	US	ASPEN (2016)	Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient[17] Specific patient populations: organ failure (pulmonary, renal, and hepatic), acute pancreatitis, surgical subsets (trauma, traumatic brain injury, open abdomen, and burns), sepsis, postoperative major surgery, chronically critically ill, obese critically ill, and end-of-life situations	When to initiate PN in the adult critically ill patient at low nutrition risk: • We suggest that, in the patient at low nutrition risk (e.g. NRS 2002 ≤ 3 or NUTRIC score ≤ 5), exclusive PN be withheld over the first 7 days following ICU admission if the patient cannot maintain volitional intake and if early EN is not feasible [quality of evidence: very low]. When to initiate PN in the critically ill patient at high nutrition risk: • Based on expert consensus, in the patient determined to be at high nutrition risk (e.g. NRS 2002 ≥ 5 or NUTRIC score ≥ 5) or severely malnourished, when EN is not feasible, we suggest initiating exclusive PN as soon as possible following ICU admission. Optimal timing for initiating supplemental PN (SPN) when EN does not meet energy or protein goals in the patient at low or high nutritional risk: • We recommend that, in patients at either low or high nutrition risk, use of SPN be considered after 7–10 days if EN alone is unable to meet > 60% of energy and protein requirements. Initiating SPN earlier than this in critically ill patients receiving some EN does not improve outcomes and may be detrimental (quality of evidence: moderate).
	International	Surviving Sepsis Campaign (2012)	International guide-lines for management of severe sepsis and septic shock (2012)[11]	Nutrition: we suggest intravenous glucose and EN rather than TPN alone or PN in conjunction with enteral feeding in the first 7 days after a diagnosis of severe sepsis/septic shock [Grade 2B].
	England & Wales	National Institute for Health and Care Excellence (NICE) (2006)	Nutrition support in adults: oral nutrition support, enteral tube feeding and parenteral nutrition[2]	If intestinal tolerance persistently limits enteral tube feeding in surgical or critical care patients, PN should be used to supplement or replace enteral tube feeding [grade B].

Table 4.4 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Renal failure	US	ASPEN (2017)	Consensus recommendation. when is parenteral nutrition appropriate?[3]	Intradialytic PN (IDPN), global recommendations: • Do not use as the sole source of nutrition intervention in malnourished patients with CKD. • Consider for adult and pediatric patients with CKD who are malnourished and unable to tolerate adequate oral intake or EN.
	US	ASPEN (2010)	Nutrition support in adult acute and chronic renal failure[18]	• This guideline does not contain specific recommendations on when to initiate PN, • Patients with renal failure who require nutrition support therapy should receive EN if intestinal function permits (Grade E).
	US	National Kidney Foundation (2000)	Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines for nutrition in chronic renal failure[19]	If oral nutrition (including nutritional supplements) is inadequate, tube feeding should be offered if medically appropriate. • If tube feeding is not used, IDPN (for hemodialysis) or intraperitoneal amino acids (IPAA; for peritoneal dialysis) should be considered if either approach in conjunction with existing oral intake meets the protein and energy requirements. • If the combination of oral intake and IDPN or IPAA does not meet protein and energy requirements, daily total or partial PN should be considered.
	Europe	European Renal Association – European Dialysis and Transplant Association (2007)	European best practice guideline on nutrition[20]	• When intensive dietary support, oral supplements, and EN have failed, a course of PN is recommended [evidence level IV]. • IDPN is recommended in malnourished patients only if spontaneous nutrient intake is > 20 kcal/kg IBW and 0.8 g protein/kg IBW/day. Otherwise, TPN infused over the entire day is indicated [opinion].

Table 4.4 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Renal failure	Europe	ESPEN (2009)	ESPEN guidelines on parenteral nutrition: adult renal failure[21]	Acute renal failure (ARF): • The indications for and contraindications to PN in ARF are comparable to those in other critically ill patients (see ICU guidelines). • PN is appropriate in ARF when the GI tract cannot be used for enteral feeding, or when EN is not enough to reach nutrient intake goals [Grade C]. Chronic renal failure (CRF): • Conservatively treated patients with CKD seldom need PN. Potential indications of PN in CKD patients are similar to the indications for PN in non-renal patients. Malnourished CKD patients requiring nutritional support should only be considered for PN when ONS and EN are impossible or fail to reach nutritional goals. Special attention should be given to CKD requiring PN during perioperative periods [Grade C]. • When nutritional requirements cannot be met by dietary intake (with or without ONS), in combination with EN or by the enteral route alone, the goals of PN in CKD patients are (a) prevention and treatment of PEW leading to cachexia; (b) ensuring provision of optimal energy, essential nutrients and trace elements; and (c) attenuation of CKD progression through protein or phosphate restriction [Grade C]. Patients on maintenance haemodialysis (HD): • In acutely ill patients with CKD on dialysis the decision to use PN should be based on the same criteria as in ARF patients. • In non-acutely ill malnourished HD patients with mild PEW as defined by insufficient spontaneous intake, dietary counseling, and, if necessary, ONS should be prescribed. • In patients exhibiting severe PEW, with spontaneous intake > 20 kcal/day: dietary counseling and ONS should be prescribed; IDPN is indicated in patients unable to comply with ONS; EN can be necessary when ONS or IDPN fail to improve nutritional status. • In patients exhibiting severe PEW, with spontaneous intake < 20 kcal/day, or in stress conditions: both ONS and IDPN are generally unable to provide satisfactory nutritional supply and are not recommended; daily nutritional support is necessary and EN should be preferred to PN; central venous PN is indicated when EN is impossible or insufficient.

Continued over

Table 4.4 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
				Patients on continuous ambulatory peritoneal dialysis (CAPD): • Intravenous PN has been poorly investigated in CAPD patients. Current data suggest that PN should be limited to malnourished and stressed CAPD patients, or patients with severe encapsulating peritonitis, when nutritional requirements cannot be ensured by oral or enteral routes [Grade C]. • In acutely ill patients with CKD on dialysis, the decision to use PN should be the same as in ARF patients [Grade C]). • In CAPD patients presenting with mild PEW as defined by insufficient spontaneous intake, dietary counseling, and, if necessary, ONS should be prescribed [Grade C]. • In patients exhibiting severe PEW, with spontaneous intake > 20 kcal/day: dietary counseling and ONS should be prescribed; IPPN may be considered in patients unable to comply with ONS; EN can be necessary when ONS are unable to improve nutritional status [Grade C]. • In patients exhibiting severe PEW, with spontaneous intakes < 20 kcal/day, or in stress conditions: daily nutritional support is necessary and EN should be preferred to PN; central venous PN is indicated when EN is impossible or insufficient [Grade C]. • In acutely ill patients with CKD on dialysis, the goal of PN is to reduce protein catabolism and nutritional depletion-associated morbidity and mortality. In chronically undernourished CAPD patients IPPN aims to improve quality of life and to reduce PEW-related complications, hospitalization rate, and mortality [Grade C].
Chronic heart failure	Europe	ESPEN (2009)	ESPEN guidelines on parenteral nutrition: cardiology and pneumology[22]	• Although there is no evidence from well-designed studies, PN is recommended to stop or reverse weight loss in patients with evidence of malabsorption, on the basis that it improves outcome in other similar conditions and there is a plausible physiological argument for it [Grade C]. • Currently there is no indication for PN in the prophylaxis of cardiac cachexia [Grade C].
Chronic obstructive pulmonary disease (COPD)	Europe	ESPEN (2009)	ESPEN guidelines on parenteral nutrition: cardiology and pneumology (2009)[22]	There is limited evidence that COPD patients intolerant of EN profit from PN. However, small studies suggest that, in combination with exercise and anabolic pharmacotherapy, PN has the potential to improve nutritional status and function [Grade C].

Table 4.4 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Gastrointestinal disease	Europe	ESPEN (2009)	ESPEN guidelines on parenteral nutrition: gastroenterology)[23]	Crohn's disease (CD): • Improvement of growth: PN should be used if enteral feeding cannot be tolerated [Grade B]. • Primary therapy for active CD: PN should be not used as a primary treatment in patients with inflammatory luminal CD [Grade A]. • Perioperative nutrition: As for other underlying diseases, PN in the perioperative period should be given to prevent or treat malnutrition in patients who are not likely to be fed orally and/or enterally. • Maintenance of remission: PN is not recommended for maintenance of remission [Grade B]. • PN is indicated when nutrition cannot be maintained via the intestine in the following situations [all Grade B]: - Obstructed bowel not amenable to feeding tube placement beyond the obstruction - Short bowel resulting in severe malabsorption or fluid and electrolyte loss which cannot be managed enterally - Severe dysmotility making enteral feeding impossible - A leaking intestine from high output intestinal fistula, or surgical anastomotic breakdown - Patient intolerant of EN whose nutrition cannot be maintained orally - Unable to access the gut for enteral feeding. Ulcerative colitis (UC): • Except in complicated UC or in the perioperative period, PN is not indicated to treat undernutrition in UC [Grade B]. • PN is indicated as an adjuvant to other forms of medical treatment – but not as a primary treatment – and is used in severe attacks of UC only when EN is not tolerated or is contraindicated (e.g., impending or established toxic megacolon, colonic perforation, massive colonic bleeding) [Grade B]. • PN does not have any role in the maintenance of remission in UC [Grade B]. Role of PN in short bowel (intestinal failure): • Post-operative phase: Most patients with a short bowel require PN for the first 7–10 days after resection but not necessarily in isolation [Grade C]. • Adaption phase: Appropriate EN and/or oral nutrition should be initiated as soon as possible and progressively increased depending on the tolerance of the gut and the patient. • Maintenance/Stabilization phase: According to the length of residual small bowel and type of anatomy (preserved colon or not), patients with short bowel may need long-term PN [Grade B]. In some, the main problem relates to stabilizing water and electrolyte balance. In some (usually with a retained colon) appropriate adaptive hyperphagia, and intestinal adaptation may improve nutritional status sufficiently such that PN can be reduced or stopped [Grade B].

Table 4.4 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Gastrointestinal disease	Europe	ESPEN (2009)	ESPEN Guideline: Clinical nutrition in inflammatory bowel disease (IBD) (2017)[24]	IBD • If oral feeding is not sufficient, tube feeding should be considered as supportive therapy. EN using formulae or liquids should always take preference over PN, unless it is completely contraindicated [Grade A — strong consensus (100% agreement)]. • PN is indicated in IBD: (i) when oral or tube feeding is not sufficiently possible, (e.g., when the GI tract is dysfunctional or in CD patients with short bowel); (ii) when there is an obstructed bowel and no possibility of placing a feeding tube beyond the obstruction or where this has failed; (iii) when other complications occur such as an anastomotic leak or a high output intestinal fistula [Grade B — strong consensus (96% agreement)]. • CD patients with a proximal fistula and/or a very high output should receive nutritional support by partial or exclusive PN [Grade B — strong consensus (96% agreement)]. • In the perioperative phase, EN should always be preferred over PN, but combinations of EN and PN should be considered if there is an indication for nutritional support and > 60% of energy needs cannot be met via the enteral route [Grade A, see ESPEN Surgery Guideline[25] — strong consensus (100% agreement)]. • In the perioperative period, PN is usually used as supplemental to EN [Grade B — strong consensus (96% agreement)]. • PN shall be used as the only intervention if EN is impossible (absence of access, severe vomiting or diarrhea) or contraindicated (intestinal obstructions or ileus, severe shock, intestinal ischemia) [Grade A — strong consensus (96% agreement)]. • Surgical patients with CD should obtain early nutritional support because, independently of the route of administration, it decreases the risk of postoperative complications [Grade B — strong consensus (100% agreement)]. • In CD patients with prolonged GI failure (such as when resection has created a short bowel), PN is mandatory and life-saving at least in the early stages of intestinal failure [Grade B, see Surgery guideline[25] — strong consensus (92% agreement)].
	US	ACG (2013)	ACG: Clinical guidelines: diagnosis and management of celiac disease)[26]	Celiac disease • Patients with refractory celiac disease should be monitored closely and receive aggressive nutritional support, including PN whenever indicated (strong recommendation, high level of evidence).

Table 4.4 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Gastrointestinal disease	Europe	ESPEN (2016)	Management of acute intestinal failure: a position paper from the European Society for Clinical Nutrition and Metabolism (ESPEN) Special Interest Group[27]	Intestinal failure (IF) • Although enteral nutrition has proven to be the most beneficial in almost all patient populations, it is relatively rare that it is sufficient in acute IF/enterocutaneous fistula (ECF) individuals because of the compromised integrity of the GI tract. Therefore, PN often represents the main option, alone or in association with EN.
	Europe	ESPEN (2016)	ESPEN guidelines on chronic intestinal failure in adults[28]	HPN is the primary treatment for chronic IF. • We recommend that patients selected for HPN have confirmed IF that, despite maximal medical therapy, would lead to deterioration of nutrition and/or fluid status [Grade of evidence: very low; strength of recommendation: strong]. • We suggest the use of enteral tube feeding in combination with oral feeding in patients with chronic IF with a low-level of HPN dependence (i.e. B1 category of clinical classification) and in whom the expected gain with tube feeding could allow them to wean off HPN{Grade of evidence: low; strength of evidence: weak]. • We recommend that HPN is not delayed in malnourished patients with chronic intestinal pseudo-obstruction (CIPO) who have chronic GI motility dysfunctions and oral/Eni s obviously inadequate [Grade of evidence: very low; strength of evidence: strong]. • We recommend HPN is not delayed in malnourished patients with radiation enteritis if oral nutrition/enteral tube feeding is obviously inadequate [Grade of evidence: very low; strength of evidence: strong]. • We recommend HPN as the primary treatment for patients with chronic IF and the early referral of patients to intestinal rehabilitation centers with expertise in both medical and surgical treatment, to maximize the opportunity of weaning off HPN, to prevent HPN failure, and to ensure timely assessment of candidacy for intestinal transplantation. • We suggest the use of EN in combination with oral feeding in patients with chronic IF with a low-level of HPN dependence (i.e. B1 category of clinical classification) and in whom the expected gain with EN could allow them to wean off HPN [Grade of evidence: low; strength of recommendation: weak].

Table 4.4 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Liver disease	Europe	ESPEN (2009)	ESPEN guidelines on parenteral nutrition: hepatology[29]	Alcoholic steatohepatitis • Immediate commencement of PN is indicated in patients with moderate or severe malnutrition who cannot be fed sufficiently orally or enterally [Grade A]. Liver cirrhosis: • Immediate commencement of PN is indicated in moderately or severely malnourished patients who cannot be sufficiently nourished orally or enterally [Grade C]. • Patients who can be fed sufficiently by the oral or enteral route but who have to abstain from food temporarily for more than 12 h (including nocturnal fasting) should be given IV glucose (2–3 g/kg/d). When this fasting period lasts longer than 72 h TPN is required (both Grade C). • PN should be considered in patients with unprotected airways and encephalopathy when cough and swallow reflexes are compromised [Grade C]. • Early postoperative (additional) PN after surgery is indicated if patients they cannot be nourished sufficiently by the oral/enteral route [Grade A]. • After liver transplantation, patients should receive early postoperative nutrition; PN is second choice to EN (Grade C). Acute liver failure • As in other critically ill patients, artificial nutrition is indicated when the patient is unlikely to resume normal oral nutrition within the next 5–7 days irrespective of current nutritional state. PN is helpful in patients who cannot be fed adequately by EN [Grade C].
Acute and chronic pancreatitis	Europe	ESPEN (2009)	ESPEN guidelines on parenteral nutrition: pancreas[30]	Acute pancreatitis • All patients who the clinician decides require nutritional support is indicated should have this commenced by the enteral route; PN is indicated only in patients who are unable to tolerate targeted requirements, that is, when the gut has failed or administration of EN is impossible for other reasons (e.g. prolonged ileus, complex pancreatic fistulae, abdominal compartment syndrome) [Grade B]. • As EN tolerance increases, the volume of PN should be decreased. When tolerated EN is associated with improved outcomes compared with PN [Grade A]. • PN does not significantly stimulate pancreatic secretion and has no adverse effects on pancreatic function [Grade A]. Chronic pancreatitis • Malnutrition is frequent because of pain-induced anorexia and continuing alcohol abuse. Resting energy expenditure may also be increased. PN may be indicated in patients with gastric outlet obstruction secondary to duodenal stenosis and in those with complex fistulating disease [Grade C].

Table 4.4 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Acute and chronic pancreatitis	US	American College of Gastroenterology (ACG) (2013)	Management of acute pancreatitis (2013)[31]	• PN should be avoided in severe acute pancreatitis, unless the enteral route is not available, not tolerated, or does not meet caloric requirements [Strong recommendation, high quality of evidence].
	International	International Consensus Guideline Committee	International consensus guidelines for nutrition therapy in pancreatitis (2012)[32]	• Use PN if nutrition therapy is indicated but EN is contraindicated or not well tolerated [Grade A: Platinum].
Cystic fibrosis	Europe	ESPEN–ESPGHAN–ECFS (2016)	Guidelines on nutrition care for infants, children, and adults with cystic fibrosis[10]	• PN should be reserved for exceptional cases when enteral feeding is not possible [Grade of evidence: low].
Surgery	Europe	ESPEN (2017)	ESPEN guideline: clinical nutrition in surgery[25]	Indication for nutritional therapy • If the energy and nutrient requirements cannot be met by oral and enteral intake alone (< 50% of caloric requirement) for more than 7 days, a combination of EN and PN is recommended (GPP). • PN shall be administered as soon as possible if nutrition therapy is indicated and there is a contraindication for EN, such as in intestinal obstruction (A) (biomedical endpoints—BM) [Grade of recommendation GPP/A – strong consensus (100% agreement)]. Preoperative PN • Preoperative PN shall be administered only in patients with malnutrition or severe nutritional risk where energy requirement cannot be adequately met by EN [A] (BM). A period of 7–4 days is recommended [0] [A/0 – strong consensus (100% agreement)]. After organ transplant • If necessary, EN and PN should be combined. Long-term nutritional monitoring and qualified dietary counseling are recommended for all transplants [GPP – strong consensus (100% agreement)]. Bariatric surgery • PN is not required in uncomplicated bariatric surgery [0 – strong consensus (100% agreement)].

Table 4.4 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Surgery	Europe	European Society of Coloproctology (2016)	Consensus on the surgical management of intestinal failure in adults[33]	• PN should be started as soon as it is anticipated that EN will be unable to meet the patient's nutritional and metabolic needs [Level of evidence: 5]. • HPN is the primary therapeutic option for intestinal failure as it is associated with better or comparable long-term survival compared with intestinal transplantation [Level of evidence: 5].
	England & Wales	National Institute for Health and Care Excellence (2006)	NICE: Nutrition support in adults: oral nutrition support, enteral tube feeding and parenteral nutrition[2]	• Peri operative SPN should be considered in malnourished surgical patients who have an inadequate or unsafe intake via the oral and/or enteral routes or a non-functional, inaccessible, or perforated (leaking) GI tract [B].
	US	ASPEN (2017)	Consensus recommendation. When is parenteral nutrition appropriate?[3]	• Consider pre-operative PN in severely malnourished patients unable to tolerate sufficient oral intake or EN. • Reserve post-operative PN for severely malnourished patients unable to tolerate EN for more than 7 days, unless initiated pre-operatively.
Bariatric surgery	US	American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic and Bariatric Surgery (2013)	Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient[34]	• EN or PN should be considered in bariatric surgery patients at high nutritional risk (e.g., NRS ≥ 3); PN should be considered in patients who are unable to meet their needs using their GI tract for at least 5–7 days with non-critical illness or 3–7 days with critical illness [Grade D]. • PN should be considered in patients with severe protein malnutrition and/or hypoalbuminemia, not responsive to oral or EN protein supplementation [Grade D]. • Severe malnutrition should prompt hospital admission for initiation of nutritional support [Grade D]. • The initiation and formulation of EN or PN should be guided by current clinical practice guidelines [Grade D].

Table 4.4 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Pressure ulcers	Europe, US, Australia, New Zealand, Hong Kong, Singapore	National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel and Pan Pacific Pressure Injury Alliance (2014)	Prevention and treatment of pressure ulcers[35]	• Consider EN or PN when oral intake is inadequate. This must be consistent with the individual's goals (strength of evidence = C; strength of recommendation = ☝) • If oral intake is inadequate, EN or PN may be recommended if consistent with the individual's wishes. EN is the preferred route if the GI tract is functioning.
Human immuno-deficiency virus (HIV) and chronic infectious diseases	Europe	ESPEN (2006)	ESPEN guidelines on enteral nutrition: wasting in HIV and other chronic infectious diseases[36]	If oral intake is possible, nutritional intervention should be implemented according the following scheme [Grade C]: • nutritional counselling • oral nutritional supplements • tube feeding • PN.

ACG, American College of Gastroenterology; ARF, acute renal failure; ASPEN, American Society of Parenteral and Enteral nutrition; BM, biomedical endpoints; CAPD, continuous ambulatory peritoneal dialysis; CD, Crohn's disease; CKD, chronic kidney disease; CRF, chronic renal failure; ECFS, European Cystic Fibrosis Society; EN, enteral nutrition; ESPEN, European Society for Clinical Nutrition and Metabolism; ESPGHAN, European Society for Paediatric Gastroenterology, Hepatology and Nutrition; GPP, good practice point; HD, hemodialysis; HPN, home parenteral nutrition; IBW, ideal body weight; ICU, intensive care unit; IDPN, Intradialytic parenteral nutrition; IF, intestinal failure; IPAA, or intraperitoneal amino acids; IV, intravenous; NICE, National Institute for Health and Care Excellence; NRS, nutrition risk score; NUTRIC, Nutrition Risk in the Critically Ill; ONS, oral nutritional supplementation; PEW, protein-energy wasting; PN, parenteral nutrition; SPN, supplemental parenteral nutrition; TPN, total parenteral nutrition; UC, ulcerative colitis

CANCER

Table 4.5 **Summary of some examples of evidence-based international and internationally recognised guidelines referring to parenteral nutrition (PN) as an integral part of patient and disease management – Oncology (parts of guidelines relevant to PN presented here, standard formulas only)**

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Patients with cancer	Europe	ESPEN (2017)	ESPEN guidelines on nutrition in cancer patients[37]	Modes of nutrition; when to escalate • If a decision has been made to feed a patient, we recommend EN if oral nutrition remains inadequate despite nutritional interventions (counseling, ONS), and PN if EN is not sufficient or feasible [strength of recommendation: strong; level of evidence: moderate]. Refeeding syndrome • If oral food intake has been decreased severely for a prolonged period of time, we recommend to increase nutrition (oral, EN or PN) slowly over several days and to take additional precautions to prevent refeeding syndrome [strong; low]. Home artificial nutrition • In patients with chronic insufficient dietary intake and/or uncontrollable malabsorption, we recommend home artificial nutrition (PN or EN) in suitable patients [strong; low]. Radiotherapy • We do not recommend PN as a general treatment in radiotherapy but only if adequate oral nutrition/EN is not possible (e.g. in severe radiation enteritis or severe malabsorption) [strong; moderate]. Medical oncology; curative or palliative anticancer drug treatment • In a patient undergoing curative anticancer drug treatment, if oral food intake is inadequate despite counsel ng and ONS, we recommend supplemental EN or, if this is not sufficient or possible, PN [strong; very low]. High-dose chemotherapy and HSCT • During intensive chemotherapy and after HSCT, we recommend to maintain physical activity and to ensure adequate nutritional intake, which may require EN or PN [strong; very low]. • If oral nutrition is inadequate, EN is preferred over PN unless there is severe mucositis, intractable vomiting, ileus, severe malabsorption, protracted diarrhea, or symptomatic GI graft versus host disease [weak; low]. Patients with advanced cancer receiving no anticancer treatment • We recommend offering and implementing nutritional interventions in patients with advanced cancer only after considering together with the patient the prognosis and both the expected benefit on quality of life and potentially survival as well as the burden associated with nutritional care [strong; low].

Table 4.5 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Patients with cancer	US	Academy of Nutrition and Dietetics (2013)	Oncology (ONC) guideline (2013)[38]	• In adult oncology patients who have pre-cachexia or cancer cachexia, prompt and aggressive intervention to address nutrition impact symptoms and preserve or prevent loss of lean body mass and weight should be initiated by the registered dietitian nutritionist. Early rather than later intervention to prevent weight loss is more likely to be effective. The metabolic derangements in cancer cachexia that promote wasting can lead to loss of weight and lean body mass and poor outcomes. Medical nutrition therapy (MNT) in adult patients undergoing chemotherapy or radiation treatment • Adult oncology patients undergoing chemotherapy or radiation treatment should receive MNT, which has been shown to improve treatment outcomes in patients undergoing chemotherapy, radiation or chemoradiotherapy in ambulatory or outpatient and inpatient oncology settings (see Table 4.17 for definition of MNT).
	US	ASPEN (2009)	Nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation (2009)[39]	Adult cancer patients undergoing anti-cancer treatment and HSCT • Nutrition support therapy is appropriate in patients undergoing HSCT who are malnourished and who are anticipated to be unable to ingest and/or absorb adequate nutrients for a prolonged period. When PN is used, it should be discontinued as soon as toxicities have resolved after stem cell engraftment [Grade B].

Table 4.5 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Non-surgical cancer patients	Europe	ESPEN (2009)	ESPEN guidelines on parenteral nutrition: non-surgical oncology[40]	• Nutritional support should be started if a patient is undernourished, if it is anticipated that they will be unable to eat for more than 7 days, or if inadequate food intake (< 60% of estimated energy expenditure) is anticipated for more than 10 days [Grade C]. If nutritional support cannot be given through the enteral route, it has to be delivered by vein. SPN should substitute the difference between the actual oral/enteral intake and estimated requirements [Grade C]. Perioperative PN • Recommended in malnourished candidates for artificial nutrition, when EN is not possible [Grade A]. Anti-cancer therapy • The routine use of PN during chemotherapy, radiotherapy, or combined therapy is not recommended [Grade A]. However, if patients are malnourished or facing longer than 1 week of starvation and EN support is not feasible, PN is recommended [Grade C]. • If patients develop GI toxicity from chemotherapy or radiation therapy, short-term PN is usually better tolerated (and more efficient) than EN to restore the intestinal function and prevent nutritional deterioration. Intestinal failure • In aphagic patients with incurable cancer, survival may be limited more by under-nutrition than by tumor progression. • Long-term PN should be offered to patients with intestinal failure if: (1) enteral nutrition is insufficient; (2) expected survival due to tumor progression is longer than 2–3 months); (3) PN is expected to stabilize or improve performance status and quality of life; (4) the patient desires this mode of nutritional support [Grade C]. Weight-losing cancer patients • SPN is of probable benefit in supporting patients with incurable cancer with weight loss and reduced nutrient intake [Grade B]. HSCT • PN should be reserved for those with severe mucositis, ileus, or intractable vomiting [Grade B]. • No clear recommendation can be made timing of PN initiation. Withdrawal should be considered when patients are able to tolerate approximately 50% of their requirements enterally [Grade C].

Table 4.5 Continued

Patient group	Country	Body	Title	Recommendation, guidance or standard [grade of evidence, where available]
Patients with cancer of the aerodigestive tract	Europe	European Society for Medical Oncology (ESMO) (2013)	Oesophageal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up[41]	• Nutritional support according to the ESPEN guidelines is an integral part of the medical care for patients with esophageal cancer in the curative and palliative settings [II, A]. Management of local/locoregional disease • Nutritional status matters and should be corrected. Endoscopic stenting should not be used in operable patients, and alternative routes of feeding (e.g., with needle catheter jejunostomy) should be preferred [II, A]. • Patient preferences taken into account.
Patients receiving palliative care	US	ASPEN (2017)	Consensus recommendation. When is parenteral nutrition appropriate?[3]	• Do not use PN solely to treat poor oral intake and/or cachexia associated with advanced malignancy. • Limit the use of PN in palliative care to carefully selected candidates, with an expected survival of 2–3 months, for whom oral intake or EN is not feasible. • Evaluate clinical factors and performance status when selecting candidates for PN at the end of life. • Involve patients and caregivers in a clear and complete dialog regarding realistic goals of PN as well as the potential risks and burdens.

ASPEN, American Society of Parenteral and Enteral nutrition; EN, enteral nutrition; ESPEN, European Society for Clinical Nutrition and Metabolism; GI, gastrointestinal; HSCT, hematopoietic stem cell transplant; MNT, medical nutrition therapy; ONS, oral nutritional supplementation; SPN, supplemental parenteral nutrition

Table 4.6 **Grading of recommendations in NICE guidelines** (adapted from NICE 2006)[2]

Grade	Evidence
A	• At least one meta-analysis, systematic review, or RCT rated as 1++(i.e. high-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias), and directly applicable to the target population, or • A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+ (i.e. well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias), directly applicable to the target population, and demonstrating overall consistency of results • Evidence drawn from a NICE technology appraisal
B	• A body of evidence including studies rated as 2++ (i.e. high-quality systematic reviews of case–control or cohort studies, high-quality case–control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal) directly applicable to the target population, and demonstrating overall consistency of results, or • Extrapolated evidence from studies rated as 1++ or 1+
C	• A body of evidence including studies rated as 2+ (i.e. well-conducted case–control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal), directly applicable to the target population and demonstrating overall consistency of results, or • Extrapolated evidence from studies rated as 2++
D	• Evidence level 3 (i.e. non-analytic studies e.g. case reports, case series) or 4 (i.e. expert opinion), or • Extrapolated evidence from studies rated as 2+, or • Formal consensus
D (GPP)	• A good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group

NICE, National Institute of Health and Care Excellence; RCT, randomized controlled trial

Table 4.7 **Grading levels of evidence used in ESPEN guidelines before 2015** (adapted from Schutz 2006)[42]

Grade	Level of evidence	Requirement
A	Ia	Meta-analysis of RCTs
	Ib	At least one RCT
B	IIa	At least one well-designed controlled trial without randomization
	IIb	At least one other type of well-designed quasi-experimental study
	III	Well-designed non-experimental descriptive studies such as comparative studies, correlation studies, case–control studies
C	IV	Expert opinions and/or clinical experience of respected authorities

RCT, randomized controlled trial

Table 4.8 **Levels of evidence and grades of recommendation used in ESPEN guidelines from 2015** (adapted from Bischoff et al., 2015)[43]

Level of evidence	
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1–	Meta-analyses, systematic reviews or RCTs with a high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies High-quality case–control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is casual
2+	Well-conducted case–control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is casual
2-	Case–control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is casual
3	Non-analytic studies (e.g. case reports, case series)
4	Expert opinion
Grade of recommendation	
A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population, or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, or A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results, or Extrapolated evidence from studies rated as 1++ or 1+
O	Evidence level 3 or 4, or Extrapolated evidence from studies rated as 2++ or 2+
GPP	Good practice point/expert consensus: recommended best practice based on the clinical experience of the guideline development group

RCT, randomized controlled trial

Table 4.9 **ESPGHAN and ESPEN grades of evidence and strength of recommendation[10]**

Grades of evidence	Definitions of evidence[44]
High	Further research is unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain
Strength of recommendation	
Strong	We recommend/do not recommend
Weak	We suggest/do not suggest

Table 4.10 **ASPEN grading of guidelines and levels of evidence** (for guidelines published before 2012)[45]

Grading of guidelines	
A	Supported by at least two level I investigations
B	Supported by one level I investigation
C	Supported by at least one level II investigation
D	Supported by at least one level III investigation
E	Supported by level IV or V evidence
Levels of evidence	
I	Large randomized trials with clear-cut results; low risk of false-positive (alpha) and/or false-negative (beta) error
II	Small randomized trials with uncertain results; moderate-to-high risk of false-positive (alpha) and/or false-negative (beta) error
III	Non-randomized cohort with contemporaneous controls
IV	Non-randomized cohort with historical controls
V	Case series, uncontrolled studies, and expert opinion

Since 2012 ASPEN has adopted a revised method of evidence grading based on the GRADE methodology (Druyan 201246) (see Table 4.11)

Table 4.11 **ASPEN grading of guidelines and levels of evidence** (for guidelines published after 2012)[46]

Quality of evidence and definitions			
High	Further research is very unlikely to change our confidence in the estimate of effect		
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate		
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate		
Very low	Any estimate of effect is very uncertain		
Quality of evidence	**Weighing risks vs benefits**	**GRADE recommendation**	**Clinical guideline statement**
High to very low	Net benefits outweigh harms	Strong	We recommend
High to very low	Trade-offs for patient are important	Weak	We suggest
High to very low	Uncertain trade-offs	Further research needed	We cannot make a recommendation at this time

Based on Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology (Druyan 2012)[46]

Table 4.12 Society of Critical Care Medicine (SCCM) and ASPEN determination of the quality of evidence[12]

Quality of evidence	Weighing risks vs benefits	GRADE recommendation	Clinical guideline statement
High to very low	Net benefits outweigh harms	Strong	We recommend
High to very low	Trade-offs for patient are important	Weak	We suggest
High to very low	Uncertain trade-offs	Further research needed	We cannot make a recommendation at this time

GRADE, Grading of Recommendations, Assessment, Development, and Evaluation

Table 4.13 Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup: determination of the quality of evidence

Underlying methodology	
A	(high) RCTs
B	(moderate) Downgraded RCTs or upgraded observational studies
C	(low) Well-done observational studies with control RCTs
D	(very low) Downgraded controlled studies or expert opinion based on other evidence
Factors that may decrease the strength of evidence	
1	Poor quality of planning and implementation of available RCTs, suggesting high likelihood of bias
2	Inconsistency of results, including problems with subgroup analyses
3	Indirectness of evidence (differing population, intervention, control, outcomes, comparison)
4	Imprecision of results
5	High likelihood of reporting bias
Main factors that may increase the strength of evidence	
1	Large magnitude of effect (direct evidence, relative risk > 2 with no plausible confounders)
2	Very large magnitude of effect with relative risk > 5 and no threats to validity (by two levels)
3	Dose-response gradient

RCT, randomized controlled trial

Table 4.14 American College of Gastroenterology: quality of evidence and strength of recommendation

Quality of evidence	Strength of recommendation
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of the effect is very uncertain

Based on Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology (Druyan 2012)[46]

Table 4.15 Academy of Nutrition and Dietetics recommendation ratings

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

Recommendations are categorized in terms of either imperative or conditional statements.

- Imperative statements are broadly applicable to the target population and do not impose restraints on their pertinence. Imperative recommendations may include terms such as “should” or “may” and do not contain conditional text that would limit their applicability to specified circumstances.
- Conditional statements clearly define a specific situation or population. Conditional recommendations are often presented in an if/then format, such that if CONDITION than ACTION(S) because REASONS(S) Fulfillment of the condition triggers one or more guideline-specified actions.

Academy Evidence-Based Nutrition Practice Guidelines published on the Evidence Analysis Library (EAL) are assigned a rating of: strong, fair, weak, consensus, or insufficient evidence based on the following criteria. Criteria for Recommendation Ratings
Adapted by the Academy of Nutrition and Dietetics from the American Academy of Pediatrics, Classifying Recommendations for Clinical Practice Guidelines, Pediatrics.2004;114;874-877s

Table 4.16 Signposts for evidence grading by other international organisations

Recommending body	Signpost for evidence grading
National Pressure Ulcer Advisory Panel (NPUAP), European Pressure Ulcer Advisory Panel (EPUAP) and Pan-Pacific Pressure Injury Alliance (PPPIA)	http://www.npuap.org/wp-content/uploads/2014/08/Quick-Reference-Guide-DIGITAL-NPUAP-EPUAP-PPPIA-Jan2016.pdf
Academy of Nutrition and Dietetics	https://www.andeal.org/recommendation-ratings
American Society for Enteral and Parenteral Nutrition (ASPEN)	http://pen.sagepub.com/content/36/1/77.full.pdf+html
North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN)	https://www.naspghan.org/content/63/en/professional-education/publications/clinical-guidelines
Surviving Sepsis Campaign	http://www.sccm.org/Documents/SSC-Guidelines.pdf
European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN)	http://www.espghan.org/fileadmin/user_upload/guidelines_pdf/Guidelines_2404/Management_of_Pediatric_Ulcerative_Colitis___Joint.24.pdf
European Society for Clinical Nutrition and Metabolism (ESPEN)	http://www.espen.org/files/ESPEN-Guidelines/0__Standard_operating_procedures_for_ESPEN_guidelines_and_consensus_papers_2.pdf

Table 4.17 Definitions of parenteral nutrition according to recommending organization

Organisation	Term	
Academy of Nutrition and Dietetics[47]	Medical nutrition therapy (MNT)	Evidence-based application of the nutrition care process. The provision of MNT (to a patient/client) may include one or more of the following: nutrition assessment/reassessment, nutrition diagnosis, nutrition intervention, nutrition monitoring, evaluation that typically results in the prevention, delay, or management of diseases and/or conditions
	Parenteral nutrition (PN)	IV administration of nutrients such as amino acids, carbohydrate, lipid, and added vitamins and minerals delivered via central (into a large-diameter vein, usually the superior vena cava adjacent to the right atrium) or peripheral route (into a peripheral vein, usually of the hand or forearm)
ASPEN[48]	MNT	Assessment of the nutrition status of a patient, followed by nutrition therapy, ranging from the diet modification to the administration of EN or PN
	PN	The administration of nutrients IV
ESPEN[49]	MNT	Encompasses oral nutritional supplements, enteral tube feeding (EN), and PN. The two latter have traditionally been called artificial nutrition, but this term is suggested to be replaced by MNT.
	PN	Nutrition therapy provided through IV administration of nutrients such as amino acids, glucose, lipids, electrolytes, vitamins and trace elements; can be central through a central venous line, or peripheral through a peripheral IV line
	Total PN (TPN) (also, exclusive PN)	The patient's complete nutritional needs (all macro and micronutrients) are covered by PN and nutrition is not given by any route other than IV
	Supplemental PN (SPN) (also, partial PN or complementary PN)	Nutrition is provided in addition to PN by any route other than IV; for example, when the oral or enteral tube routes cannot independently achieve the defined nutritional care plan target
	Home PN (HPN)	PN used outside the hospital Home TPN or SPN is often used for patients with chronic intestinal failure, malignant obstruction or partial obstruction of the gastrointestinal tract
	Intra-dialytic PN (IDPN)	PN given IV through the venous line of the dialysis circuit, and thus given cyclically during the dialysis session IDPN is not a routine technique for supplemental nutrition therapy but may be indicated to prevent nutritional deterioration in patients receiving dialysis treatment when other methods of nutrition therapy have proved insufficient to meet nutritional and metabolic needs

ASPEN, American Society of Parenteral and Enteral nutrition; ESPEN, European Society for Clinical Nutrition and Metabolism; IV, intravenous

4.3.2 Guidelines: From theory to practice for enhanced patient care

PN is indicated for use in adults, children, and infants across a variety of medical conditions and is therefore considered an integral part of nutrition care. However, given that PN is classified as a high-alert medication (i.e., carries a heightened risk of causing harm if used in error), development of evidence-based guidance on how to safely manage this complex therapy in both the hospital and community setting (including the transition from EN to PN) is essential to maximize clinical benefit while minimising risk for error and harm.

The decision to initiate PN and its implementation requires input from multiple disciplines and agencies and may also involve ethical considerations for certain patients, such as those nearing the end of life and patients who do not have the capacity to take part in the decision-making process. Consequently, internationally recognised organizations such as the European Society for Clinical Nutrition and Metabolism (ESPEN), the European Society for Paediatric Gastroenterology Hepatology and Nutrition, the American Society for Parenteral and Enteral Nutrition (ASPEN), and the UK National Institute for Health and Care Excellence have produced practical guidance for healthcare providers to aid the delivery of PN. Details of key publications focusing on the practical and ethical aspects of PN are shown in Table 4.18.

Table 4.18 Key publications focusing on the practical and ethical aspects of parenteral nutrition

Country/region	Organization	Ages	Title
Europe	ESPEN	All	ESPEN guideline on ethical aspects of artificial nutrition and hydration (2016)[50]
		Adults in home care setting	ESPEN guidelines on parenteral nutrition: home parenteral nutrition (HPN) in adult patients (2009)[51]
	ESPGHAN and ESPEN, supported by the ESPR (2005)	Paediatric	Home parenteral nutrition in children[52]
UK	NICE	Adults in hospital and community	Nutrition support quality standard 24 (2012)[53]
US	ASPEN	All	Standardized Competencies for Parenteral Nutrition Prescribing: The American Society for Parenteral and Enteral Nutrition Mode (2015) I[54]
		All	A.S.P.E.N. Parenteral Nutrition Safety Consensus Recommendations (2014)[55]
		Home and alternate site	A.S.P.E.N. Standards for Nutrition Support: Home and Alternate Site Care (2014)[5]
		Paediatric	Standards for Nutrition Support: Pediatric Hospitalized Patients (2013)[14]

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I PREVALENCE OF MALNUTRITION – Tables A1.1 to A1.8

Table A1.1 **Prevalence of malnutrition or risk of malnutrition in some examples of studies reported after 2002 according to country and healthcare setting – hospital (general)**

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
EUROPE						
Bosnia-Herzegovina	Vanis & Mesihovic (2008)[1]	Randomly chosen hospitalised patients	2200	Hospital (during hospital stay)	**58.3** **52** **55.3**	'MUST' (no further details given) Nutrition Risk Screening 2002 (NRS-2002) (no further details given) MNA (no further details given)
Denmark	Rasmussen et al. (2004)[2]	> 14 years of age	590	Hospital – internal medicine, gastro and orthopaedic surgery (hospitalised patients on the specific day of investigation)	**39.9**	NRS-2002 but note no adjustment made for age
Denmark	Kondrup et al. (2002)[3]	> 15 years of age	740	Hospital – university, regional & local (on admission)	**22**	**Nutritionally at risk = score ≥ 3**. Severe malnutrition = score 3 (BMI < 18.5 kg/m^2, recent weight loss > 5% in the last month or an intake of 0–25% of requirement). Moderate malnutrition = score 2 (BMI 18.5–20.5 kg/m^2, recent weight loss > 5% in the last 2 months or an intake of 25–50% of requirement). Slight malnutrition = score 1 (recent weight loss > 5% in the last 3 months or an intake of 50–75% of requirement). Patients' general condition and disease severity also taken into account
Germany	Pirlich et al. (2006)[4]	> 18 years of age	1886	Hospital – community, teaching & university (on day of admission)	**27.4** (17.6 + 9.8)	SGA (**moderate + severe**)
Germany	Pirlich et al. (2003)[5]	> 18 years of age	502	Hospital – university & district (on day of admission)	**24.2**	SGA (**moderate + severe**). Not reported separately

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Table A1.1 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
Hungary	Lelovics et al. (2008)[6]	All adult patients	1266	Hospital – teaching (on admission)	**41** (13 + 28)	'MUST' (**medium + high**)
Iceland	Westergren et al. (2010)[7]	All adults > 18 years of age	95 (2006) 92 (2007)	Hospital (point prevalence on specified day in 2006 & 2007)	**25** (2006) **17** (2007)	**Nutritionally at risk** defined by presence of at least 2 of: involuntary weight loss; BMI < 20 kg/m² if ≤ 69 years, BMI < 22 kg/m² if ≥ 70 years; eating difficulties according to Minimal Eating Observation Form Version II
Italy	Cereda et al. (2010)[8]	> 18 years of age	559	Regional hospitals with > 400 beds (within 36 hours of admission)	**57.2**	NRS-2002
Italy	Lucchin et al. (2009)[9]	Adults aged > 18 years of age	1284	Regional hospitals with > 400 beds (within 36 hours of admission)	**28.6**	NRS-2002. '**At risk**' of malnutrition = score ≥ 3
Poland	Dzieniszewski et al. (2005)[10]	Adults aged 16–100 years of age	3310	Hospital – teaching, provincial & county (first day of admission & day of discharge)	**10.43** (admission) **11.21** (discharge)	BMI (classification of risk of malnutrition BMI < 20 kg/m²)
Portugal	Amaral et al. (2010)[11]	> 18 years of age	1144	Hospital – university, district & oncology (on admission)	**36**	NRS-2002
Portugal	Amaral et al. (2007)[12]	> 18 years of age	469	Hospital (on admission)	**42**	NRS-2002 (based on BMI, % recent weight loss, recent change in food intake and disease severity). Mild/slight: score 1, moderate: score 2, severe: score 3. For patients > 70 years of age, one point was added to the score. Patients with a total **score of ≥ 3 were considered nutritionally at risk**, patients with a score < 3 were not considered nutritionally at risk
Republic of Ireland	Russell & Elia (2012)[13] (spring 2011)	Adults ≥ 18 years of age	1102	Hospital (within 72 hours of admission)	**27** (7 + 20)	'MUST' (**medium + high**)

Table A1.1 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
Republic of Ireland	Russell & Elia (2011)[14] (winter 2010)	Adults ≥ 18 years of age	1602	Hospital (within 72 hours of admission)	**33** (8 + 25)	'MUST' (**medium + high**)
Spain	Velasco et al. (2011)[15]	≥ 18 years of age	400	University hospitals (within 36 hours of admission)	**34.5** **31.5** (14 +17.5) **35.3** (28.5 + 6.8) **58.5** (44 + 14.5)	NRS-2002 MUST (**medium + high**) SGA (**suspected malnourishment + severe**) MNA (**at risk + poor nutritional status**)
Spain	Martinez Olmos et al. (2005)[16]	> 18 years of age	360	Hospital (stratified random sample of hospitalised patients on specified days)	**46.9** (37.2 + 9.7)	SGA (**moderate + severe**)
Spain	Planas et al. (2004)[17]	Adult patients	400	Hospital – university-affiliated (within 48 hours of admission)	**26.7** (anthropometry) **46** (SGA)	Anthropometry (classification as undernourished: BMI < 18.5 kg/m^2 or BMI < 20 kg/m^2 and TSFT or Arm Muscle Circumference < 15th centile) SGA (**moderate + severe**). Not reported separately
Spain	Pablo et al. (2003)[18]	> 18 years of age	60	Hospital – public general (within 48 hours of admission)	**63.3** (36.7, 18.3 + 8.3) SGA 90 (6.7, 60 + 23.3) Nutritional Risk Index **80** (20, 15 + 45) INA **78.3** Combined Index	SGA (**mild, moderate + severe**) NRI: 1.519 x serum albumin (g/l) + 41.7 x (present/usual weight)) (**mild:** NRI 97.5–100, **moderate:** NRI 83.5 to < 97.5, **severe:** NRI < 83.5 Instant Nutritional Assessment (INA) **1st degree:** serum albumin ≥ 3.5 g/dl; blood lymphocyte count < 1500 cells/mm^3, **2nd degree:** serum albumin < 3.5 g/dl; blood lymphocyte count < 1500 cells/mm^3, **3rd degree:** serum albumin < 3.5 g/dl; blood lymphocyte count ≥ 1500 cells/mm^3, **4th degree:** serum albumin < 3.5 g/dl; blood lymphocyte count < 1500 cells/mm^3

Table A1.1 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment	Prevalence % (risk category)	Method and details of risk category where reported
Sweden	Westergren et al. (2009)[19]	>18 years of age	1197 824 370	Large hospitals > 500 beds Medium hospitals 200–500 beds Small hospitals < 200 beds (point prevalence, data collected on hospitalised patients on a single day)	**34** (26.4 + 7.6) **26.2** (21.1 + 5.1) **21.6** (17.7 + 3.9)	**Moderate/high risk** of under-nutrition defined as the occurrence of at least two of: involuntary weight loss, BMI below limit (BMI < 20 kg/m^2 if ≤ 69 years, BMI < 22 kg/m^2 if ≥ 70 years), eating difficulties according to Minimal Eating Observation Form – Version II
Sweden	Westergren et al. (2008)[20]	All patients	874	Hospitals (hospitalised patients, timing not specified)	**27**	At risk of under-nutrition if 2–3 of the following 3 criteria fulfilled: (1) involuntary weight loss (irrespective of time and amount), (2) BMI below limit (< 20 kg/m^2 if ≤ 69 years, < 22 kg/m^2 if ≥ 70 years), and (3) presence of eating difficulties. **Low risk:** 1 criterion fulfilled, **moderate risk:** 2 criteria fulfilled, **high risk:** 3 criteria fulfilled. Not reported separately
Switzerland	Imoberdorf et al. (2010)[21]	All adult medical admissions	32837	Hospital (on day of admission)	**18.2** (range 13–20% across 7 participating hospitals)	NRS-2002. Severe under-nutrition or high risk for developing under-nutrition: score ≥ 3
Switzerland	Venzin et al. (2009)[22]	All medical admissions	430	Hospital – medium-sized general teaching (MNA within 24 hours of admission, physician's assessment on admission)	**30.5** (20.1 + 10.4) **14**	MNA. **At risk of malnutrition**: score of 17–23.5, **frank malnutrition** score of < 17 Physician's assessment (judgement based on patient history, physical examination and laboratory results)

Table A1.1 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
Switzerland	Kyle et al. (2006)[23]	All adult medical/ surgical admissions	995	Hospital (on hospital admission)	**39** (29 + 10) **37** (10 +27) **28** (19 + 9) **25** (20 + 5)	SGA (**moderate + severe**) MUST (**medium + high**) NRS-2002 (**medium + high risk**) NRI (**medium + high risk**) (1.519 x serum albumin g/l) = (14.7 x present/usual body weight [BW]). NRI score > 100 indicates no risk, 97.5–100 low risk, 83.5–97.5 medium risk, ≤ 83.5 high risk
Switzerland	Kyle et al. (2002)[24]	All adult medical/ surgical admissions	995	Hospital (within 3 hours of admission)	**61.4** (38.3 + 23.1)	SGA (**moderate + severe**)
The Netherlands	Meijers et al. (2009)[25]	≥ 18 years of age	8028	Hospital (cross-sectional, point prevalence on specified day)	**23.8**	Malnutrition defined according to one of the 3 following criteria: (1) BMI < 18.5 kg/m^2 (2) unintentional weight loss (6 kg in previous 6 months or 3 kg in the previous month) or (3) BMI 18.5–20 kg/m^2 in combination with no nutritional intake for 3 days or reduced intake for > 10 days
The Netherlands	Bavelaar et al. (2008)[26]	All newly admitted patients	395	Hospital general medical wards (within 72 hours of admission)	**31.9** (31.1 + 0.8)	BMI and/or SNAQ score (**severe:** BMI < 18.5 kg/m^2 and/or SNAQ score ≥ 3 points + **moderate:** BMI 18.5–20.0 kg/m^2 and/or SNAQ score ≥ 2 points)
The Netherlands	Kruizenga et al. (2003)[27]	> 18 years of age	6150	Hospital (convenience sample, timing not clear)	**26** (13 + 13)	Involuntary weight loss (**at risk:** 5–10% unintentional weight loss during the past 6 months + **malnourished:** unintentional weight loss > 10% during the past 6 months)

Table A1.1 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
Turkey	Nursal et al. (2005)[28]	All adult patients admitted to wards	2211	University referral centre (within 48 hours of admission)	**11** **15.6**	SGA (**moderate + severe**). Not reported separately Combination criteria: diagnosed with malnutrition if positive for at least 2 of the following 6 criteria: (1) > 10% weight loss during the past 6 months; (2) BMI < 20 kg/m^2; (3) TSFT no higher than the 5th centile; (4) MAMC no higher than the 5th centile; (5) serum albumin level < 3 g/dl; and (6) serum prealbumin level < 0.2 g/dl
UK	Lamb et al. (2009)[29]	Adult inpatients ≥ 16 years of age	328 226	Hospital – general medicine, general surgery, orthopaedics and critical care (all patients assessed on a single day, 1st May 2007)	**43.9** (11.9 + 32) **32.7** (19 + 13.7)	'MUST' (**medium + high**) Northumbria Nutrition Score Chart (NNSC) validated for reproducibility and ease of use only. Patients scored according to psychological state, BMI, weight loss, ability to swallow and co-morbid medical illness. **Low** risk of malnutrition: 0-3, **moderate** risk: 4–5, **high** risk: ≥ 6
UK	Russell & Elia (2012)[13] (spring 2011)	Adults ≥ 18 years of age	7541	Hospital (within 72 hours of admission)	**25** (7 + 18)	'MUST' (**medium + high**)
UK	Russell & Elia (2011)[14] (winter 2010)	Adults ≥ 18 years of age	9669	Hospital (within 72 hours of admission)	**34** (14 + 21)	'MUST' (**medium + high**)
UK	Russell & Elia (2009)[30] (summer 2008)	Adults ≥ 18 years of age	5089	Hospital (within 72 hours of admission)	**28** (6 + 22)	'MUST' (**medium + high**)
UK	Russell & Elia (2008)[31] (autumn 2007)	Adults ≥ 18 years of age	9336	Hospital (within 72 hours of admission)	**28** (6 + 22)	'MUST' (**medium + high**)

Table A1.1 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
USA & CANADA						
Canada	Singh et al. (2006)[32]	Adults ≥ 20 years of age	48	Hospital – medical admission/teaching unit (within 10 days of admission)	**69** (39 + 30)	SGA (**moderate + severe**)
USA	Robinson et al. (2003)[33]	≥ 18 years of age	320	Hospital – tertiary (blood taken within 48 hours of admission & nurse screening within 24 hours of admission)	**51** **33**	Plasma prealbumin concentration Standard hospital nutrition screening/assessment protocol (nursing screening questionnaire regarding nutritional status and nutritional intake). If any positive responses, a dietitian informed and perform a formal nutrition assessment within 48 hours
USA	Liang et al. (2008)[34]	Adults 18–80 years of age	200	Hospitals – teaching, Baltimore, USA (newly admitted + 2 weeks post admission or discharge)	**51** (admission) **41.4** (discharge or 2 weeks post discharge)	NRS-2002
CENTRAL & SOUTH AMERICA						
Argentina	Wyszynski et al. (2003)[35]	Adults > 18 years of age	997	Hospital (not specified June-November 1999)	**47.3** (36.1 + 11.2)	SGA (**moderate + severe**)
Brazil	Leandro-Merhi et al. (2011)[36]	Adults 20-60 years of age	230	Hospital – surgical wards (preoperatively)	**20.1** (19.3 + 0.8)	SGA (**slightly malnourished + moderately malnourished**)
Brazil	Correia & Campos (2003)[37]	Adults > 18 years of age	9348	Hospitals – general and at least 200 beds	**50.2** (39.0 + 11.2)	SGA (**moderate + severe**)
Cuba	Barreto Penié (2005)[38]	Adults > 19 years of age	1905	Hospitals – secondary & tertiary (not specified)	**41.2** (30.1 + 11.1)	SGA (**moderate + severe**)

Table A1.1 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
ASIA						
China	Liang et al. (2008)[34]	Adults 18–80 years of age	300	Hospitals – teaching (newly admitted and 2 weeks post admission or discharge)	**39** (admission) **38.5** (discharge or 2 weeks post admission)	NRS-2002
Singapore	Lim et al. (2011)[39]	Adults 18–74 years of age	818	Acute tertiary hospital (within 48 hours of admission)	**29** (25 + 4)	SGA (**moderate + severe**)
Singapore	Raja et al. (2004)[40]	Adults	715 (admission episodes) 681 (patient episodes) 152 (cases)	Hospitals – medical & surgical wards (within 72 hours of admission by dietitian using MST)	**14.7** **22.3** **69.1** (37.5 + 31.6)	Those episodes identified as at risk of malnutrition/malnourished by both MST and SGA Initial assessment by dietitians using Ferguson, Bauer, Banks & Capra MST. MST is a questionnaire developed and validated in an Australian hospital. Patients are scored based on the following criteria: recent weight loss; if yes, how much; eating poorly due to decreased appetite? Score ≥ 2 classified as at **risk of malnutrition** SGA (**moderate + severe**)
Vietnam	Pham et al. (2006)[41]	Abdominal surgery patients	438 total of which major surgery 274	Hospital – general (not specified)	**55.7** (28.8 + 26.9) **77.7** (35.4 + 42.3)	SGA (**moderate + severe**) SGA (**moderate + severe**)
MIDDLE EAST						
Iran	Hosseini et al. (2006)[42]	≥ 18 years of age	156	Hospital > 400 beds (within 24 hours of admission + on discharge)	**5.8** (admission) **10.9** (discharge) **0.6** (admission) **1.3** (discharge)	BMI **severely undernourished** < 16 kg/m^2 BMI **undernourished** < 18.5 kg/m^2

Table A1.1 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
AUSTRALIA & NEW ZEALAND						
Australia & New Zealand	Agarwal et al. (2012)[43]	≥ 18 years of age	3080	Acute care hospitals (data collected over 1–3 24 hour periods during June & July 2010)	**32** **30** (24 + 6) **8** **41**	Combined SGA + BMI SGA (**suspected or moderately malnourished + severely malnourished**) BMI < 18 kg/m^2 Malnutrition risk (MST)
Australia	Thomas et al. (2007)[44]	> 18 years of age	64	Hospital Acute Admissions Unit (within 48 hours of admission)	**53** (43.8 + 9.4)	Patient Generated-SGA (PG-SGA) (**moderately malnourished + severely malnourished**). An extension of SGA, with a higher numerical score reflecting a greater risk of deterioration of nutritional status. PG-SGA global rating can identify malnutrition and the score is used to assess subtle changes in nutritional status/nutritional risk that cannot be detected by SGA. (No further details given)
Australia	Lazarus & Hamlyn (2005)[45]	≥ 18 years of age	324	Hospital: not-for-profit private (not specified August–October 1999)	**42.3** (36.4 + 5.9)	SGA (**moderate + severe**)
Australia	Banks et al. (2007)[46]	All available subjects (excluding paediatric, obstetric, mental health and same-day patients)	774 1434	Hospitals (a single day for each facility 2002 + 2003)	**34.7** (27.8 + 7.0) **31.4** (26.1 + 5.3)	Mean MNA (**moderate + severe**) Mean MNA (**moderate + severe**)

Table A1.2 **Prevalence of malnutrition or risk of malnutrition in some examples of studies reported after 2002 according to country and healthcare setting – hospital (older people)**

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
EUROPE						
Belgium	Vanderwee et al. (2011)[47]	≥ 75 years of age	2094	Hospital – geriatric wards (cross-sectional survey between 16th May &15th June 2007)	**31.9** (range 0–90.9% across participating wards)	MNA-SF
Germany	Volkert et al. (2010)[48]	≥ 75 years of age	205	Community hospital – geriatric ward (first day after admission)	**25.4** **60** (34.6+ 25.4) **90.2** (60.0 + 30.2) **5.9**	BMI (**undernourished** < 22 kg/m²) SGA (**moderate + severe**) MNA (**at risk + undernourished**) Clinical judgement of physician
Italy	Orsitto et al. (2009)[49]	> 65 years of age	588	Hospital – geriatric ward (on admission)	**82** (58 + 24)	MNA (**at risk + malnourished**)
Norway	Söderhamn et al. (2011)[50]	> 65 years of age	153 154 153 158	Hospital – medical wards (during the first days on the wards)	**60.8** (43.8 + 17) **64.9** **44.4** **62** (29.1 + 32.9)	MNA (**at risk + undernourished**) MNA-SF (**at risk**) NRS-2002 (**at risk**) Nutritional Form for the Elderly (Norwegian) (NUFFE-NO) (≥ 6 indicating **medium risk of under-nutrition** + ≥ 11 indicating **high risk of under-nutrition**). Ordinal scale containing 15 3-point items: weight loss, changes in dietary intake, appetite, intake of prepared food, portion size, intake of fruit and veg, possibility of obtaining food products, company at meals, activity, dental and swallowing difficulties, fluid intake, GI problems, eating assistance, number of drugs, difficulties in eating because of impaired health

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Table A1.2 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
Portugal	Cansado et al. (2009)[51]	≥ 65 years of age	341	Hospital – surgery (within 48 hours of admission and 24 hours of discharge)	**93.3** (0.0 + 93.3) admission **61.5** (8.2 + 53.3) discharge	'MUST' (**medium + high**)
					77.9 (26.6 + 51.3) admission **77.1** (33.7 + 43.4) discharge	MNA (**at risk + undernourished**)
			190	Hospital – medicine (within 48 hours of admission and 24 hours of discharge)	**92.6** (0.0 + 92.6) admission **50.9** (15.2 + 35.7) discharge	'MUST' (**medium + high**)
					91.5 (48.9 + 42.6) admission ***95.7*** (44.7 + 51.0) discharge	MNA (**at risk + undernourished**)
Republic of Ireland	Russell & Elia (2012)[13] (spring 2011)	Adults ≥ 65 years of age	Total study population *n* = 1262, of which 51% aged ≥ 65 years. ('MUST' data only available for *n* = 1102)	Hospital (within 72 hours of admission)	**28**	'MUST' (**medium + high**)

Table A1.2 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
Republic of Ireland	Russell & Elia (2011)[14] (winter 2010)	Adults ≥ 65 years of age	Total study population *n* = 1636, of which 48% aged ≥ 65 years. ('MUST' data only available for *n* = 1602)	Hospital (within 72 hours of admission)	**34**	'MUST' (**medium + high**)
Spain	de Luis et al. (2011)[52]	> 65 years of age	493	Hospital (not specified)	**72.1** (49.6 + 22.5)	MNA (at risk + undernourished)
Spain	de Luis & Lopez Guzman (2006)[53]	> 70 years of age	213	Hospital internal medicine departments (randomly selected hospitalised patients)	**74.1** (23.9 + 50.2)	MNA (**malnourished:** score < 17 points + **at risk:** score 17–23.5)
Switzerland	Drescher et al. (2010)[54]	78–89 years of age	104	Hospital – geriatric ward (within 3 days of admission)	**70** (48 + 22) **34**	MNA (**at risk + undernourished**) NRS-2002
Switzerland	Imoberdorf et al. (2010)[21]	Adults	Total study population *n* = 32,837, no details of number of patients aged > 65 years available	Hospital – general medical departments 65–84 years of age > 85 years of age (day of admission)	 **22** **28**	 NRS-2002 NRS-2002 Patients ≥ 70 years were given an additional score point

Table A1.2 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
UK	Russell & Elia (2012)[13] (spring 2011)	Adults ≥ 65 years of age	Total study population *n* = 9132, of which 56% aged ≥ 65 years. ('MUST' data only available for *n* = 7541)	Hospital (within 72 hours of admission)	**28**	'MUST' (**medium + high**)
UK	Russell & Elia (2011)[14] (winter 2010)	Adults ≥ 65 years of age	Total study population *n* = 9932, of which 59% aged ≥ 65 years. ('MUST' data only available for *n* = 9669)	Hospital (within 72 hours of admission)	**39**	'MUST' (**medium + high**)
UK	Russell & Elia (2009)[30] (summer 2008)	Adults ≥ 65 years of age	Total study population *n* = 6068, of which 52% aged ≥ 65 years. ('MUST' data only available for *n* = 5089)	Hospital (within 72 hours of admission)	**32**	'MUST' (**medium + high**)

Table A1.2 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
UK	Russell & Elia (2008)[31] (autumn 2007)	Adults ≥ 65 years of age	Total study population *n* = 9563, of which 55% aged ≥ 65 years. ('MUST' data only available for *n* = 9208)	Hospital (within 72 hours of admission)	**30**	'MUST' (**medium + high**)
UK	Stratton et al. (2006)[55]	Acutely ill older people	150	Hospital elderly care wards (within 48–72 hours of admission)	**58** (17 + 41)	'MUST' (**medium + high**)
USA & CANADA						
USA	Covinsky et al. (1999)[56]	> 70 years of age	369	Hospital – general medical unit (between 2nd & 4th day after discharge)	**40.7** (24.4 + 16.3)	SGA (**moderate + severe**)
CENTRAL & SOUTH AMERICA						
Brazil	Leandro-Merhi et al. (2011)[36]	≥ 60 years of age	120	Hospital – surgical wards (preoperatively)	**43.9** (32.9 + 11.0)	MNA (**at risk + malnourished**)
Brazil	Coelho et al. (2006)[57]	≥ 60 years of age	192	Hospital – geriatric unit (between October 2004 & March 2005)	**29.7** **54.7**	BMI (WHO classification **underweight** < 18.5 kg/m^2) BMI (Nutrition Screening Initiatives classification **underweight** < 22 kg/m^2)

Table A1.2 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
ASIA						
China	Lei et al. (2009)[58]	> 60 years of age	184	Hospital (within 5 days of admission)	**72.8** (53.2 + 19.6)	MNA (**at risk + malnourished**)
China	Shum et al. (2005)[59]	≥ 60 years of age	77 120	Convalescent & rehabilitation hospital – geriatric wards (within 48 hours of admission)	**61.1** (44.2 +16.9) **16.7**	Chinese MNA (**at risk:** 18.5–23.5 + **malnourished:** score < 18.5) (no further details given) BMI < 18.5 kg/m^2 and albumin level of < 35g/l: at risk
China	Woo et al. (2005)[60]	≥ 65 years of age	867	Hospitals & nursing homes (not specified)	**36** (25.8 + 10.1)	Chinese Nutrition Screening (CNS) (**at risk + malnourished**). A questionnaire based on MNA, specifically orientated to Chinese elderly in hospitals and nursing homes. 16 questions regarding lifestyle, health and dietary care tailored to suit Chinese healthcare system, diet, culture and customs. It omits anthropometry and has a maximum score of 32. The higher the score, the better the nutrition status. Further detail unavailable
India	Karmakar et al. (2010)[61]	> 60 years of age	76	Hospital – tertiary, inpatients and outpatients (not specified)	**27.6** (of which 61.9) **42.1** (of which 57.1)	BMI undernourished < 18.5 kg/m^2 (**severely undernourished** < 16 kg/m^2) IBW undernourished < 85% (**severely undernourished** < 70%)
MIDDLE EAST						
Israel	German et al. (2008)[62]	≥ 65 years of age	195	Hospital (within 24 hours of admission)	**39**	MNA (no further details given)

Table A1.2 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
AUSTRALIA & NEW ZEALAND						
Australia	Vivanti et al. (2011)[63]	Older people	194	Hospital – geriatric assessment and rehabilitation unit (within 72 hours of admission)	**39** (35.1 + 3.6)	SGA (**moderate + severe**)
Australia	Adams et al. (2008)[64]	≥ 70 years of age	100	Hospital – tertiary (within 24–48 hours of admission)	**91** (61 + 30)	MNA (**at risk + malnourished**)

Table A1.3 **Prevalence of malnutrition or risk of malnutrition in some examples of studies reported after 2002 according to country and healthcare setting – outpatients**

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting†	Prevalence % (risk category)	Method and details of risk category where reported
EUROPE						
Italy	Bozzetti (2009)[65]	Adults with cancer	1000	Outpatients	**33.8** **39.7**	NRS-2002. Score ≥ 3 = **malnourished** Significant weight loss (≥ 10%)
The Netherlands	Leistra et al. (2009)[66]	> 18 years of age	2288	General outpatient departments in 9 hospitals	**7.1** (2 + 5.1) Wide variation depending on type of department	**Moderate malnutrition** = BMI ≥ 18.5 kg/m^2 with 5–10% unintentional weight loss in the last 6 months. **Severe malnutrition** = one or more of the following present: BMI < 18.5 kg/m^2 and/or intentional weight loss of > 5% in the last 1 month or > 10% in the last 6 months
The Netherlands	Neelemaat et al. (2008)[67]	Adults aged > 18 years	705 979	General outpatients Preoperative outpatients	**12** (7 + 5) **17** (9 + 8)	SNAQ. 3 questions: 'Did you lose weight unintentionally (> 6 kg in the last 6 months and/or > 3 kg in the last 1 month)? Did you use supplemental drinks or tube feeding over the last month? Did you experience difficulties when eating and drinking over the last month? (**moderate** = score of ≥ 2 and severe = score of ≥ 3)
The Netherlands	Vermeeren et al. (2006)[68]	Adults aged 40–75 years with COPD	389	Outpatients in 39 centres	**27**	Nutritional depletion defined as BMI ≤ 21 kg/m^2 and or Fat-Free Mass Index (FFMI) ≤ 15 kg/m^2 (females) or ≤ 16 kg/m^2 (males)
Turkey	Halil (2009)[69]	Older people aged ≥ 65 years	2327	Geriatric medicine outpatient clinic	**28**	MNA-SF. **Malnutrition risk** = MNA ≤ 11 points
UK	Collins et al. (2010)[70]	Adults with COPD	425	Outpatients (overall) Mild disease Moderate disease Severe disease	**21** (7 + 14) **13** **12** **26**	'MUST' (**medium + high risk**)
UK	Rust et al. (2010)[71]	Adults	321	General hospital outpatients	**15.9** (10.9 + 5)	'MUST' (**medium + high risk**)

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Table A1.3 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting†	Prevalence % (risk category)	Method and details of risk category where reported
UK	Renshaw et al. (2008)[72]	Adults with cancer	207	Medical oncology outpatients	**83** (upper GI) **76** (lung/ mesothelioma) **73** (gynaecological) **60** (breast) **50** (colorectal) **45** (urological)	Nutritional risk determined using local trust validated Nutrition Screening Tool (includes questions on unintentional weight loss, appetite reduction in previous 3–6 months, height, usual and current weight and BMI). Details of validation not given
UK	Stratton et al. (2004)[73]	Adults	50	Gastroenterology outpatients	**30** (18 + 12)	'MUST' (**medium + high risk**)

†Timing not specified in studies; assume on attendance during the period of the study

Table A1.4 **Prevalence of malnutrition or risk of malnutrition in some examples of studies reported after 2002 according to country and healthcare setting – care homes (majority of participants were older people)**

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
EUROPE						
Austria	van Nie-Visser et al. (2009)[74]	Residents of care homes (age not reported)	221	Care homes (on admission)	**28**	**Malnutrition** prevalence measured by assessing BMI, undesired weight loss and nutritional intake (no further details given)
Denmark	Beck & Ovesen (2002)[75]	> 65 years of age	180	Nursing homes (not specified)	**33** (22)	BMI < 20 kg/m^2 (BMI < 18.5 kg/m^2)
Finland	Suominen et al. (2009)[76]	Older people	1043	Long-term elderly care facilities (all patients during 2 weeks in September 2003)	**97.4** (40.7 + 56.7) **15.2**	**At risk** MNA 17–23.5 points, malnourished MNA < 17 points Nurse assessment using BMI
France	Bourdel-Marchasson et al. (2009)[77]	Older people	517	Nursing Homes† (random sample of 15 residents from each home at the time of the interview visit)	**54.9** (13.1)	**At risk** MNA-SF score ≤ 11 (of whom **malnourished** MNA score < 17)
			84	Long-term care homes† (random sample of 15 residents from each home at the time of the interview visit)	**90.4** (42.9)	**At risk** MNA-SF score ≤ 11 (of whom **malnourished** MNA score < 17)
Germany	Volkert et al. (2011)[78]	> 65 years of age	350	Nursing home (not specified)	**79.6** (52.9 + 26.7)	MNA (**at risk + malnourished**)
Germany	Smoliner et al. (2009)[79]	Older people	114	Nursing home (not specified)	**80.7** (57.9 + 22.8)	**At risk** MNA 17–23.5 points, **malnourished** < 17 points
Germany	van Nie-Visser et al. (2009)[74]	Residents of care homes (age not reported)	2444	Care homes (on admission)	**26**	**Malnutrition** prevalence measured by assessing BMI, undesired weight loss and nutritional intake (no further details given)

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Table A1.4 **Prevalence of malnutrition or risk of malnutrition in some examples of studies reported after 2002 according to country and healthcare setting – care homes (majority of participants were older people)**

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
Germany & Austria	Valentini et al. (2009)[80]	> 50 years age	2137	Nursing homes (one-day cross-sectional audit on 22nd February 2007)	**16.7** (13.9) **9.2** (14.3)	**Malnourished:** BMI < 20 kg/m^2 (at **risk of malnutrition:** BMI 20–21.9 kg/m^2) Subjectively assessed by staff. (**Malnourished (at risk of malnutrition**)
Germany	Norman et al. (2007)[81]	Age range 79.1–91.4 years	112	Nursing home (not specified)	**80.3** (71.4 + 8.9)	MNA (**at risk + malnourished**)
Hungary	Lelovics et al. (2009)[82]	Older people > 60 years	1381	Nursing homes (unclear)	**38.1** (8.0 + 30.1)	'MUST' (**medium + high**)
Italy	Santomauro et al. (2011)[83]	≥ 65 years of age	463	Nursing homes	**80.8** (58.3 + 22.5)	MNA (**at risk + malnourished**)
Italy	Cereda et al. (2009)[84]	Older people	241	Long-term care for older people (not specified)	**51.8** (39 + 12.8) **56.8** (36.1 + 20.7)	**At risk** MNA 17–23.5 points, **malnourished** < 17 points GNRI **moderate risk:** GNRI 92–98, **high risk:** GNRI < 92
Italy	Pezzana et al. (2009)[85]	Older people	738	Nursing homes (not specified)	**78**	MNA-SF (no further details given)
Republic of Ireland	Russell & Elia (2012)[13] (spring 2011)	> 18 years of age*	29 (Note: only 6 homes took part)	Care homes (overall) Nursing homes only Residential homes only Other homes (restricted to adults admitted within the previous 6 months)	**21** (7 + 14)** **25** **0** **20**	'MUST' (**medium + high**)

Table A1.4 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
Republic of Ireland	Russell & Elia (2011)[14] (winter 2010)	> 18 years of age*	153	Care homes (overall) Nursing homes only Residential homes only Other homes (restricted to adults admitted within the previous 6 months)	**32** (16 + 16)** (*n* = 143) **34** **9** **32**	'MUST' (**medium + high**)
Spain	Ruiz-Lopez et al. (2003)[86]	Women aged 72–98 years	89	Nursing homes – private	**69.7** (61.8 + 7.9)	MNA (**at risk + malnourished**)
Sweden	Westergren et al. (2008)[20]	All residents*	1726	Special accommodation –nursing home-type setting (not specified)	**27**	At risk of under-nutrition if 2–3 of the following 3 criteria fulfilled: (1) involuntary weight loss (irrespective of time and amount), (2) BMI below limit (< 20 kg/m^2 if ≤ 69 years, < 22 kg/m^2 if ≥ 70 years), and (3) the presence of eating difficulties. **Low risk:** 1 criterion fulfilled, **moderate risk:** 2 criteria fulfilled, **high risk:** 3 criteria fulfilled. Not reported separately
The Netherlands	Meijers et al. 2009)[25]	≥ 18 years of age*	2061	Nursing homes (cross-sectional, point prevalence on specified days)	**19.2**	Malnutrition defined according to one of the 3 following criteria: (1) BMI < 18.5 kg/m^2 (2) unintentional weight loss (6 kg in previous 6 months or 3 kg in previous month) or (3) BMI 18.5–20 kg/m^2 in combination with no nutritional intake for 3 days or reduced intake for > 10 days
The Netherlands	van Nie-Visser et al. (2009)[74]	Residents of care homes (age not reported)	583	Care homes (on admission)	**27**	Malnutrition prevalence measured by assessing BMI, undesired weight loss and nutritional intake (no further details given)
The Netherlands	Kruizenga et al. (2003)[27]	> 18 years of age*	808	Nursing homes (convenience sample, timing not clear)	**18** (12 + 6)	**At risk of malnutrition:** 5–10% unintentional weight loss during the past 6 months , **malnourished:** unintentional weight loss > 10% during the past 6 months

Table A1.4 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
UK	Parsons et al. (2010)[87]	Residents of care homes*	1176	Care homes – overall (not specified)	**39** (14 + 25)	'MUST' (**medium + high**)
UK	Parsons et al. (2009)[88]	Residents of care homes*	1176	Nursing homes Residential homes (cross-sectional survey)	**40** **36**	'MUST' (**medium + high**)
UK	Russell & Elia (2012)[13] (spring 2011)	Adults ≥ 18 years of age*	523	Care homes (overall) Nursing homes only Elderly mentally ill homes only Residential homes only Other homes (restricted to adults admitted within the previous 6 months)	**41** (16 + 25)** **46** **40** **41** **39**	'MUST' (**medium + high**)
UK	Russell & Elia (2011)[14] (winter 2010)	Adults ≥ 18 years of age*	821	Care homes (overall) Nursing homes only Elderly mentally ill homes only Residential homes only Other homes (*n* = 815) (restricted to adults admitted within the previous 6 months)	**37** (15 + 23)** **45** **26** **30** **36**	'MUST' (**medium + high**)

Table A1.4 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
UK	Russell & Elia (2009)[30] (summer 2008)	> 18 years of age*	614	Care homes (overall) Nursing homes only Elderly mentally ill homes only Residential homes only Other homes (*n* = 581) (restricted to adults admitted within the previous 6 months)	**42** (11 + 30)** **46** **59** **36** **43**	'MUST' (**medium + high**)
UK	Russell & Elia (2008)[31] (autumn 2007)	> 18 years of age*	1610	Care homes (overall) Nursing homes only Residential homes only Other homes (restricted to adults admitted within the previous 6 months)	**30** (10 + 20) **35** **22** **32**	'MUST' (**medium + high**)
UK	Elia & Stratton (2005)[89]	> 65 years of age	202	Institution (secondary analysis of the National Diet and Nutrition Survey)	**20.8** (8.9 + 11.9)	'MUST' type criteria applied, i.e. a score of current weight status added to the weight loss score (**medium + high**)

Table A1.4 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
ASIA						
China	Woo et al. (2005)[60]	≥ 65 years of age	867	Nursing homes & hospitals (not specified)	**36** (25.8 + 10.1)	CNS (**at risk + malnourished**). A questionnaire based on MNA, specifically orientated to Chinese elderly in nursing homes and hospitals. 16 questions regarding lifestyle, health and dietary care tailored to suit Chinese health care system, diet, culture and customs. It omits anthropometry and has a maximum score of 32. The higher the score, the better the nutrition status. Further details unavailable
Singapore	Chan et al. (2010)[90]	Older people	154	Nursing homes – voluntary welfare (not specified)	**52** **97** **39**	BMI – **underweight** < 18.5 kg/m^2 MNA-SF (**at risk**) MNA (**malnourished** score < 17)
Taiwan	Chang & Roberts (2011)[91]	≥ 60 years of age with dementia	83	Nursing homes with > 15 residents with dementia (not specified)	**90.4** **19**	MNA-SF BMI (< 18.5 kg/m^2)
MIDDLE EAST						
Saudi Arabia	Alhamdan (2004)[92]	Adult males < 60 years of age Elderly males ≥ 60 years of age	39 45	Nursing homes (not specified)	**12.8** **11.1**	BMI – **underweight** < 18.5 kg/m^2

Table A1.4 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
AUSTRALIA & NEW ZEALAND						
Australia	Grieger et al. (2009)[93]	Aged care residents	74	High-level care nursing homes & low-level care hostels (not specified)	**53** (37 + 16)	MNA (**at risk + malnourished**)
Australia	Gaskill et al. (2008)[94]	Older people	346	Residential aged care facilities (6-week period, late 2005)	**49.5** (43.1 + 6.4) (range 72.1–31.8% across 8 facilities)	SGA (**moderate + severe**)
Australia	Banks et al. (2007)[46]	Older people	381 (2002) 458 (2003)	Residential aged care facilities (a single day for each facility 2002 + 2003)	**50.0** (41.6 + 8.4) **49.2** (41.6 + 8.4)	Median MNA (**moderate + severe**) Median MNA (**moderate + severe**)

†In France, long-term care homes receive older people with functional impairment and severe disease requiring continuous medical care; in contrast, nursing homes do not provide continuous presence of nurses
*Participants' age in years mean (±SD): special accommodation 85.4 (±7.7),[20] nursing homes 80.3 (±10.0),[25] nursing homes well-nourished 80 (±11), at risk 81 (±11), malnourished 83 (±9),[27] care homes 86.5 (±8.7),[87;88] UK care homes 83.3 (±9.5),[30] 84.2 (±8.4),[31] 83.1 (±9.7),[14] 80.4 (±11.8)[13]. Republic of Ireland care homes 80.8 (±9.3),[14] 83.5 (±7.0)[13]
** Figures rounded to the nearest 1%

Table A1.5 **Prevalence of malnutrition or risk of malnutrition in some examples of studies reported after 2002 according to country and healthcare setting – sheltered accommodation (majority of participants were older people)**

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
EUROPE						
Finland	Vikstedt et al. (2011)[95]	> 60 years of age	375	Serviced housing (not specified)	**86** (21 + 65)	MNA
Sweden	Odlund Olin et al. (2008)[96]	Frail older people	49	Serviced flats (before and after intervention with additional meal)	**90** (27 + 63) (baseline)	MNA (**malnourished:** score < 17 + **at risk of malnutrition** score: 17–23.5)
Sweden	Ödlund Olin et al. (2005)[97]	Elderly 68–96 years of age	80	Serviced flats (not specified)	**89** (59 + 30)	MNA (**at risk + malnourished**)
UK	Ralph et al. (2010)[98]	Individuals in sheltered housing*	1353	Sheltered housing schemes (overall) > 80 years of age < 80 years of age (individuals screened during invited coffee mornings over 6-month period)	**12** (7 + 5) **14** **9**	'MUST' (**medium + high**)
UK	Elia & Russell (2009)[99]	Older people	335	Sheltered accommodation (not specified)	**14** (5 + 9)	'MUST' (**medium + high**)
UK	Harris et al. (2007)[100]	> 65 years of age	100	Sheltered accommodation (not specified)	**10** **12** **17**	Dietitian assessment 'MUST' (**medium + high risk**). Not reported separately MNA (screening score < 12)

* Participants' age in years mean (±SD): 78 (±10.4)

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Table A1.6 **Prevalence of malnutrition or risk of malnutrition in some examples of studies reported after 2002 according to country and healthcare setting – free-living (majority of participants were older people)**

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
EUROPE						
Denmark	Beck & Ovesen (2002)[75]	> 65 years of age	200	Home care districts (not specified)	**30** (12)	BMI < 20 kg/m^2 (BMI < 18.5 kg/m^2)
Republic of Ireland	O'Dwyer et al. (2009)[101]	Older people	63	Meals on wheels recipients (not specified)	**36.5** (27 + 9.5)	**At risk** MNA 17–23.5, **malnourished** MNA < 17
Sardinia	Buffa et al. (2010)[102]	≥ 70 years of age**	170	Free-living (not specified, in 2005)	**37.1** (35.9 +1.2)	MNA (**at risk + malnourished**)
Spain	de la Montana & Miguez (2011)[103]	> 65 years of age	728	Home-living	**59** (46.7 + 12.4) **70.1** (57.6 + 12.5)	MNA-SF (**at risk + malnourished**) MNA (**at risk + malnourished**)
Spain	Cuervo et al. (2008)[104]	> 65 years of age	22007	Community-dwelling (cross-sectional survey)	**29.7** (25.4 + 4.3)	**At risk** MNA ≥ 17 to ≤ 23.5, **malnourished** MNA < 17
Sweden	Johansson et al. (2009)[105]	Older people	579	Home-living Baseline At follow-up 1–4 (between 2001 & 2006) (prospective study, assessed at baseline & follow-up as above)	**14.5** **7.6 –16.2**	**At risk** MNA 17–23.5, **malnourished** MNA < 17
The Netherlands	Meijers et al. (2009)[25]	≥ 18 years of age*	2794	Home care (cross-sectional, point prevalence)	**21.7**	**Malnutrition** defined according to one of the 3 following criteria: (1) BMI < 18.5 kg/m^2 (2) unintentional weight loss (6 kg in previous 6 months or 3 kg in previous month) or (3) BMI 18.5–20 kg/m^2 in combination with no nutritional intake for 3 days or reduced intake for > 10 days
The Netherlands	Kruizenga et al. (2003)[27]	> 18 years of age*	533	Home care (convenience sample, timing not clear)	**13** (7 + 6)	**At risk of malnutrition:** 5–10% unintentional weight loss during the past 6 months , **malnourished:** unintentional weight loss > 10% during the past 6 months

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Table A1.6 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
UK	Skinner et al. (2010)[106]	Older people	111	Meals on wheels recipients (not specified)	**31** (16 + 15)	'MUST' (**medium + high**)
UK	Elia & Stratton (2005)[89]	> 65 years of age	953	Free-living (secondary analysis of the National Diet and Nutrition Survey)	**12.5** (6.6 + 5.9)	'MUST' type criteria applied, i.e. a score of current weight status added to the weight loss score (**medium + high**)
USA & CANADA						
USA	Fodero & Wunderlich (2008)[107]	≥ 60 years of age	34	Convenience sample enrolled on Congregate Dining Programme and tai chi classes (not specified)	**5.9** (5.9 + 0)	MNA (**at risk + malnourished**)
CENTRAL & SOUTH AMERICA						
Brazil	De Andrade et al. of age (2009)[108]	> 60 years	834	Non-institutionalised – participating in Family Health Programme & Community Agents Health Programme (not specified)	**2.1**	BMI (**underweight** < 18.5 kg/m^2)
Cuba	Da Silva Coqueiro et al. (2010)[109]	≥ 60 years of age	1688	Free-living (Data from Survey on Health, Aging and Well-being of the Elderly SABE 2000)	**33**	BMI (**underweight** < 22 kg/m^2)

Table A1.6 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
ASIA						
China	Han et al. (2008)[110]	≥ 65 years of age	162	Community-dwelling (convenience sample, July–September 2007)	**44.4** (36.4 + 8.0)	MNA (**at risk + undernourished**)
Japan	Iizaka et al. (2008)[111]	≥ 65 years of age	130 (missing data *n* = 3)	Attendees of Setagya Senior College (November–December 2006)	**12.6** (12.6 + 0)	MNA (**at risk + undernourished**)
Taiwan	Tsai et al. (2010)[112]	≥ 65 years of age	2802 (1534 male, 1268 female)	Free-living (data from 'Survey of Health and Living Status of the Elderly in Taiwan' SHLSET)	**18** (15.1 + 2.9) male **24** (21.2 + 2.8) female	MNA (**at risk + malnourished**)
					14.3 (12.0 + 2.3) male **17.3** (15.6 + 1.7) female	MNA-Taiwan version-1 (MNA-T1) (**at risk + malnourished**). Modified version of MNA altering the questions on protein intake to emphasise the frequency of consumption rather than the number of servings. Also contains Taiwanese-specific anthropometric cut-offs (no details given)
					14.3 (12.3 + 2.0) male **16.3** (14.8 + 1.5) female	MNA-Taiwan version-2 (MNA-T2) (**at risk + malnourished**). Modified version of MNA with questions relating to protein intake as MNA-T1. Also, the BMI question omitted and redistributed BMI score to MAC – 1 point and calf circumference (CC) – 2 points
Taiwan	Tsai et al. (2008)[113]	≥ 65 years of age	2400	In-home interviews, part of population-based "The Survey of Health & Living Status of the Elderly in Taiwan" (not specified)	**15.1** (13.1 + 2.0)	MNA (**at risk + undernourished**)

Table A1.6 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
AUSTRALIA & NEW ZEALAND						
Australia	Leggo et al. (2008)[114]	Older people requiring help with daily tasks and younger people with impaired functional ability	1145	Home and Community Care recipients (not specified September 2003 – June 2005)	**15**	MST. The MST was modified with an additional question 'client appears very underweight or frail', with 'yes' recommending dietetic referral, score 0–1 indicates **low risk**, 2 **at risk**, 3–4 **higher level of risk**, 5 **very high risk of malnutrition**
Australia	Visvanathan et al. (2003)[115]	≥ 65 years of age	250	Domiciliary care service recipients (between January and December 2000)	**43.0** (38.4 + 4.8)	MNA (**at risk + malnourished**)
New Zealand	Teh et al. (2010)[116]	75–79 years of age (Maori) 85 years of age (non-Maori)	108	Free-living (not specified January – August 2008)	**52**	Seniors in the Community: Risk evaluation for Eating and Nutrition Version II (SCREEN II). Weight change, food intake, risk factors for food intake (meal frequency, diet restriction, appetite, chewing and swallowing difficulties, meal replacement, eating alone, meal preparation, shopping difficulties). Each item scores 0–4, lower scores indicating problems indicating nutrition risk. Total scores 0–64, < 50 = **at significant nutrition risk**
New Zealand	Wham et al. (2011)[117]	80–85 years of age	51	Free-living (convenience sample April – July 2006)	**31**	SCREEN II < 50 score = **at significant nutrition risk**

*Participants' age in years mean (±SD): home care 76.2 (±12.0),[25] home care well-nourished 59 (±20), at risk 64 (±23), malnourished 66 (±23)[27]
**Age ranges of sample: 70–79 years *n* = 103, 80–89 years *n* = 66, 90+ years *n* = 31

Table A1.7 **Prevalence of malnutrition or risk of malnutrition in some examples of studies reported after 2002 according to country and healthcare setting – other care settings**

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
EUROPE						
The Netherlands	Poels et al. (2006)[118]	Stroke patients > 18 years of age*	69	Stroke rehabilitation centre (on admission)	**35** (primary criteria) **73** (if malnutrition defined by the presence of at least one of the primary or secondary criteria)	Malnutrition assessed by a dietitian. Primary criteria for malnutrition were unintentional weight loss of > 5% in 1 month or > 10% in 6 months or a BMI < 18 kg/m^2 (< 65 years) or < 22 kg/m^2 (≥ 65 years). Secondary criteria for malnutrition: (1) serum albumin < 25 g/l, (2) Free-fat Mass (FFM) ≤ 16 kg/m^2 (men), ≤ 15 kg/m^2 (women), (3) TSFT < 90% of 12.5 mm (men) or 16.5 mm (women), (4) MAMC < 90% of 25.3 cm (men) or 23.3 cm (women)
UK	Russell & Elia (2012)[13] (spring 2011)	Adults ≥ 18 years of age*	543	Mental health units (Acute units within 72 hours of admission, long-stay/rehab units within previous 6 months)	**19** (9 + 10)	'MUST' (**medium + high**)
UK	Russell & Elia (2011)[14] (winter 2010)	Adults ≥ 18 years of age*	146	Mental health units (Acute units within 72 hours of admission, long-stay/rehab units within previous 6 months)	**18** (12 + 7)**	'MUST' (**medium + high**)
UK	Russell & Elia (2009)[30]	Adults ≥ 18 years of age*	185	Mental health units (Acute units within 72 hours of admission, long-stay/rehab units within previous 6 months)	**20** (5 + 15)	'MUST' (**medium + high**)

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Table A1.7 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening/assessment)	Prevalence % (risk category)	Method and details of risk category where reported
UK	Russell & Elia (2008)[31]	Adults ≥ 18 years of age*	332	Mental health units (Acute units within 72 hours of admission, long-stay/rehab units within previous 6 months)	**19** (7 + 12)	'MUST' (**medium + high**)
ASIA						
China	Chai et al. (2008)[119]	Adults with history of stroke, mean age 76 years	61	Cheshire Home Infirmary (not specified)	**8.2**	BMI < 18.5 kg/m^2 + serum albumin <35 g/l
Taiwan	Tsai et al. (2011)[120]	Adults with schizophrenia bipolar disorder major depression	120	Mental health units (convenience sample, not specified)	**21.1** (11.5 + 9.6) **12.5** (12.5+0) **55.6** (50.0 + 5.6)	MNA-Taiwan version 1 (MNA-T1) (**at risk + malnourished**). Content-equivalent version of MNA. MNA-T1 adopted Taiwanese-specific anthropometric cut-off points. For Item G 'can live independently', those psychiatrically stable individuals who could carry out daily activities were considered to live independently and given one point in the study
MIDDLE EAST						
Iran	Amirkalali et al. (2010)[121]	≥ 65 years of age	221	Kahrizak Charity Foundation† (not specified)	**46.6** (43.4 + 3.2)	MNA (**at risk + malnourished**)

*Participants' age in years mean (±SD): stroke rehabilitation centre 56.7 (±11.0),[118] mental health units 59.2 (±20.0),[31] 66.4 (±20.1),[30] 50.0 (±19.0),[14] 55.9 (±21.6)[13]
**Figures do not add up due to rounding
†Private non-governmental non-profit charitable organisation where physically handicapped or elderly with no financial resources are cared for free of charge

Table A1.8 Prevalence of malnutrition or risk of malnutrition in children in hospital in studies reported after 2000 according to country

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening /assessment)	Prevalence % (risk category)			Method and details of risk category where reported
					Acute	Chronic	Overall	
EUROPE								
Austria	Wildham et al. (2007)[122]	Children aged 3–18 years	100	Hospital (admission)	**3** (2 + 1) **18** (13 + 5)	**17** (8 + 9)	**15** (15 + 0)	Waterlow Score (stunting)** (**moderate + severe**) Waterlow Score (wasting)* (**moderate + severe**) Gomez score (WFA)† (**moderate + severe**) Vienna score (**moderate + severe**): Based on albumin, total lymphocyte count, haemoglobin measures (see Wildham et al. 2007 for cut-off points), total weight loss of > 5% relative to pre-illness body weight (4 weeks), weight/height centile < 10th centile and lack of appetite
France	Lambe et al. (2010)[123]	All children admitted to paediatric neurology and orthopaedic surgery wards with length of stay > 2 days	348	Tertiary care paediatric hospital (Timing of assessment not specified)			**4.9** (4 + 0.9) **2.3** (1.4 + 0.9) **20**	Orthopaedic surgery (**moderate + severe**) Neurology (**moderate + severe**) All (**mild, moderate + severe** for both specialities) Data collection (weight, height, growth charts, clinical history) performed by a dietitian. Nutritional status assessed by a specialist paediatrician. No details given regarding cut-off points for mild, moderate or severe protein-energy malnutrition
France	Marteletti et al. (2005)[124]	Children aged between 2 months & 16 years hospitalised for > 48 hours	280 No age break-down	One-day cross-sectional study over 3 different seasons	**11**			**Malnourished:** WFH z-score less than -2 SD

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Table A1.8 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening /assessment)	Prevalence % (risk category)			Method and details of risk category where reported
					Acute	Chronic	Overall	
France	Hankard et al. (2001)[125]	Children aged > 6 months admitted to medical or surgical wards for > 48 hours	58 No age break-down	One-day cross-sectional study			**21** **12**	**Malnourished:** BMI below -2 SD When patients with anorexia nervosa excluded Note: Patients receiving nutritional support (parenteral, enteral or special regimens for metabolic diseases) were excluded (represented 19% of total number of patients admitted on the day of the survey)
France	Sermet-Gaudelus et al. (2000)[126]	Children aged > 1 month with a hospital stay of ≥ 48 hours admitted to medical or surgical wards	296 1–12 months *n* = 133 12–72 months *n* = 87 > 72 months *n* = 76	Within 48 hours of hospital admission			**26** **85.2** (40.9 + 44.3) No age breakdown	**Undernourished:** percentage IBW < 85% Simple Paediatric Nutritional Risk Score: Takes account of food intake, pain and pathology. Maximum score 5 (see Sermet-Gaudelus et al. 2000 for further details). **Low risk** of nutritional depletion: score 0 **Moderate risk:** score 1–2 **High risk:** score ≥ 3 Note: Children with conditions that involved large variations in hydration were excluded

Table A1.8 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening /assessment)	Prevalence % (risk category)			Method and details of risk category where reported
					Acute	Chronic	Overall	
Germany	Pawellek et al. (2008)[127]	All children admitted to 1 of 2 general paediatric wards or 1 surgical ward	475 (< 1–17 years) < 1 year *n* = 28 2–5 years *n* = 164 6–12 years *n* = 186 13–17 years *n* = 97	Hospital admission	**6.1** (4.4+1.7)	 **14.2** (7.1+7.1) **4.3** (4.3+0.0) **5.9** (4.8+1.1) **7.2** (3.1+4.1)	**17.2** (7.5+9.7)	Waterlow criteria: **Mild** malnutrition: 81–90% centile WFH **Moderate** malnutrition: 70–80% centile WFH **Severe** malnutrition: < 70% centile WFH TSFT: Malnutrition: 5th–9th centile **Severe** malnutrition: < 5th centile

Table A1.8 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening /assessment)	Prevalence % (risk category)			Method and details of risk category where reported
					Acute	Chronic	Overall	
Italy	Campanozzi et al. (2009)[128]	All children aged 1 month to 16 years admitted to medical paediatric ward with ±Grade 1 conditions	496 1–12 months *n* = 174 13–24 months *n* = 72 25–36 months *n* = 48 37–72 months *n* = 84 > 72 months *n* = 118	Hospital admission			**10.2** No age breakdown	**Malnourished:** BMI z-score < -2 ±Grade 1 conditions involve mild stress factors, e.g. admissions for diagnostic procedures, minor infection, other episodic illnesses or minor surgery (American Academy of Pediatrics and American Dietetic Association criteria) Patients with < 72 hour hospital stay, patients aged < 1 month, patients with chronic conditions and patients requiring IV fluid/electrolyte therap or who were dehydrated were excluded
The Netherlands	Hulst et al. (2010)[129]	Children aged > 1 month, admission to paediatric ward and expected stay at least 1 day	424 No age break-down	Hospital admission			**62** (54+8)	STRONG$_{kids}$ includes: 1) SGA 2) high risk disease 3) nutritional intake and losses and 4) weight loss or poor weight increase (**moderate + high risk**)

Table A1.8 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening /assessment)	Prevalence % (risk category)			Method and details of risk category where reported
					Acute	Chronic	Overall	
The Netherlands	Joosten et al. (2010)[130]	Children aged > 1 month, admission to medium care unit and expected stay at least 1 day	424 < 1 year 2–5 years 6–12 years 13–17 years	Hospital admission	**11** **14** **14** **7** **10**	**9** **6** **8** **12** **11**	**19** **18** **21** **17** **19**	**Acute** malnutrition: WFH < -2 SD **Chronic** malnutrition: HFA < -2 SD Overall malnutrition rate: presence of **acute** and/or **chronic malnutrition**
Poland	Horvath et al. (2008)[131]	Series of unselected children (age not specified)	96 No age break-down	Timing of assessment not specified Paediatric teaching hospital			**16** **14** **19**	Malnutrition was defined as: BMI < 3rd centile for age BMI z-score < -2 SD MAC < 5th centile for age
Spain	Moreno Villares et al. (2005)[132]	Children aged 1 month to 19 years	268 < 2 years *n* = 132 2–7 years *n* = 69 > 7 years *n* = 62				**17.2**	

Table A1.8 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening /assessment)	Prevalence % (risk category)			Method and details of risk category where reported
					Acute	Chronic	Overall	
Turkey±	Dogan et al. (2005)[133]	Children aged 1 month to 23 years No age breakdown	528 (223 female)	Hospital admission	**52.4** **40.9**	**27**	**45.7**	**Acute** malnutrition: based on WFA based on WFH Chronic malnutrition (based on HFA) BMI below -2 SD
Turkey±	Ozturk et al. (2003)[134]	Children aged > 1 month to 17 years	170	Hospital admission			**30.4** (21.7 + 5.8 + 2.9)	**Mild, moderate and severe** malnutrition **Mild:** 80–89% of ideal body WFH **Moderate:** 70–79% of ideal body WFH **Severe:** < 70% of ideal body WFH
UK	McCarthy et al. (2012)[135]	All children aged 2–17 years admitted to participating medical & surgical wards No age breakdown	238	Timing of screening/ assessment not reported Large paediatric hospital			**18** **14**	STAMP. Consists of 3 scored elements: clinical diagnosis, nutritional intake, anthropometric measures. An overall score of ≥ 4 considered as 'at nutrition risk' Full nutritional assessment by a RD, consisting of a face-to-face interview to obtain dietary, personal and clinical information from medical and nursing notes

Table A1.8 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening /assessment)	Prevalence % (risk category)			Method and details of risk category where reported
					Acute	Chronic	Overall	
UK	Gerasimidis et al. (2010)[136]	All children aged 1 - 16 years admitted to 4 paediatric wards (Tertiary paediatric hospital [TPH], 3 medical & 1 surgical, District general hospital [DGH] 1 general paediatric)	247 No age break-down	Within 24 hours of hospital admission District general hospital (DGH) Tertiary paediatric hospital (TPH)			DGH **19.4** (10.4 + 9) TPH **19.5** (9 + 10.5)	PYMS (**medium + high risk**) STEP 1: BMI below 2nd centile (-2 SD) on UK 1990 growth chart STEP 2: history of recent weight loss STEP 3: recent change in nutritional intake for at least the past week STEP 4: the likely effect of the current medical condition on the nutritional status of the patient for at least the next week. Each step bears a score of 0–2 and the total score reflects the degree of the nutrition risk of the patient **Low risk of malnutrition:** score of 0 **Moderate risk of malnutrition:** score of 1 **High risk of malnutrition:** score of ≥ 2 Note: Patients from cardiology, renal and orthopaedic specialities, critical care and day assessment were not included
USA & CANADA								
Canada	Groleau & Babakissa (2008)[137]	Children aged 0–18 years No age breakdown	173	On hospital admission			**79.8** **28** **35**	Nutritional paediatric nutrition score published in 2000 (likely to be Sermet-Gaudelus et al. 2000) Canadian Paediatric Society's recommendations (no details given) Waterlow score (no details given on whether this was acute or chronic)

Table A1.8 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening /assessment)	Prevalence % (risk category)			Method and details of risk category where reported
					Acute	Chronic	Overall	
Canada	Secker & Jeejeebhoy (2007)[138]	Consecutive children aged 31 days to 17.9 years scheduled for surgery	175 31 days –2 years *n* = 51 2–5 years *n* = 22 5–12 years *n* = 45 12–17 years *n* = 57	Nutritional assessment undertaken either the day before surgery or the morning of surgery for same-day admissions Large paediatric academic hospital			**51** (36 + 15) No age-related breakdown of prevalence	Subjective Global Nutritional Assessment (SGNA) (**moderate + severe**) Note: requiring major abdominal or non-cardiac thoracic surgery on a nonemergency basis and who had not undergone surgery in the 30 days before screening
CENTRAL & SOUTH AMERICA								
Brazil±	Fernandez et al. (2008)[139]	Children aged < 3 years	67 (46% < 2 years old)	Within 48 hours of admission Hospital general paediatric unit	**43**			Gomez score (WFA) Categories not reported separately, prevalence reported as 'had some degree of malnutrition'

Table A1.8 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening /assessment)	Prevalence % (risk category)			Method and details of risk category where reported
					Acute	Chronic	Overall	
Brazil±	Rocha et al. (2006)[140]	Children: average age 21.6 ±15.4 months (62.2% aged < 24 months)	203 Aged 3–11 months *n* = 69 12–23 months *n* = 57 24–59 months *n* = 77	Within 48 hours of admission	**18.7** **6.9**		 **18.2**	Weight for? age (**moderate and/or severe**) Weight/stature (**moderate and/or severe**) Stature for? age (**moderate and/or severe**) Classified in accordance with WHO criteria¥: **Mild** malnutrition: z-score from -1 to -2 SD **Moderate** malnutrition: z-score from -2 to -3 SD **Severe** malnutrition: z-score less than -3 SD Ages corrected for children with gestation age < 37 weeks Note: Children with chronic liver or renal disease, surgical pathologies or cerebral palsy or who were admitted to intensive care or oncology units with rehospitalisation during the study period were excluded
Cuba±	Jimenez et al. (2008)[141]	All children (age not specified) No additional data	162	On admission Tertiary level national paediatric hospital			**17.3**	Malnutrition: < 3rd centile WFH; National Growth Charts (**severe malnutrition**)
MIDDLE EAST								
Iran±	Mahdavi et al. (2009)[142]	Consecutive admissions aged 2–12 years	140 No age breakdown	Within 3 days of hospitalisation Paediatric hospital			**70.7** **48.5**	SGA (SGA B/C) Objective assessment (Waterlow criteria) includes **mild, moderate and severe** malnutrition Note: Admissions to surgical, inflectional, oncology, ENT and internal medicine wards (gastroenterology, nephrology, respiratory, neurology, cardiology, metabolic disorder)

Table A1.8 Continued

Country	Author (year)	Study population	Patients (*n*)	Healthcare setting (and timing of nutritional screening /assessment)	Prevalence % (risk category)			Method and details of risk category where reported
					Acute	Chronic	Overall	
AFRICA								
South Africa±	Marino et al. (2006)[143]	Patients in all medical and surgical wards and in some specialist outpatient clinics	227	Timing of assessment not reported			**35**	Undernourished defined as ≤ 2 z-scores for following: WFA/WFH and HFA
			< 12 months		**40/27**	**33.5**	**34**	
			13–60 months	Hospital	**27/21**	**31**	**32**	
			Children > 60 months		**29/14**	**31**	**19**	
AUSTRALIA & NEW ZEALAND								
Australia	Aurangzeb et al. (2012)[144]	Aged > 1 month	157	Tertiary paediatric hospital (new admissions during one week in September 2006)	**4.5**			WFA z-score ≤ -2
					2.5			WFH z-score ≤ - 2
						8.9		HFA z-score ≤ -2
							47.8	NRS (No nutritional risk: 0–3, **moderate risk:** 4–5 and **high risk:** ≥ 7)

*Acute malnutrition Waterlow score (wasting):[145] mild: 80–90% WFH; moderate: 70–80% WFH; severe: < 70% WFH
**Chronic malnutrition Waterlow score (stunting):[145] mild: 95–87.5% HFA; moderate: 87.5–80% HFA; severe: < 80% HFA.
†Acute malnutrition Gomez score (WFA)[146:] mild: 75–90% WFA; moderate: 60–74% WFA; severe: < 60% WFA.
ᵞWHO criteria:[147] moderate: symmetrical oedema – no, WFH -3 ≤ SD-score < -2 (70-79%), HFA -3 ≤ SD-score < -2 (85-89%); severe: symmetrical oedema – yes, WFH SD-score < -3 (<70%), HFA SD-score < -3 (<85%).
±Countries classed as Upper Middle Income Economies see http://data.worldbank.org/about/country-classifications/country-and-lending-groups for more information.

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II FUNCTIONAL BENEFITS OF ONS – Table A2.1

Table A2.1 **Some examples of trials reported after 2002 describing significantly improved functional outcomes with ONS in a variety of healthcare settings**

Trial	Design	Subjects (setting)	Intervention (n)	Control (n)	Duration	Functional outcomes
Parsons et al. (2016)[1]	Randomised, parallel, open-label trial	Adults aged >50y at risk of malnutrition (Care homes)	ONS ad libitum (range of styles, flavours, volume, energy density; 87% took ONS with energy density between 1.5-2.4kcal/ml). Target provision 600kcal and 16g protein daily. ONS group also seen by dietitian (53)	Dietary advice by dietitian with leaflet at baseline and at week 6 (51)	12 weeks	• Significantly higher scores in two out of the three QoL measures in intervention vs. control (EQ-5D TTO $p = 0.005$, VASr $p = 0.006$) in ITT analysis and significantly higher scores in all measures in intervention vs. control in per protocol analysis (EQ-5D TTO $p = 0.002$, VASr $p = 0.004$, Visual Analogue Scale $p = 0.027$) at 12 weeks. • Responses to questions about appetite sensations did not differ between groups at any time points except for "fullness" which was experienced in a smaller proportion of subjects in the intervention vs. control group at week 12 (41% vs 70%; $p < 0.05$).
Ng et al. (2015)[2]	RCT - 5 arms (49 ONS, 50 cognitive, 48 physical, 49 combination, 50 control)	Frail older people, ≥ 65 y, able to ambulate without personal assistance, identified door-to door using cardio-vascular health study (CHS) criteria for frailty (Community-free-living)	ONS, (49) ONS with exercise and cognitive training (49)	Usual care (50), Placebos identical in appearance to ONS and vitamin/mineral supplements. Artificially sweetened vanilla flavoured liquid made with water and non-dairy creamer	24 weeks/ 6 months	• Significant reductions in frailty scores were seen in all groups 12 month follow up compared with baseline and control groups- nutritional (odds ratio (OR) 2.98), cognition (OR 2.89), physical (OR 4.05) and combination (OR 5.00) for intervention groups. • Significant increase in levels of physical activity also seen in the nutritional intervention arm compared with baseline $p < 0.01$ vs control at 6 and 12 months.
Huynh et al. (2014)[3]	RCT- 2 arm	Moderate and severely malnourished patients (Hospitals)	ONS + DC (104)	Standard diet + DC (103)	12 weeks	• Patients who were in the lowest tertile at baseline for handgrip strength score in the ONS group had a greater improvement at week 4 ($p = 0.042$) compared to the control group.

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Table A2.1 Continued

Trial	Design	Subjects (setting)	Intervention (n)	Control (n)	Duration	Functional outcomes
Kim and Lee (2012)[4]	RCT - 2 arms	Frail older people, ≥ 65 y, low socioeconomic status (Community-free-living)	ONS + DC? (43)	Visited monthly - no placebo ONS/ counseling but a small gift given. Home healthcare services suspended during trial period (44)	12 weeks	• Short physical battery remained stable in the intervention group while decreasing by 12.5% in controls ($p = 0.039$). • Usual gait speed decreased by 1.0% in the intervention group and decreased by 12.5% in controls ($p = 0.039$). • Timed up and go improved by 7.2% in the intervention group but decreased by 3.4% in controls ($p = 0.038$)
Neelemaat et al. (2012)[5]	RCT	Malnourished elderly (> 60 years) patients, various conditions. (Community - post hospital discharge)	ONS (105)	Usual care (105)	3 months	• Significant decrease in functional limitations (mean difference -0.72, 95% CI -1.15 to -0.28) with no difference in costs
Feldblum et al. (2011)[6]	RCT-3 arm	Older medical patients (hospital + follow-up post discharge)	Individualised DC + ONS in hospital and post discharge (78)	Individualised DC + ONS in hospital (73) Routine care (108)	6 months	• Significantly lower mortality in group 1 (3.8%) vs groups 2 and 3 (11.6%, $p = 0.046$). No significant differences in other functional cognitive parameters
Rufenacht et al. (2010)[7]	RT	Undernourished patients (hospital)	Individualised DC + ONS (18) ONS (18)		10–15 days	• Both groups demonstrated improved QOL parameters from baseline to discharge (NT group $p < 0.001$, ONS group $p < 0.003$). No significant differences between groups. NT group showed further significant improvement in QOL 2 months post discharge ($p = 0.016$)
McMurdo et al. (2009)[8]	RCT	Older people, malnourished. (Community-dwelling, admitted to hospital with acute illness. Residents of care homes excluded. ONS provided upon discharge)	ONS (126)	Control supplement (127)	4 months	• Significant improvement in hand-grip strength in ONS group compared with controls • Significantly more vector movement (objective measure of physical activity using accelerometry) in the ONS group compared with controls

Table A2.1 Continued

Trial	Design	Subjects (setting)	Intervention (*n*)	Control (*n*)	Duration	Functional outcome
Norman et al. (2008)[9]	RCT	Adult malnourished SGA B or C, benign GI disease (post hospital)	HP ONS + DC (38)	DC (42)	3 months	• Significant improvement in hand-grip strength and peak expiratory flow in ONS group, unchanged in DC group • Significant improvement in all 8 scales of QOL in ONS group, whereas improvement in 3 scales in DC group only. Significantly higher increases in physical functioning, role physical, vitality and general health scales in ONS group • Change in hand-grip strength correlated with the change in 2 physical scales (physical functioning and physical role)
Rabadi et al. (2008)[10]	RDB Trial	Undernourished (2.5% weight loss in 2 weeks) (patients admitted to a stroke rehabilitation unit)	Intensive ONS	Standard ONS	From within 72 hours of arrival on unit to discharge	• Significant improvement in the Intensive ONS group in total FIM score, FIM motor sub-score, 2-minute walk and 6-minute walk
Gariballa & Forster (2007)[11]	RDBPCT	Acutely ill older people (hospital and post discharge)	NHD + HP ONS (106)	NHD + placebo (119)	6 weeks	• Significant increase in number of patients with no symptoms of depression and decrease in those with symptoms of mild or severe depression among ONS group compared with placebo group
Gariballa & Forster (2007)[12]	RDBPCT	Acutely ill older people (hospital and post discharge)	NHD + HP ONS (106)	NHD + placebo (119)	6 weeks	• Significantly better QOL scores in the ONS group compared with placebo group at 6 months but not at 6 weeks. Effect of supplementation was seen in higher physical function, role physical and social function scores
Persson et al. (2007)[13]	RCT	Older acutely ill/trauma patients at risk of malnutrition MNA-SF (on hospital discharge to home/nursing home)	ONS + DC (29)	Brief written DA (25)	4 months	• Treated-as-protocol analyses showed Katz ADL index improved in the ONS + DC group
Price et al. (2005)[14]	RCT	Undernourished* older people (on hospital discharge to community)	ONS (70)	Usual care (66)	8 weeks	• Improvement in hand-grip strength in both groups, but ONS group showed significantly greater increase over 12 weeks compared with controls Intention-to-treat analysis showed a 13.9% increase in the ONS group compared with 7.2% in the control group

Table A2.1 Continued

Trial	Design	Subjects (setting)	Intervention (*n*)	Control (*n*)	Duration	Functional outcome
Edington et al. (2004)[15]	RCT	Older malnourished** patients (community)	ONS (51)	Standard care (49)	8 weeks	• Significant improvement in hand-grip strength during supplementation but not sustained from week 8 to week 24 • No difference between groups in QOL utility score or health status; however, ONS group scored significantly higher on the mobility score at week 24 than controls, possibly indicating an improvement in strength
Payette et al. (2002)[16]	RCT	Frail older people at high nutritional risk (community)***	ONS + DC (41)	Visited monthly, no advice/ONS (42)	16 weeks	• When results analysed by gender, significant reduction in the meantime to execute 'up and go' test was seen in women in the ONS group, and knee extensor strength increased in men in the ONS group • The number of days subjects had to stay in bed significantly increased in the control group over the course of the study compared with baseline; in contrast, no change in bed disability days seen in the ONS group

HP: high-protein (> 20% energy from protein), DC: dietary counselling, RDBPCT: Randomised Double Blind Placebo Controlled Trial, NHD: Normal hospital diet, OR: Odds Ratio, QoL: Quality of Life, EQ-5D TTO: EuroQol Time Trade Off Data, VASr: Visual Analogue Scale rescaled, VAS: Visual Analogue Scale.
*BMI ≤ 24 kg/m^2, TSFT or MAMC below the 10th centile and/or weight loss ≥ 5% during hospital stay
**(a) BMI < 20 kg/m^2 or (b) BMI ≥ 20 kg/m^2 but < 25 kg/m^2 with documented evidence of weight loss of ≥ 10% in the 6 months prior to study period or ≥ 5% in the 3 months prior to study period
***(a) involuntary weight loss > 5% body weight in the past month, > 7.5% in the past 3 months or > 10% in the past 6 months and BMI < 27 kg/m^2 or (b) BMI < 24 kg/m^2

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III SUMMARY OF TRIALS: SETTING, POPULATION, INTERVENTION & OUTCOME – Tables A3.1 to A3.4

The studies listed here are key individual trials that have been mentioned within the text to illustrate specific points; therefore, this list is not an exhaustive list of all trials using ONS. For example, studies which have been included in key systematic reviews and meta-analyses have not been listed here.

For trials up to 2002, see Stratton et al. (2003)[1]. Key systematic reviews and meta-analyses include: Stratton et al. (2003)[1], Langer et al. (2003)[2], Stratton et al. (2005)[3], Milne et al. (2005, 2006 & 2009)[4-6], NICE (2006)[7], Elia et al. (2006)[8], Lidder et al. (2009)[9], Cawood et al. (2012)[10], Burden et al. (2012)[11], Geeganage et al. (2012)[12], Stratton et al. (2013)[13], Allen et al. (2013)[14], Smyth et al. (2014)[15], Collins et al. (2015)[16], Liu et al. (2015)[17], Francis et al. (2015)[18].

Table A3.1 Summary of trials: setting, population, intervention and outcome – community studies

Trial	Setting	Popula-tion	Design	Sample size	Intervention (n)	Control (n)	Duration	Outcome
Allen et al. (2013)[19]	Nursing homes* *The majority of patients were recruited from nursing homes (18/26) others were recruited from hospitals (8/26)	Older adults with dementia >65y	Prospective controlled crossover study	26	ONS on alternate days (26)	No ONS on alternate days (26)	1 week	**Nutritional** Significantly more energy consumed on intervention days compared to control days (p <0.001). No significant difference between energy consumed from food on intervention days compared to paired control days (p = 0.641). 55.8% of patients met their caloric goals on intervention days, compared to 17.3% on their adjacent control day (p <0.0001). Significantly more total protein consumed on intervention days vs. control days (p <0.0001). No difference in protein intake from food on intervention vs. control days (p = 0.576). On intervention days RDA for protein was more frequently met compared to on control days (p <0.0001) **Clinical** NR **Functional** NR **Economic** NR
Bonnefoy et al. (2003)[20]	Retirement homes	Frail older people	RCT factorial design	57	2 x 200 ml daily given at 10.00 & 16.00 hours Group 1 – ONS plus memory Group 2 – ONS plus exercise	Placebo in identical packaging, contained no energy, protein or micronutrients Group 3 – placebo plus exercise Group 4 – placebo plus memory	9 months	**Nutritional** Increase in BMI at 3 and 9 months with ONS (p = 0.004, p = 0.007 respectively) Trend towards increase in FFM in ONS group and decrease in placebo group at 3 and 9 months **Functional** ONS improved muscle power at 3 months (+ 56.8%, p = 0.03) Improved 5-time chair rise with exercise at 9 months (p = 0.014) but no significant effect on muscle function or nutritional status at 3 or 9 months

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Table A3.1 Continued

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Bunout et al. (2001)[21]	Community -dwelling (free-living)	Older people	RCT	149	Two servings soup/ porridge-style supplement daily Group 1 – ONS plus resistance exercise training Group 2 – ONS, no training Group 3 – no ONS, resistance exercise training	Group 4 – no ONS, no training	18 months	**Nutritional** No change in body weight or FFM, fat mass increased in all groups. Bone mineral density decreased less in ONS groups than in trained groups ($p < 0.01$) **Functional** ADL remained constant in ONS groups and decreased in non-ONS groups. Exercise had no effect Mini-mental scores increased in all groups, no differences among groups No effect of ONS on walking capacity, muscle strength and maximal inspiratory pressure
Edington et al. (2004)[22]	Community (post discharge from hospital)	Older people, malnourished	RCT	100	Intakes between 600 kcal and 1000 kcal/day prescribed in order to achieve a weight gain of at least 0.5 kg/ week (plus telephone contact by dietitian)	Standard care	8 weeks*	**Nutritional** Higher energy intake at week 12 ($p = 0.041$) Improved nutritional status (BMI, weight and TSFT) between baseline and 24 weeks in ONS group but no significant difference between groups **Functional** Improvement in hand-grip strength at 8 weeks in ONS group ($p = 0.04$) (not sustained), trend towards significance at 8 weeks between groups Fewer mobility problems in ONS vs control group at 24 weeks ($p = 0.022$) **Economic** No difference in health economic outcomes between groups at 24 weeks

*Mean actual duration of supplementation was 99.4 days (range 6–169).

Table A3.1 Continued

Trial	Setting	Population	Design	Sample size	Intervention (n)	Control (n)	Duration	Outcome
Jobse et al. (2014)[23]	Nursing homes	Nursing home residents, ≥65y	RCT- 2 arms (45 ONS, 42 control)	87	HP ONS (45)	Usual care (42)	12 weeks	**Nutritional** Median ONS intake in the intervention group was 438kcal/d. Significantly higher body weight increases in subjects with high compliance median (+3.0kg) than in those with low compliance (-0.2 kg) p <0.001. Residents with high compliance showed a clear increase of nutritional parameters; 3kg body weight gain, improved BMI by 1.2 kg/m^2 and increased MNA-SF score by 2 points. High compliance was more often observed in residents with malnutrition (66.7 vs. 27.3%) and chewing difficulties (77.8% vs. 24.2%) than in those without the conditions. Immobility, depression and presence of gastrointestinal complaints were related to a low compliance. **Functional**: NR **Economic**: NR
Kim and Lee (2013)[24]	Community - (free-living)	Frail older people, ≥ 65y,	RCT - 2 arms (43 ONS, 44 control)	87	ONS + DC? (43)	Visited monthly - no placebo ONS/ counselling but a small gift given. Home healthcare services suspended during trial period	12 weeks	**Nutritional** Significant improvements in energy, protein, essential amino acid intake and mean adequate ratio were observed in the intervention group relative to the control group ($p \leq 0.008$). **Clinical:** The serum level of blood nitrogen urea in the intervention group was increased significantly ($p = 0.011$) as was the estimated creatinine clearance ($p = 0.018$). **Functional:** Short physical battery remained stable in the intervention group while decreasing by 12.5% in controls ($p = 0.039$). Usual gait speed decreased by 1.0% in the intervention group and decreased by 12.5% in controls ($p = 0.039$). Timed up and go improved by 7.2% in the intervention group but decreased by 3.4% in controls ($p = 0.038$). **Economic:** NR

Table A3.1 Continued

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Lauque et al. (2004)[25]	Geriatric wards and day care centres	Older people with Alzheimer's disease, at risk of under-nutrition	RCT	91	300–500 kcal/day in addition to the patients' spontaneous food intake	Usual care (some patients from the control group who received ONS prescribed during the study not excluded but ONS prescription recorded)	3 months	**Nutritional** Improved energy and protein intakes between baseline and 3 months in the intervention group leading to significant improvement in weight and FFM **Functional/clinical** No difference in dependence, cognitive function or biological markers at 3 months or in fractures, pressure ulcers or hospitalisation at 6-month follow-up
Manders et al. (2009)[26]	Residents of care homes for older people	Older people	RDBPCT, parallel	176	2 x 125 ml dairy drinks between meals (250 kcal/day)	Placebo drink, no energy, vitamins or minerals. Contained water, cloudifier, thickener, flavouring, colourant and non-calorific sweetener	6 months	**Nutritional** Weight gain, 1.6 kg difference in change ($p = 0.035$) Increased CC, 0.9 cm difference in change ($p = 0.48$) Improved plasma vitamin D, B12, B6, homocysteine, folate and methylmalonic acid ($p < 0.01$) **Functional** Better performance on language sub-score of Alzheimer's Disease Assessment Scale in a subgroup with BMI < 24.4 kg/m^2 ($p = 0.01$) No significant effects on physical performance (e.g. hand-grip strength, ADL), verbal fluency or depression score

Table A3.1 Continued

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Manders et al. (2009)[27]	Residents of care homes for older people (homes for the elderly *n* = 3, nursing homes *n* = 3, mixed homes *n* = 3)	Older people	RDBPCT, parallel	176	2 x 125 ml dairy drinks between meals (250 kcal/day) in addition to usual diet	Placebo drink, no energy, vitamins or minerals. Contained water, cloudifier, thickener, flavouring, colourant and non-calorific sweetener	6 months	**Nutritional** Increased intake of vitamins and minerals except vitamin A ($p < 0.001$) (non-randomised sub-sample $n = 66$) Most vitamin deficiencies normalised, most notably vitamin D (10% vs 75% remained deficient in ONS vs placebo group) (vitamin levels also reported in Manders 2009)[26] Non-significant positive effect on macronutrient intake and body weight. Energy intake decreased to the same extent in both groups. No effect on blood proteins or biochemical indicators of general health
McMurdo et al. (2009)[28]	Community-dwelling (admitted to hospital with acute illness). Residents of care homes excluded	Older people, under-nourished	RCT	253	2 x 200 ml ONS daily	Control supplement based on skimmed milk containing 200 kcal, 12.4 g protein	4 months	**Nutritional** Weight gain† mean difference of 1.17 kg (95% CI 0.07–2.27, $p = 0.04$) **Functional** Hand-grip strength¥ mean difference of 1.48 kg (95% CI 0.46–2.50, $p = 0.005$) Physical activity (accelerometry)¥ mean difference in % change in vector movement 1.71 (95% CI 0.26–3.17, $p = 0.02$) No change to ADL, health-related QOL, falls, rehab input, time spent walking, death, unplanned admissions or other adverse events, trend towards improvement in sit-to-stand test in ONS group

¥Intention to treat analysis. †Per protocol analysis.

Table A3.1 Continued

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Neelemaat et al. (2011)[29] Neelemaat et al. (2011)[30]	Community (post hospital discharge)	Malnourished elderly (> 60 years) patients, various conditions	RCT	210	2 x 200 ml HP ONS daily plus 500mg Calcium and 400IE vitamin D supplement and DC	Usual care	3 months	**Nutritional** Patients in the intervention group tended to gain more weight than controls (mean difference 1.5 kg, 95% CI -0.2–3.1 ns). A significant increase in weight was demonstrated in the highest body weight category > 63.9 kg (mean difference + 3.4 kg, 95% CI 0.2–6.6). No differences in FFM and hand-grip strength Compliance with ONS 80% **Functional** A positive though non-significant trend of a reduction in functional limitations for both men and women in intervention group after 3 months (mean difference -0.5, 95% CI -1.0–0.1). No significant improvement seen in physical activities and performance **Cost-effectiveness** Second paper reported significant decrease in functional limitations (mean difference -0.72, 95%CI -1.15 to -0.28) with no difference in costs
Ng et al. (2015)[31]	Community - (free-living)	Frail older people, ≥ 65y	RCT - 5 arms (49 ONS, 50 cognitive, 48 physical, 49 combination, 50 control)	246	ONS (49), ONS with exercise and cognitive training (49)	Usual care (50), Placebos identical in appearance to ONS and vitamin/mineral supplements. Artificially sweetened vanilla flavoured liquid made with water and non-dairy creamer	6 months	**Nutritional:** NR **Clinical:** No significant difference of IADL-ADL dependency, hospitalization between groups as small numbers and low frequency of occurrence. **Functional:** Significant reductions in frailty scores were seen in all groups 12 month follow up compared with baseline and control groups-nutritional (odds ratio (OR) 2.98), cognition (OR 2.89), physical (OR 4.05) and combination (OR 5.00) for intervention groups. Significant increase in levels of physical activity also seen in the nutritional intervention arm compared with baseline p <0.01 vs control at 6 and 12 months. **Economic:** NR

Table A3.1 Continued

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Norman et al. (2008)[32]	Community	Malnourished patients with GI disease	RCT	101	Up to 3 x 200 ml daily. Patients advised to drink ONS slowly and between meals (≥ 1 h before a meal) (plus standard DC session as per control, contacted once per month)	Standard DC session (verbal advice, 45 min) by an RD. Advised on improving protein and energy intake with normal food. All patients actively contacted once per month	3 months	**Nutritional** Higher energy and protein intake in ONS group vs control ($p < 0.0001$) **Functional** Improved hand-grip strength and peak flow in ONS group vs controls ($p = 0.002$, $p = 0.047$ respectively) Body weight and BMI increased in both groups Significantly improved QOL in 4 areas in ONS group vs controls (physical functioning, physical role, general health and vitality, $p < 0.05$) **Clinical** Control patients had more readmissions than ONS group ($n = 20$ vs $n = 10$, $p = 0.041$)
Payette et al. (2002)[33]	Community	Frail older under-nourished people	RCT	83	2 x 235 ml daily. Choice of ONS. Encouraged to attain max tolerable energy intake to gain 0.5 kg body weight per week. Instructed to use ONS and increase overall food intake (plus nutrition counselling by phone every 2 weeks between visits)	Visited monthly, no advice/ONS	16 weeks	**Nutritional** ONS group had higher energy intake ($p < 0.001$) and weight gain ($p < 0.001$) No significant differences in other anthropometric indexes, muscle strength or functional measures **Clinical** Number of bed disability days significantly increased in control group compared with baseline ($p = 0.04$), no change in bed disability days seen in ONS group

Table A3.1 Continued

Trial	Setting	Population	Design	Sample size	Intervention (n)	Control (n)	Duration	Outcome
Parsons et al (2016)[34]	Care homes	Adults aged >50 y at risk of malnutrition	Randomised, parallel, open-label trial	104	ONS *ad libitum* (range of styles, flavours, volume, energy density; 87% took ONS with energy density between 1.5-2.4kcal/ml). Target provision 600kcal and 16g protein daily. ONS group also seen by dietitian (53)	Dietary advice by dietitian with leaflet at baseline and at week 6 (51)	12 weeks	**Nutritional** No significant changes in the total intake of energy, protein or other nutrients over time in control group. Total energy and protein intakes were significantly greater in intervention group vs. control group at 12 weeks by 423kcal/day ($p<0.001$) and 14.7g protein/day ($p<0.01$). Intakes of many micronutrients were significantly greater in intervention vs. control groups at same time point. Body weight increased significantly from baseline in intervention group ($p = 0.010$), but not in the control group ($p > 0.05$) but no significant difference between the groups. **Clinical:** NR **Functional** QoL (adjusted for baseline QOL, malnutrition risk, type of care received [nursing or residential]) was significantly higher in the ONS than the dietary advice group (intention to treat analysis at week 12; $n = 104$). EQ-5D TTO scores (mean ± SE) were 0.50 ± 0.04 vs 0.36 ± 0.05 ($p = 0.005$), VAS rescaled scores were 0.54 ±0.03 vs 0.046 ± 0.03 ($p = 0.006$) and VAS scores were 61.3 ± 4.5 vs 54.6 ± 6.3 ($p = 0.533$) for ONS vs dietary advice respectively. Significantly higher scores for all three measures (TTO [0.611 v 0.425; $p = 0.002$]; VASr [0.608 v 0.491; $p = 0.004$]; VAS [66.3 v 57.0; $p = 0.027$]) according to the per protocol analysis at 12 weeks. Responses to questions about appetite sensations did not differ between groups at any time points except for "fullness" which was experienced in a smaller proportion of subjects in the intervention vs. control group at week 12 (41% vs 70%; $p < 0.05$).

Table A3.1 Continued

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Persson et al. (2007)[35]	Community (recruited in hospital, ONS on discharge)	Older people at risk of malnutrition	RCT	108	1–2 x 200 ml daily of a choice of either a complete or an incomplete formula (plus 2 individualised counselling sessions by a dietitian, telephone contact from dietitian at 3 time points, advised to increase fat and eat more snacks between meals)	Brief written DA	4 months	**Nutritional** In both intention to treat and per protocol analyses, ONS group maintained weight while controls lost weight ($p < 0.001$) **Functional** Improved ADL in ONS group in the treated-as-protocol analyses ($p < 0.05$ between groups)
Price et al. (2005)[36]	Community, on discharge from hospital (nursing home residents excluded)	Older people following acute illness	RCT	136	2 x 200 ml daily	Usual care	8 weeks	**Nutritional** Higher energy intake in ONS group vs controls ($p = 0.022$) **Functional** Improved hand-grip strength in ONS group vs controls over 12 weeks ($p = 0.02$), mean increase of 19.9% vs 6.6%; intention to treat analysis 13.9% vs 7.2%, ($p = 0.055$)

Table A3.1 Continued

Trial	Setting	Popula-tion	Design	Sample size	Intervention (n)	Control (n)	Duration	Outcome
Simmons et al. (2015)[37]	Long term care facilities	Nursing home/ long stay residents	RCT - 3 arms (52 supplement ONS, 53 snack, 49 control)	154	ONS liquid or solid (52) or Snack (53)	Usual care (49)	6 months	**Nutritional** The ONS intervention group took in an average of 265 calories more per day and the snack intervention group an average of 303 calories more per day than the control group. Neither intervention had a significant effect on body weight, despite positive trends **Clinical:** NR **Functional:** NR **Economic** Both interventions were cost effective in increasing caloric intake. Cost effectiveness ratios were 103 kcal per dollar for the supplement intervention and 79kcal per dollar for the snack intervention.
Wouters-Wesseling et al. (2002)[38]	Nursing homes	Physco-geriatric patients	RCT	42	2 x 250 ml daily during day between main meals. Patients were helped and encouraged by nursing staff to drink the ONS (plus regular dietary intake)	Placebo (2 x 250 ml) consisting of water, cloudifier, flavourant and non-calorific sweetener to resemble ONS in taste and appearance. No energy, no vitamins, no minerals	3 months	**Nutritional** Improved body weight with ONS vs placebo (p = 0.03) Significant improvement in homocysteine, vitamins B1, B6, B12, D, thiamine diphosphate and folic acid levels in ONS group vs placebo group **Functional** No significant change in ADL

Note that actual intake often not recorded, may differ from target level.

Table A3.2 Summary of trials: setting, population, intervention and outcome – hospital studies and hospital to community

Trial	Setting	Popula-tion	Design	Sample size	Intervention (n)	Control (n)	Duration	Outcome
Anbar et al. (2013)[39]	Hospital	Geriatric hip fracture patients >65 y	RCT – 2 arms (22 intervention, 28 control)	50	Normal diet + ONS prescribed according to measured energy requirements/ intake (22)	Normal diet + ONS if already prescribed (28)	14 days or ad-mission length if earlier	**Nutritional** The intervention group had a significantly higher mean daily intake of energy and protein vs. control group during the first 11 postoperative days (p = 0.001). The calculated daily energy balance was significantly more positive in the intervention group (p <0.05) from days 3 to 10 of the study. **Clinical** The total complication rate was significantly lower in the intervention group vs. control group (27.3% vs. 64.3%, p = 0.012). This was mainly due to a reduction in the number of infectious complications in the intervention group (13.6% vs. 50%, p = 0.008). No difference in mortality. **Functional:** NR **Economic** There was a trend for shorter length of hospitalization in the intervention group (10.1 ±3.2 days vs. 12.5± 5.5 days for the control group, p = 0.06)
Bos et al. (2001)[40]	Hospital inpatients	Malnour-ished older people	Controlled trial	23	2 units daily providing total of 400 kcal, 30 g protein. Advised to consume between meals or at bedtime	No ONS, but careful nutrition attention from nursing staff (advice on finishing meals)	10 days	**Nutritional** Increased energy and protein intake, (p < 0.005 and p < 0.0002 respectively) **Functional** FFM and BMI changes between day 7 and 17 (p < 0.02 and p < 0.005 respectively) No significant effect on biological markers or hand-grip strength

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Table A3.2 Continued

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Botella-Carretero et al. (2008)[41]	Hospital (ONS started 48 h after surgery and continued until after discharge)	Normally nourished or mildly under-nourished older hip fracture patients	RCT (3-arm)	90	Group A: 4 x 10 g packets protein powder providing 36 g protein and 152 kcal/day dissolved in water, milk or soup Group B: 2 x 200 ml liquid ONS providing 37.6 g and 500 kcal/day	Standard or texture-modified diet	ONS started 48 hours after operation and maintained after hospital discharge	**Nutritional** No significant effects on nutritional status (albumin, prealbumin, BMI, tricipital fold or midbrachial circumference **Functional/clinical** No differences in hospital stay, mobilisation, blood transfusions, complications
Botella-Carretero et al. 2010)[42]	Hospital (ONS started on admission prior to surgery and continued until discharge)	Normally nourished or mildly under-nourished older hip fracture patients	RCT	60	2 x 200 ml liquid ONS providing 40 g protein and 400 kcal/day	Standard or texture-modified diet	ONS started 48 hours after operation and maintained after hospital discharge	**Nutritional** Larger decrease in serum albumin ($p = 0.002$) and prealbumin ($p = 0.045$) in control group after surgery and worse postoperative recovery vs intervention group No significant effects on anthropometric parameters (BMI, tricipital fold or midbrachial circumference) Compliance with supplement was 52.2±12.1% of prescribed amount daily. Intervention group had significantly higher total energy and protein intake vs control group ($p < 0.05$) **Clinical** Non-significant tendency for higher postoperative complication rate in the control group

Table A3.2 Continued

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Burden et al. (2011)[43]	Hospital (ONS started on admission prior to surgery and continued until surgery min 10 days)	Elective curative surgery for colorectal cancer	RCT	116	2 x 200 ml HP ONS providing 24 g protein and 600 kcal/day plus DA (*n* = 54)	DA (*n* = 62)	> 10 days preoperatively	**Nutritional** Intervention group had significantly higher total energy intake preoperatively: 1722 (489) kcal/d vs 745 (366), *p* = 0.001). No difference demonstrated for protein intake preoperatively: intervention group 51.8 (33.6) g vs control group 33.0 (16.0) g, *p* = 0.157 Full compliance with ONS 72% No significant benefit of ONS on postoperative complications demonstrated. Subgroup analysis showed significant reduction in surgical site infections (Buzby criteria) in weight-losing patients from intervention group preoperatively (*p* = 0.034)
Feldblum et al. (2011)[44]	Hospital and post discharge	Elderly medical under-nourished patients (MNA-SF < 10 or > 10% weight loss in previous 6 months) stratified into at risk or under-nourished	RCT (3-arm)	259	Group 1: in hospital and community treatment Group 2: in hospital treatment Treatment: individualised plans to ensure > 35 kcal/kg/d and 1–1.5 g protein/kg/d using diet and food/ONS supplements	Group 3: standard in-hospital care	Contact monthly for 6 months	**Nutritional** Mean change in MNA score significantly higher in group 1 (3.0±2.6) than in groups 2 and 3 (1.8±3.0, *p* = 0.004). Group 1 gained 0.5± 2.84 kg weight over 6 months vs 0.15±2.72 kg in groups 2 and 3 (ns). Trend towards higher intakes of macronutrients seen in group 1 after 3-month follow-up but not significant No significant haematological/ biochemical differences seen between groups, apart from significantly fewer patients in group 1 had low albumin levels (< 3.5 g/dl) after 6 months (9.7%) compared with groups 2 and 3 (22.9%, *p* = 0.03) **Functional** No significant impact of intervention on functional cognitive or depression status Lower mortality in group 1 (3.8%) vs groups 2 and 3 (11.8%, *p* = 0.046)

Table A3.2 Continued

Trial	Setting	Population	Design	Sample size	Intervention (n)	Control (n)	Duration	Outcome
Deutz et al. (2016)[45] & Zhong et al. (2016)[46]	Hospital stay and post discharge	Older (≥65 years) hospitalised patients with a primary diagnosis of acute myocardial infarction, congestive heart failure, pneumonia or chronic obstructive pulmonary disease and with moderate or severe malnutrition	Prospective DBPC RCT	652	Standard care plus ONS (containing high protein beta-hydroxy-beta-methylbutyrate (HP-HMB)) (328)	Standard care plus placebo (324)	90 days	**Nutritional**: Significant improvements in the experimental group, compared with the control group, observed in: - odds of achieving a better SGA nutritional class after 90 days ($p = 0.009$) - day 30 body weight ($p = 0.035$) - serum 25(OH)D concentration at days 30 and 60 ($p = 0.035$ and $p = 0.008$ respectively) **Clinical:** There was no significant difference between groups for the primary composite end-point (event of death or nonelective readmission within 90 days of discharge). Ninety-day mortality rate significantly decreased in the experimental group compared with the control group (4.8% vs 9.7%; $p = 0.018$), but no significant difference was observed between the groups for 90-day readmission rates. The Kaplan-Meier curve for mortality showed significantly greater survival in the experimental group compared with the control group ($p = 0.013$). No significant effects on mean total LOS found. **Functional:** No significant difference in ADL between groups at all time points. **Economic:** Mean 90-day costs for the experimental group were slightly greater than those for the control group ($22,506/person vs $22,133). Through the 90-day follow-up period, the experimental group gained 0.011 more QALYs than the control group, reflecting the experimental group's significantly greater probability of survival through 90 days follow-up. The 90-day follow-up period ICER was $33,818/QALY. Estimated lifetime expectancy for the experimental group was greater than that of the control group by 0.71 years. Lifetime ICER was $524/LYS.

Table A3.2 Continued

Trial	Setting	Population	Design	Sample size	Intervention (n)	Control (n)	Duration	Outcome
Flodin et al. (2014)[47]	Hospital	Elderly hip fracture hospitalised patients, >60 y	RCT- 3 arms (28 Ca/Vit D + Bisphos, 26 Ca/VitD + Bisphos +ONS, 25 Ca/Vit D)	79	ONS group: Calcichew D3 + 35mg risedronate daily 12m + 2 x 200ml daily milk based ONS (26)	Control group: Calcichew D3 (25)	6-12 m	**Nutritional**: NR **Clinical** Between baseline and 12 months, the percentage change in total body BMD was -0.02% for the ONS group and -0.9% and -1.6% for the bisphos. and control groups, respectively ($p = 0.03$). There was a mean increase in serum-25-OHD of between 17 nmol/L and 20 nmol/L in all three groups. **Functional:** NR **Economic:** NR
Gariballa et al. (2007)[48]	Hospital, continued in the commu-nity	Older people with acute illness	RDBPCT	225	2 bottles x 200 ml daily at 8.00 a.m. and 12 noon (plus NHD)	NHD plus placebo (identical to the supplement but contained no protein or micro-nutrients and with a minimal kcal content [60 kcal])	6 weeks	**Functional** Increase in number of patients with no depressive symptoms and decrease in patients with mild or severe depression with ONS compared to placebo ($p = 0.007$)

Table A3.2 Continued

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Gariballa et al. (2007)[49]	Hospital, continued in the community	Older people with acute illness	RDBPCT	225	2 x 200 ml daily at 8.00 a.m. and 12 noon (plus NHD)	NHD plus placebo (identical to the supplement but contained no protein or micronutrients and with a minimal kcal content [60 kcal])	6 weeks	**Functional** After adjustment for baseline QOL, age and gender, better QOL score with ONS at 6 months (physical function $p = 0.04$, physical role $p = 0.047$, and social function $p = 0.05$) but not at 6 weeks Overall QOL scores better at 6 months with ONS ($p = 0.003$), no significant difference in cumulative change between the two groups No difference in ADL
Gariballa et al. (2006)[50]	Hospital, continued in the community	Older people with acute illness	RDBPCT	445	2 x 200 ml daily at 8.00 a.m. and 12 noon (plus NHD)	NHD plus placebo (identical to the supplement but contained no protein or micronutrients and with a minimal kcal content [60 kcal])	6 weeks	**Nutritional** Improved red-cell folate and plasma vitamin B12 in ONS group compared to decrease seen in controls At 6 months, no difference between groups in weight, BMI, MUAC, TSFT or transferrin **Clinical** Reduced readmission rate (29% vs 40%, $p < 0.05$)
Gazzotti et al. (2003)[51]	Hospital, continued in the community	Older people at risk of malnutrition	RCT	80	2 x 200 ml daily (one of each energy density to provide total of 500 kcal and 21 g protein daily) (plus standard diet)	No nutritional supplementation	2 months	**Nutritional** MNA scores higher in ONS group vs control group at day 60 ($p < 0.01$) Spontaneous protein and energy intake higher in ONS group vs controls ($p < 0.01$) Mean weight loss in controls 1.23±2.5 kg ($p = 0.01$), ONS groups showed non-significant weight increase 0.28±3.8 kg ($p = 0.6$) **Clinical** No difference in LOS or discharge destination

Table A3.2 Continued

Trial	Setting	Population	Design	Sample size	Intervention (n)	Control (n)	Duration	Outcome
Hegerova et al. (2015)[52]	Hospital stay and post discharge	Acutely ill hospitalised older patients, >78 y	RCT - 2 arms (100 ONS plus exercise, 100 standard care)	200	ONS plus intense rehabilitation exercise program (100)	standard care (100)	Admis-sion length (11 ± 7d) then follow up 3 monthly for 1 year.	**Nutritional** The total daily energy and protein intakes were significantly higher in ONS group vs control (p <0.001). Intake of hospital food was not reduced. Both groups experienced decreases in body weight and BMI during the hospital stay but the ONS group started to regain both body weight and BMI immediately after discharge and achieved their original weight by 6 month post discharge. LBM did not change during hospital stay in the intervention group compared to the control group and was only 0.4 kg lower at 3 months as opposed to 3.5 kg lower in the control group. **Clinical:** NR **Functional:** NR **Economic:** NR
Huynh et al. (2014)[53]	Hospital	Moderate and severely malnourished patients	RCT- 2 arm (106 ONS, 106 control)	112	ONS + DC (104)	Standard diet + DC (103)	12 weeks	**Nutritional** Significant increases in energy and carbohydrate intakes at week 12 (560 vs 230 kcal) in intervention group vs control (p <0.05). At week 12 ONS significantly increased weight compared to control (2.0 vs 0.9kg) (p <0.001) and BMI (0.76 vs 0.37 kg/m^2) (p <0.001). **Functional** Patients who were in the lowest tertile of baseline handgrip strength score in the ONS group had a greater improvement in handgrip strength at week 4 (p = 0.042) compared to the control group. **Clinical** No significant differences between the groups in Albumin, pre-albumin or CRP after 12 weeks. **Economic:** NR

Table A3.2 Continued

Trial	Setting	Population	Design	Sample size	Intervention (n)	Control (n)	Duration	Outcome
Kabata et al. (2015)[54]	Hospital	Preoperative non-malnourished gastrointestinal cancer patients	Prospective RCT - 2 arm (54 ONS, 48 control)	102	ONS 14 days pre-surgery (54). ONS post-surgery if required.	Standard diet pre surgery (48). ONS post-surgery if required.	14 days, followed up 30 days post -surgery.	**Nutritional** Body weight decreased significantly in the control group (p <0.001) to borderline level of malnutrition, whereas in supplementation group their levels increased. **Clinical** In postoperative period, patients in control group suffered from significantly higher (p <0.001) number of serious complications compared with patients receiving ONS. Especially wound infections. Levels of albumin and total protein declined significantly (p <0.001) in the control vs the ONS group where they remained stable. Significant increases in median levels of Transferrin (p = 0.032) and TLC (p = 0.05) in the intervention group. **Functional:** NR **Economic:** NR
Lauque et al. (2004)[25]	Geriatric wards and day care centres	Older people with Alzheimer's disease at risk of under-nutrition	RCT	91	300–500 kcal/day in addition to the patients' spontaneous food intake	Usual care (some patients from the control group who received ONS prescribed during the study not excluded but ONS prescription recorded)	3 months	**Nutritional** Improved energy and protein intakes between baseline and 3 months in intervention group leading to significant improvement in weight and FFM **Functional/clinical** No difference in dependence, cognitive function or biological markers at 3 months or in fractures, pressure ulcers or hospitalisation at 6-month follow-up

Table A3.2 Continued

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Miller et al. (2006)[55]	Hospital, continued in the community (on discharge 52 went to rehab programme, 12 to community hospital, 16 to higher level care and 20 returned to pre-injury admission accommod-ation)	Older people at risk of under-nutrition with fall-related lower limb fracture	RCT	100	Supplement volumes were prescribed to meet 45% of individual estimated total energy requirements (range 580–800 ml/day). 4 doses of equal volume administered daily plus usual clinical care Group 1: ONS Group 2: ONS plus resistance training exercise Group 3: resistance training exercise	Group 4 – Attention control (received tri-weekly visits to match the home visits of the active intervention groups; discussions limited to general information, e.g. benefits of regular exercise and nutrient-dense meals)	42 days	**Nutritional** Patients in resistance training group lost more weight than those in ONS plus exercise group ($p = 0.029$) **Functional/clinical** No significant difference in quadriceps strength, gait speed, QOL or healthcare utilisation

Table A3.2 Continued

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Neumann et al. (2004)[56]	Rehabilitation hospital	Older people following hip fracture	RDB, parallel	46	At least 2 x 8 oz (227 ml*) daily	Compared with standard ONS (110 kcal and 3.9 g protein per 100ml†)	28 days	**Nutritional** Protein, fibre, calcium, vitamin K and phosphorus intake greater in HP ONS group **Clinical** Trend towards shorter rehab LOS but not significant (23 vs 28 days, $p = 0.27$) **Functional** No differences in FIM
Rabadi et al. (2008)[57]	Stroke rehabilitation hospital	Under-nourished patients	RDBCT	102	120 ml dose of an intensive ONS every 8 hours by mouth	Compared with standard ONS (127 kcal, 5 g protein). Standard ONS contained 36 mg vitamin C compared with 90 mg in the intensive ONS	From within 72 hours of arrival on unit to discharge	**Nutritional** Non-significant greater increase in body weight in intensive group **Functional** Improved total FIM and motor FIM sub-score ($p < 0.001$) and 2-minute and 6-minute walk test ($p < 0.001$) in the intensive ONS group vs controls Higher % returned home in the intensive group (63% vs 43%, $p < 0.05$)

*1 fluid oz = 28.4 ml. †Calculated from the description of the ONS used in the study. Note that actual intake often not recorded, may differ from target level

Table A3.2 Continued

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Rufenacht et al. (2010)[58]	Hospital	Under-nourished patients	RT	36	NT group – Individualised nutritional plan including fortified diet, snacks and energy-dense ONS ONS group – energy-dense ONS (2 x 200 ml 1.5 kcal/ml 12 g protein), no other advice		Length of hospital stay (10–15 days)	**Nutritional** Both groups demonstrated significant improvements in both energy intake ($p < 0.001$) and protein ($p < 0.001$) intake from baseline. No significant differences seen between groups Both groups demonstrated improved QOL parameters from baseline to discharge (NT group $p < 0.001$, ONS group $p < 0.003$). No significant differences between groups. NT group showed further significant improvement in QOL 2 months post discharge ($p = 0.016$)
Stratton et al. (2006)[59] Stratton et al. (2006)[60] Stratton et al. (2007)[61]	Hospital	Patients with fractured neck of femur at risk of malnutrition	RCT	50	Choice of liquid ONS ad libitum	Isoenergetic food snacks, e.g. cakes, biscuits, puddings	Postoper-atively until discharge	**Nutritional** Significantly greater energy and protein intake with ONS vs snacks Significantly greater mean total intake of all water-soluble vitamins in ONS group vs snack group Significantly fewer patients in ONS group had complications than in snack group (27% vs 58%, $p = 0.04$) Non-significant reduction in the incidence of specific complications, i.e. infections 17% vs 33% and wound-related complications (poor wound healing, pressure ulcers) 17% vs 38%

Table A3.3 Summary of trials in children: setting, population, intervention and outcome

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Alarcon et al. 2003[62]	Community	Mean age 48.5 months (range 36.0–61.0 months) Picky eaters below 25th percentile WFH (children with underlying acute/chronic disease excluded)	Multi-centre randomised, parallel group, open study	92	Physician-directed nutritional counselling with ONS	Physician-directed nutritional counselling without ONS	90 days	Significantly greater increase in WFH percentiles from baseline to day 60 ($p = 0.002$) and day 90 ($p < 0.001$) in study group vs controls Significantly greater increase in WFH percentiles from baseline to day 90 ($p < 0.001$) in study group vs controls – Philippines only Significantly greater increases for weight, height, WFH, WFA and HFA percentiles in study group compared to control group at all time points ($p < 0.05$) except HFA at day 30 Upper respiratory tract infections significantly lower in the study group vs controls (28% vs 51% respectively, $p = 0.027$)
Bayram et al. 2009[63]	Not specified	Mean age 7.5±3.0 years Children with malignant disease undergoing intensive chemo-therapy	Prospective randomised single centre open label study	52	Protein- and energy-dense EPA containing ONS in addition to normal dietary intake (2 x 240 ml/day)	Usual dietary care	3 months	At 3 months, significantly fewer patients in treatment group showed a loss in body weight (6.1% vs 47.4%, $p = 0.001$) and BMI (12.1% vs 52.6%, $p = 0.002$), and a negative deviation in weight percentile (6.1% vs 31.6%, $p = 0.021$) compared to the control group After 6 months ($n = 23$), the % of patients with weight loss was significantly lower in the treatment group vs controls (6.7% vs 50%, $p = 0.03$). No significant differences in BMI and negative deviation from weight percentile at this time point At 3 months, the remission rate in the treatment group was significantly greater vs controls (87.9% vs 63.2%, $p = 0.036$)

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Table A3.3 Continued

Trial	Setting	Population	Design	Sample size	Intervention (ONS)	Control	Duration	Outcome
Soylu et al. 2008[64]	Community	Children with spastic quadriplegia (mal-nourished)	Un-controlled intervention study	45	Nutritional support including DA and ONS	No control group	6 months	Significant changes in weight, height, MAC, TSFT, weight z-score, WFA, WFH, BMI and number of infections after treatment compared to baseline

Table A3.4 Summary of trials of EPA-enriched ONS in cancer patients: design, population, intervention and outcome

Trial	Design	Population	Intervention	Control	Duration	Outcome
Fearon et al. (2003)[65]	Multi-centre RCT	Advanced pancreatic cancer patients with cachexia	474 ml EPA-enriched ONS (providing 2.2 g EPA, 620 kcal, 32 g protein and enhanced levels of antioxidants) (n = 95)	474 ml Isocaloric, isonitrogenous standard ONS (n = 105)	8 weeks	Significant increase in total (diet plus supplement) energy and protein intake from baseline in experimental group completing 8 weeks (mean 224 kcal, $p = 0.001$ and 15 g protein/day, $p < 0.001$) compared to control group increase 68 kcal/day, ns and 6 g protein ($p = 0.036$) Post hoc analysis demonstrated significant correlation between supplement intake and weight gain in the EPA group ($r = 0.5$, $p < 0.001$) and an increase in LBM ($r = 0.33$, $p = 0.036$) in the study group that were not seen in the control group Significant correlation between 8-week plasma EPA level and an increase in weight ($r = 0.50$, $p < 0.001$) and LBM ($r = 0.51$, $p < 0.001$) were also seen in the study group Intake of EPA-enriched supplement correlated positively with QOL (EQ-5D index) ($r = 0.46$, $p < 0.001$)

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Table A3.4 Continued

Trial	Design	Population	Intervention	Control	Duration	Outcome
Guarcello et al. (2007)[66]	Blinded RCT	Malnourished patients with lung cancer undergoing chemotherapy	474 ml EPA-enriched ONS (providing 2.2 g EPA, 590 kcal, 32 g protein and enhanced levels of antioxidants) (n = 46)	474 ml isocaloric, isonitrogenous standard ONS (n = 105)	60 days	Significant improvements seen in body weight, oral energy and protein intake from diet seen from baseline (T0) in EPA-enriched ONS group (weight T0: 57.7 kg [42.7–70.6] – end 58.6 kg [46.0–73.0], $p < 0.05$; kcal intake T0: 1300 kcal [850–1700] – end 2000 [900–3300], $p < 0.05$; protein intake T0: 40 g [20–55] – end 60 g [35–80], $p < 0.05$). No differences seen in control group No between-group comparisons reported
Read et al. (2007)[67]	Open label phase II study	Stage IV colorectal cancer patients undergoing chemotherapy	480 ml EPA-enriched ONS (providing 2.2 g EPA, 0.92 g DHA, 600 kcal, 32 g protein and enhanced levels of antioxidants) (n = 23)	-	9 weeks	Mean weight increase 2.5 kg seen after 3 weeks (p = 0.03) prior to commencement of treatment; weight was then maintained through course of treatment. No significant increase in LBM seen
Van der Meij et al. (2010)[68]	RDBPCT	Stage 3 non-small -cell lung cancer undergoing multi-modality treatment	480 ml EPA-enriched ONS (providing 2.2 g EPA, 0.92 g DHA, 600 kcal, 32 g protein and enhanced levels of antioxidants) (n = 20)	400 ml Ensure plus® (n = 20)	5 weeks	EPA-enriched ONS group demonstrated significant improvements in energy and protein intakes after 4 weeks – 2456 kJ (p = 0.03) and 25.0 g (p = 0.01) respectively. The intervention group demonstrated better weight maintenance (by 1.7 kg, p = 0.04) after 4 weeks and a smaller reduction in LBM (by 1.9 kg, $p < 0.05$) after 5 weeks compared with control group
Weed et al. (2011)[69]	Prospective observational study	Perioperative head and neck small-cell cancer (SCC) (grade II+) patients with weight loss < 5% in previous 6 months	480 ml EPA-enriched ONS (providing 2.2 g EPA, 0.92 g DHA, 600 kcal, 32 g protein and enhanced levels of antioxidants) (n = 38)	-	Approx. 4 weeks	70% maintained or gained weight prior to surgery (mean + 0.71 kg), with 57% continuing to maintain or gain weight during hospital admission (mean + 0.66 kg). There was a statistically significant increase in LBM (+ 3.21 kg over the course of the study ($p < 0.01$) and a reduction in fat mass by 3.19 kg ($p < 0.001$)

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IV NUTRIENT CONTENT OF ONS vs TYPICAL FOOD SNACKS – Table A4.1

Table A4.1 Comparison of average nutrient content of some examples of ONS with typical snack foods used with the aim of increasing nutrient intake

		Fortisip† (Nutricia)	Ensure Plus† (Abbott Nutrition)	Fresubin Energy Drink† (Fresenius Kabi)	Resource Energy† (Nestle Health Sciences)	Nutricomp Drink plus Vanilla (B Braun)	Fruit yogurt	Cheese & crackers	Chocolate cake	Mars Bar
		per 200ml	per 220ml	per 200ml	per 200ml	per 100ml	per 150g	per portion*	per portion**	Per 65g bar
Energy	kcal	300	330	300	303	150	164	299	313	307
Protein	g	11.8	13.8	11.2	11.2	6	6	11.6	3.7	2.9
Carbohydrate	g	36.8	44.4	37.6	42	20	26.6	9.7	33.1	50.2
Sugars	g	13.4	14.3	7.8-12.6‡	11.4	-	24.9	0.1	22.3	43
Fat	g	11.6	10.8	11.6	10	5	4.5	24	19.3	11.9
Saturates	g	1.2	0.99	0.8	1.4	1.2	3	14.6	N/A	6.7
Dietary fibre	g	0¥	0¥	0¥	0¥	< 0,1	0	0.4	1	0.3
Sodium	mg	180	202	160	160	100	87	435	273	98
Potassium	mg	318	352	270	340	170	255	50	91	163
Chloride	mg	174	242	200	370	60	269	632	299	195
Calcium	mg	182	264	270	160	72	183	313	38	62
Phosphorus	mg	156	220	160	160	115	144	220	104	72
Magnesium	mg	46	66	42	56	27	20	15	23	21
Iron	mg	4.8	4.6	4	3.4	1.7	0.18	0.36	0.98	0.78
Zinc	mg	3.6	4.0	3	3	1.2	0.6	1.75	0.59	0.46
Copper	µg	540	396	0.6	0.3	170	0	0.04	0.2	0.20
Manganese	mg	1	1.1	0.8	0.7	0.58	0	0.01	0.1	0
Fluoride	mg	0.3	0	0.4	0.3	0.15	N/A	N/A	N/A	N/A
Molybdenum	µg	30	35	30	26	N/A	N/A	N/A	N/A	N/A
Selenium	µg	17.2	18	20	16	8.3	3	3	3	1
Chromium	µg	20	17	20	15	16	N/A	N/A	N/A	N/A
Iodine	µg	40	48	60	32	N/A	41	18	19	0
Vitamin A	µg RE	246 (54µg carotenoids)	257 (beta-carotene 64µg)	240 (beta-carotene 600µg)	276	0.15	54	241 (117 µg carotene)	0	20 µg retinol (26 µg carotene)
Vitamin D	µg	2.2	4.4	4	3.6	1.8	0.15	0.21	1.83	0.2
Vitamin E	mg-α-TE	3.8	4.7	6	6	2.0	0.27	0.57	1.96	0.31
Vitamin K	µg	16	26	33.4	28	12	0	2.62	0	3.12
Thiamin B1	mg	0.46	0.44	0.46	0.46	0.18	0.18	0.04	0.05	0.03
Riboflavin B2	mg	0.48	0.59	0.64	0.44	0.22	0.24	0.17	0.06	0.13
Niacin B3	mg NE	5.4	5.7	6	2.2	2.4	0.15	0.28	0.26	0.13
Pantothenic acid B5	mg	1.0	2.4	2.4	1.7	1.1	0.6	0.25	0.26	0.59
Vitamin B6	mg	0.52	0.59	0.66	0.7	0.22	0.02	0.08	0.03	0.02
Folic acid	µg	80	88	100	90	45	15	15	6	3
Vitamin B12	µg	0.64	1.2	1.2	0.44	0.55	0.45	0.99	0.65	0
Biotin	µg	12	13	15	13	8.0	1.7	2.1	3.9	1.3
Vitamin C	mg	30	26	30	30	15	1.5	0	0	0
Choline	mg	110	121	53.4	0	30	N/A	N/A	N/A	N/A
Data Source		www.nutricia.co.uk. Accessed 06.06.17	www.abbottnutrition.co.uk Accessed 06.06.17	www.fresenius-kabi.co.uk Accessed 06.06.17	www. nestlehealth-science.co.uk Accessed 06.06.17	www. bbraun.-co.uk	McCance and Widdowson The Composition of Foods[1]			

†Required to comply with the minimum and maximum values for vitamins, minerals and trace elements within Regulation No 2016/128. *Portion = 2 crackers, 40g cheddar cheese & 10g butter, **portion = 65g chocolate cake with butter icing. ‡Depending on flavour. ¥Fibre variants available. N/A, not available. [1]Food Standards Agency (2002) McCance and Widdowson's The Composition of Foods. 6th Summary ed. Cambridge: Royal Society of Chemistry.

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V SUMMARY OF TRIALS: TYPE, REGIMEN AND DURATION OF ONS USED – Tables A5.1 to A5.3

Table A5.1 Community studies

Table A5.2 Hospital studies and hospital to community studies

Table A5.3 Studies in children

- A variety of different ONS were used in the trials discussed, but in general, liquid multi-nutrient ONS were used.
- The duration of supplementation with ONS ranged from 10 days to 18 months (not specified in some trials).
- The energy density ranged from 0.85 kcal/ml to 2.5 kcal/ml and protein content ranged from 3.4 g/100 ml to 13 g/100 ml.
- Energy intakes from ONS ranged from 400 kcal to 1000 kcal per day and 17 g to 50 g of protein per day.

Table A5.1 **Summary of trials: Type, regimen and duration of ONS used – community studies**

Trial	Setting	Population	Design	Sample Size	Intervention					Control (n)	Duration
					ONS Type	ONS regimen	Energy (kcal) per 100ml	Protein (g) per 100ml	Micro-nutrients		
Allen et al. (2013)[1]	Nursing homes*	Older adults with dementia >65y	Prospective controlled crossover study	26	ONS drinks - various	3 x ONS per day on alternate days	130 (average by calculation)	6.3 (average by calculation)	Contains vitamins and minerals	No ONS on alternate days (26)	1 week
Bonnefoy et al. (2003)[2]	Retirement homes	Frail older people	RCT factorial design	57	1 kcal/ml	2 x 200ml daily given at 10.00 and 16.00 hours Group 1: ONS plus memory Group 2: ONS plus exercise	100	7.5	ONS provided 50% of Recommended Daily Allowances for vitamins and minerals	Placebo in identical packaging, contained no energy, protein or micronutrients Group 3: placebo plus exercise Group 4: placebo plus memory	9 months

*The majority of patients were recruited from nursing homes (18/26) others were recruited from hospitals (8/26).

Table A5.1 Continued

Trial	Setting	Population	Design	Sample Size	Intervention					Control (n)	Duration
					ONS Type	ONS regimen	Energy (kcal) per 100ml	Protein (g) per 100ml	Micro-nutrients		
Bunout et al. (2001)[3]	Community (free-living)	Older people	RCT	149	N/R	2 servings soup/ porridge-style supplement daily Group 1: ONS plus resistance exercise training Group 2: ONS, no training	400 (per 100g)	13 (per 100g)	Contained 25% of daily vita-min and mineral re-quirements	Group 3: no ONS, resistance exercise training Group 4: no ONS and no training	18 months
Edington et al. (2004)[4]	Community (post-discharge from hospital)	Older people malnourished	RCT	100	Various - N/R	Intakes between 600 kcal and 1000 kcal/ day prescribed in order to achieve a weight gain of at least 0.5 kg/week (plus telephone contact by dietitian)	Choice offered. Variety of different energy/ protein contents - N/R		N/R. Some known to be nutritionally complete	Standard care	8 weeks
Jobse et al. (2014)[5]	Nursing homes	Nursing home residents, ≥ 65y, with or at risk of malnutrition	RCT- 2 arms (45 ONS, 42 control)	87	2.4 kcal/ ml	Intervention group: 2 x 125ml bottles daily (low volume HPE ONS) (600kcal/day) given between meals or as part of dessert	240	19.2	Contains all essential, minerals, vitamins and trace elements	Usual care (42)	12 weeks

Table A5.1 Continued

Trial	Setting	Population	Design	Sample size	Intervention					Control	Duration
					ONS Type	ONS regimen (+ other care, if provided)	Energy (kcal) per 100ml	Protein (g) per 100ml	Micronutrients		
Kim and Lee (2013)[6]	Community-(free-living)	Frail older people, ≥ 65y, low socio-economic status	RCT - 2 arms (43 ONS, 44 control)	87	1.0 kcal/ml	Intervention group: 2 x 200ml cans daily (400 kcal/day) in addition to usual diet	100	6.25	Contains vitamins and minerals	Visited monthly - no placebo ONS/counselling but a small gift given. Home healthcare services suspended during trial period.	12 weeks
Lauque et al. (2004)[7]	Geriatric wards and day care centres	Older people with Alzheimer's disease, at risk of under-nutrition	RCT	91	Various (1-1.5 kcal/ml)	300 - 500 kcal/day in addition to the patients spontaneous food intake	100 - 150	5 - 8	Enriched with vitamins and minerals	Usual care (some patients from the control group who received ONS prescribed during the study not excluded, but ONS) prescription recorded	3 months
Manders et al. (2009)[8]	Residents of care homes for older people	Older people	RDBPCT parallel	176	1 kcal/ml	2 x 125ml dairy drink between meals (250 kcal/day)	100	3.5	Added vitamins, minerals & trace elements (25-175% of U.S. RDA, enhanced levels of antioxidants)	Placebo drink, no energy, vitamins or minerals. Contained water, cloudifier, thickener, flavouring, colourant and non-calorific sweetener	6 months
Manders et al. (2009)[9]	Residents of care homes for older people (homes for the elderly *n* = 3, nursing homes *n* = 3, mixed homes *n* = 3)	Older people	RDBPCT parallel	176	1 kcal/ml	2 x 125ml dairy drink between meals (250 kcal/day) in addition to usual diet	100	3.5	Added vitamins, minerals & trace elements (25-175% of Dutch RDA, with added antioxidants)	Placebo drink, no energy, vitamins or minerals. Contained water, cloudifier, thickener, flavouring, colourant and non-calorific sweetener	6 months

Table A5.1 Continued

Trial	Setting	Population	Design	Sample size	Intervention					Control	Duration
					ONS Type	ONS regimen (+ other care, if provided)	Energy (kcal) per 100ml	Protein (g) per 100ml	Micronutrients		
McMurdo et al. (2009)[10]	Community (admitted to hospital with acute illness). Residents of care homes excluded	Older people, under-nourished	RCT	253	1.5 kcal/ml	2 x 200ml daily	150	10	Nutritionally complete	Control supplement based on skimmed milk containing 200 kcal, 12.4 g protein	4 months
Neelemaat et al. (2012)[11]	Community (post hospital discharge)	Mal-nourished elderly (> 60 years) patients, various specialities	RCT	210	1.5 kcal/ml HP	2 x 200 ml daily. Alongside high energy/protein diet. Also received 400IE vitamin D3 and 500 mg calcium/d	150	6	Nutritionally complete	Usual care	3 months
Norman et al. (2008)[12]	Community	Mal-nourished patients with GI disease	RCT	101	1.5 kcal/ml, HP**	Up to 3 x 200ml daily. Patients advised to drink ONS slowly and in between meals (≥1 h before a meal) (plus standard DC session as per control, contacted once/month)	150	10	Nutritionally complete	Standard DC session (verbal advice, 45 min) by a registered dietitian. Advised on improving protein and energy intake with normal food. All patients actively contacted once/month.	3 month

Table A5.1 Continued

Trial	Setting	Population	Design	Sample Size	Intervention					Control (n)	Duration
					ONS Type	ONS regimen	Energy (kcal) per 100ml	Protein (g) per 100ml	Micro-nutrients		
Ng et al. (2015)[13]	Commu-nity-(free-living)	Frail older people, ≥ 65y, able to ambulate without personal assistance, identified door-to door using cardiovas-cular health study (CHS) criteria for frailty	RCT - 5 arms (49 ONS, 50 cognitive, 48 physical, 49 combi-nation, 50 control)	246	1.5kcal/ml	Group 1: 1x 200ml daily with 4.6g fibre (300 kcal/day) plus 29mg iron, 1mg folate, 200mg B6, 200mcg B12, 600mg Calcium and 200 IU Vit D supplements daily. In addition to usual diet Group 2: Physical exercise Group 3: Cognitive training Group 4: Combination of ONS, exercise and cognitive training Group 5: Control group	154	6	ONS nutritionally complete supplement with 4.6g fibre, plus 29mg iron, 1mg folate, 200mg B6, 200mcg B12, 600mg Calcium and 200 IU Vit D sup-plements daily.	Usual care (50), placebos identical in appearance to ONS and vitamin/ mineral supplements. Artificially sweetened vanilla flavoured liquid made with water and non-dairy creamer	24 weeks/ 6 months
Parsons et al. (2016)[14]	Care homes	Adults aged >50y at risk of malnutrition	Ran-domised, parallel, open-label trial (53 ONS, 51 control)	104	Range of styles (drinks, soups, puddings, modules), flavours and volumes	Target provision 600kcal and 16g protein daily (87% took ONS with energy density between 1.5-2.4kcal/ml).	130-450	NR	Some were complete in micronutri-ents	Dietary advice by dietitian with leaflet at baseline and at week 6. (51)	12 weeks

Table A5.1 Continued

Trial	Setting	Population	Design	Sample size	Intervention					Control	Duration
					ONS Type	ONS regimen (+ other care, if provided)	Energy (kcal) per 100ml	Protein (g) per 100ml	Micronutrients		
Payette et al. (2002)[15]	Community	Frail, older under-nourished people	RCT	83	Various: N/R	2 x 235 ml daily. Choice of ONS. Encouraged to attain max tolerable energy intake to gain 0.5 kg body weight per week. Instructed to use ONS and increase overall food intake (plus nutrition counselling by phone every 2 weeks between visits)	Choice offered. Variety of different energy/protein contents - N/R		N/R. Some known to be nutritionally complete	Visited monthly, no advice/ONS	16 weeks
Persson et al. (2007)[16]	Community (recruited in hospital, ONS on discharge)	Older people at risk of mal-nutrition	RCT	108	1.2 kcal/ml or 0.85 kcal/ml	1 - 2 x 200ml daily of a choice of either a complete or an incomplete formula (plus 2 individual-ised counselling sessions by a dietitian, telephone contact from dietitian at 3 time points, advised to increase fat, eat more snacks between meals)	120 (complete) 85 (in-complete)	5 4	Vitamins D, B6, B12, Folacin, Mg, Ca, Zn + multi vitamin supplement (nutrients as above except Mg, Ca)	Brief written dietary advice	4 months

Table A5.1 Continued

Trial	Setting	Population	Design	Sample Size	Intervention					Control (n)	Duration
					ONS Type	ONS regimen	Energy (kcal) per 100ml	Protein (g) per 100ml	Micro-nutrients		
Price et al. (2005)[17]	Community, on discharge from hospital (nursing home residents excluded)	Older people, following acute illness	RCT	136	1.5kcal/ml	2 x 200 ml daily	150	12	N/R. Known to be nutrition-ally complete	Usual care	8 weeks
Simmons et al. (2015)[18]	Long term care facilities	Nursing home/long stay resi-dents, with orders for nutritional supplemen-tation	RCT - 3 arms (52 supple-ment ONS, 53 snack, 49 control)	154	Various (twice per day morning and after-noon 5 days per week)	Group 1: supplement intervention - liquid and solid supplement options. Group 2: Snack intervention offered variety of foods e.g. yogurts, puddings and beverages (assorted juices and liquid supplements)	NR	NR	NR	Usual care (49)	24 weeks/ 6 months
Wouters-Wesseling et al. (2002)[19]	Nursing Homes	Psycho-geriatric patients	RCT	42	1.1 kcal/ml	2 x 250 ml daily during the day between main meals. Patients were helped and encouraged by nursing staff to drink the ONS (+ regular dietary intake)	109†	3.4†	Contained a range of vitamins and minerals	Placebo (2 x 250ml) consisting of water, cloudifier, flavouring and non-caloric sweetener to resemble ONS in taste and appearance. No energy, no vitamins, no minerals	3 months

N/R Not reported. *Mean actual duration of supplementation was 99.4 days (range 6–169). **HP ≥ 20% energy from protein.[6] †Calculated from the description of the ONS used in the study. Note that actual intake often not recorded, may differ from target level

Table A5.2 Summary of trials: Type, regimen and duration of ONS used – hospital studies and hospital to community studies

Trial	Setting	Population	Design	Sample Size	Intervention					Control (n)	Duration
					ONS Type	ONS regimen	Energy (kcal) per 100ml	Protein (g) per 100ml	Micro-nutrients		
Anbar et al. (2013)[20]	Hospital	Geriatric hip fracture hospi-talised patients >65y	RCT – 2 arms (22 interven-tion, 28 control)	50	1.5 kcal/ml (Ensure Plus) and 1.0 kcal/ml (Glucerna)	Intervention: amount of ONS adjusted to make up the difference between energy received from hospital food and measured energy expenditure.	150 and 100	5.7 and 4.2	Complete	Normal diet + ONS if already prescribed (28)	14 days or admission length if earlier
Bos et al. (2001)[21]	Hospital inpatients	Mal-nourished older people	Controlled trial	23	N/R	2 units daily providing total of 400 kcal, 30 g protein. Advised to consume between meals or at bedtime	N/R	N/R	Con-tained a range of vitamins and minerals	No ONS, but careful nutrition attention from nursing staff (advice on finishing meals)	10 days
Botella-Carretero et al. (2008)[22]	Hospital (ONS started 48 hrs after surgery and contin-ued until after dis-charge)	Normally nourished or mildly under-nourished older hip fracture patients	RCT (3-arm)	90	N/R 1.25 kcal/ml	Group A - 4 x 10g packets protein powder providing 36 g protein and 152 kcal/day dissolved in water, milk or soup Group B - 2 x 200 ml liquid ONS providing 37.6 g and 500 kcal/day	N/R 125	N/R 9.4	N/R N/R	Standard or texture modified diet	Started 48 hours operation and maintained after hospital discharge

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Table A5.2 Continued

Trial	Setting	Population	Design	Sample Size	Intervention					Control (n)	Duration
					ONS Type	ONS regimen	Energy (kcal) per 100ml	Protein (g) per 100ml	Micro-nutrients		
Botella-Carretero et al. 2010)[23]	Hospital (ONS started on admission prior to surgery and continued until discharge)	Normally nourished or mildly undernourished older hip fracture patients	RCT	60	1.kcal/ml	2 x 200 ml daily	100	10	ONS provided full range vitamins and minerals	No ONS	Up to 23 days
Burden et al. 2011)[24]	Hospital pre-operative	Elective colorectal cancer	RCT	116	1.5 kcal/ml HP ONS	2 x 200 ml daily advised between meals. Advised on high protein and energy menu choices	150	6	Nutritionally complete	DA only	Until discharge
Deutz et al. (2016)[25] & Zhong et al. (2016)[26]	Hospitals and post-dischage	Older, nourished adults hospitalised for congestive heart failure, acute myocardial infarction, pneumonia, or chronic obstructive pulmonary disease.	RDBPCT	654	1.4kcal/ml HP-HMB*	2 x 237ml servings per day during hospitalisation and for 90 days post-discharge	136	8.4	Contains essential micronutrients	Placebo in identical packaging provided per serving: 48 kcal, 12 g carbohydrate, and 10 mg vitamin C, but no other macro- or micronutrients	Admission length followed by 90 days post discharge

* HP-HMB, high-protein beta-hydroxy-beta-methylbutyrate.

Table A5.2 Continued

Trial	Setting	Population	Design	Sample Size	Intervention					Control (n)	Duration
					ONS Type	ONS regimen	Energy (kcal) per 100ml	Protein (g) per 100ml	Micro-nutrients		
Feldblum et al. (2011)[27]	Hospital and post dis-charge	Elderly medi-cal under-nourished patients (MNA-SF < 10, or > 10% weight loss in previous 6 months), stratified into at risk or under-nourished	RCT 3-arm	259	Liquid or pudding 1.5.kcal/ml 237 g can	Varied according to individualised patient plan (including fortified meals and snacks, multivitamin supplement as appropriate)	150	6.5	15% RDI for vitamins and minerals in 237 ml pack	Usual care (some pa-tients in control group received ONS prescribed during the study as part of routine care)	6 months
Flodin et al. (2014)[28]	Hospitals	Elderly hip fracture hospitalised patients, >60y	RCT- 3 arms (28 Ca/Vit D + Bisphos, 26 Ca/VitD + Bisphos +ONS, 25 Ca/Vit D)	79	1.5 kcal/ml	Group 1: Calcichew D3 (1000mg Ca & 800 IU Vit D daily) 12m. Group 2: Calcichew D3 + 35mg Risedronate daily 12m. Group 3: Calcichew D3 + 35mg Risedronate daily 12m + 2 x 200ml daily (600kcal and 40g protein) 6m.	150	10	NR	Control group: Calcichew D3 (25)	6-12 m

Table A5.2 Continued

Trial	Setting	Population	Design	Sample size	Intervention					Control	Duration
					ONS Type	ONS regimen (+ other care, if provided)	Energy (kcal) per 100ml	Protein (g) per 100ml	Micronutrients		
Gariballa et al. (2007)[29]	Hospital, continued in the community	Older people with acute illness	RDBPCT	225	2.5 kcal/ml, HP†	2 bottles x 200ml daily at 8.00 am and 12 noon (plus NHD)	249*	12.4*	100% RNI for vitamins & minerals for healthy older person	Normal hospital diet plus placebo (identical to the supplement but contained no protein or micronutrients and with a minimal kcal content (60 kcal))	6 weeks
Gariballa et al. (2007)[30]	Hospital, continued in the community	Older people with acute illness	RDBPCT	225	2.5 kcal/ml, HP†	2 bottles x 200ml daily at 8.00 am and 12 noon (+ NHD)	249*	12.4*	100% RNI for vitamins & minerals for healthy older person	Normal hospital diet plus placebo (identical to the supplement but contained no protein or micronutrients and with a minimal kcal content (60 kcal))	6 weeks
Gariballa et al. (2006)[31]	Hospital, continued in the community	Older people with acute illness	RDBPCT	445	2.5 kcal/ml, HP†	2 bottles x 200ml daily at 8.00 am and 12 noon (+ NHD)	249*	12.4*	100% RNI for vitamins & minerals for healthy older person	Normal hospital diet plus placebo (identical to the supplement but contained no protein or micronutrients and with a minimal kcal content (60 kcal))	6 weeks
Gazzotti et al. (2003)[32]	Hospital, continued in the community	Older people, at risk of malnutrition	RCT	80	1 kcal/ml 1.5 kcal/ml	2 x 200ml cups daily (1 of each energy density to provide total of 500 kcal and 21 g protein daily) (+ standard diet)	100 150	N/R	N/R - ? Nutritionally Complete	No nutritional supplementation	2 months

N/R Not reported. †HP ≥ 20% energy from protein. *Calculated from the description of the ONS used in the study. †1 fluid oz = 28.4 ml. Note that actual intake often not recorded, may differ

Table A5.2 Continued

Trial	Setting	Population	Design	Sample Size	Intervention					Control (n)	Duration
					ONS Type	ONS regimen	Energy (kcal) per 100ml	Protein (g) per 100ml	Micro-nutrients		
Hegerova et al. (2015)[33]	Hospital stay and post discharge	Acutely ill hospitalised older patients, >78y	RCT - 2 arms (100 ONS plus exercise, 100 standard care)	200	Sipping nutritional supplement (total 600 kcal/d)	Group 1:ONS plus exercise: ONS given at 14:00 and 19:00 in addition to usual diet (providing 600 kcal/d and 20 g protein/d)	NR	NR	NR	Standard care (100)	Admission length (11 ± 7d) then follow up 3 monthly for 1year.
Kabata et al. (2015)[34]	Hospitals	Pre-operative non-malnourished gastrointestinal cancer patients	Prospective RCT - 2 arms (54 ONS, 48 control)	102	1.5 kcal/ml	Intervention group: 2 x 200ml bottles daily (low volume HPE ONS) 14 days pre-surgery. (Nutridrink Protein N.V Nutricia)	150	10	Contains all essential, minerals, vitamins and trace elements	Standard diet pre surgery (48). ONS post surgery if required.	14 days, followed up 30 days post surgery.
Lauque et al. (2004)[7]	Geriatric wards and day care centres	Older people with Alzheimer's disease, at risk of undernutrition	RCT	91	Various (1-1.5 kcal/ml)	300-500 kcal/day) in addition to the patients' spontaneous food intake	100 - 150	5 - 8	Enriched with vitamins and minerals	Usual care (some patients from the control group who received ONS prescribed during the study not excluded but ONS prescription recorded)	3 months

Table A5.2 Continued

Trial	Setting	Population	Design	Sample size	Intervention					Control	Duration
					ONS Type	ONS regimen (+ other care, if provided)	Energy (kcal) per 100ml	Protein (g) per 100ml	Micronutrients		
Miller et al. (2006)[35]	Hospital, continued in the community (on discharge 52 went to rehab programme, 12 to community hospital, 16 to higher level care and 20 returned to pre-injury admission accommod-ation)	Older people at risk of under-nutrition with fall-related lower limb fracture	RCT	100	1.5 kcal/ml	Supplement volumes were prescribed to meet 45% of individual estimated total energy requirements (range 580–800 ml/day). 4 doses of equal volume administered daily + usual clinical care Group 1: ONS Group 2: ONS + exercise	150	6*	Complete	Group 3 – exercise Group 4 –attention control (received tri-weekly visits to match the home visits of the active intervention groups; discussions limited to general information, e.g. benefits of regular exercise and nutrient-dense meals)	42 days
Neumann et al. (2004)[36]	Rehabilitation hospital	Older people following hip fracture	RDB, parallel	46	1.1 kcal/ml HP	At least 2 x 8 oz (227 ml¥) daily	106*	6.6	Contains vitamins and minerals	Compared with standard ONS (110 kcal and 3.9 g protein per 100ml*)	28 days
Rabadi et al. (2008)[37]	Stroke rehabilitation hospital	Under-nourished patients	RDBCT	102	N/R	120 ml dose of an intensive ONS every 8 hours by mouth	240 kcal per ?	11 g protein per ?	Accompanied by multivitamins with minerals. ONS nutritionally complete	Compared with standard ONS (127 kcal, 5 g protein). Standard ONS contained 36 mg vitamin C compared with 90 mg in the intensive ONS	From within 72 hours of arrival on unit to discharge

N/R Not reported. †HP ≥ 20% energy from protein. *Calculated from the description of the ONS used in the study. †1 fluid oz = 28.4 ml. Note that actual intake often not recorded, may differ

Table A5.2 Continued

Trial	Setting	Population	Design	Sample size	Intervention					Control	Duration
					ONS Type	ONS regimen (+ other care, if provided)	Energy (kcal) per 100ml	Protein (g) per 100ml	Micronutrients		
Rufenacht et al. (2010)[38]	Hospital	Under-nourished	RT	36	1.5 kcal/ml	NT group: Individualised regimen including fortified meals and energy-dense snacks + ONS	150	6	N/R (Assume as per ONS group drink)		10–15 days
						ONS group: 2 x 200 ml 1.5 kcal/ml ONS with 12 g protein. Nutritionally complete (Nutridrink, Nutricia)	150	6	Full range of vitamins, minerals and trace elements		
Sanchez-Lara et al. (2014)[39]	Hospital setting	Malnourished patients with advanced NSCLC under-going chemo-therapy, ≥ 18y	RCT-2 arms (64 ONS, 46 control)	92	1.3 kcal/ml +EPA 600 kcal/day	Intervention group: 2 x 200ml bottles daily (low volume HPE ONS) 14 days pre-surgery. (Nutridrink Protein N.V Nutricia)	150	10	Contains all essential minerals, vitamins and trace elements	Standard diet pre surgery (48). ONS post surgery if required	14 days followed up 30 days post surgery
Stratton et al. (2006) [40;41;42]	Hospital	Patients with fractured neck of femur, at risk of malnutrition	RCT	50	1.5 kcal/ml	Choice of liquid ONS ad libitum	150	Various	Contained vitamins and minerals	Isoenergetic food snacks, e.g. cakes, biscuits, puddings	Post-opera-tively until discharge

Table A5.3 Summary of trials: Type, regimen and duration of ONS used – children

Trial	Setting	Population	Design	Sample size	Intervention					Control	Duration
					ONS Type	ONS regimen (+ other care, if provided)	Energy (kcal) per 100ml	Protein (g) per 100ml	Micronutrients		
Alarcon et al. 2003[43]	Community	Mean age 48.5 months (range 36.0–61.0 months) Picky eaters below 25th percentile WFH (children with underlying acute/chronic disease excluded)	Multi-centre randomised, parallel group, open	92	1 kcal/ml nutritionally complete paediatric supplement (Paediasure)	40 ml/kg/day in addition to diet (physician-directed nutritional counselling)	100	2.8	Complete	Physician-directed nutritional counselling without ONS	90 days
Bayram et al. 2009[44]	Hospital	Mean age 7.5±3.0 years Children diagnosed with malignant disease undergoing intensive chemotherapy	Prospective, randomised, single centre, open	52	1.25 kcal/ml HP ONS containing EPA (Prosure)	2 x 240 ml cartons daily	125	6.67	Range of vitamins, minerals, anti-oxidants and EPA	No ONS	3 months
Soylu et al. 2008[45]	Community	Children with spastic quadriplegia (malnourished)	2-centre intervention study	45	1–1.5 kcal/ml nutritionally complete paediatric supplement (Paediasure/ Fortini)	DA including texture modification and ONS	100–150	2.8–3.4	Nutritionally complete	No control	6 months

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