

## Conference on ‘Malnutrition matters’

### Symposium 2: The skeleton in the closet: malnutrition in the community Encouraging appropriate, evidence-based use of oral nutritional supplements

Rebecca J. Stratton\* and Marinos Elia

*Institute of Human Nutrition, School of Medicine, University of Southampton, F Level, MP 113, Southampton General Hospital, Southampton SO16 6YD, UK*

With the considerable cost of disease-related malnutrition to individuals and to society (estimated to be  $>£13 \times 10^9$  for the UK, 2007 prices), there is a need for effective and evidence-based ways of preventing and treating this condition. The wide range of oral nutritional supplements that may be prescribed for the dietary management of malnutrition and other conditions account for only about 1% (about  $£99 \times 10^6$ , 2007 data) of the prescribing budget in England. Systematic reviews and meta-analyses consistently suggest that ready-made, multi-nutrient liquids which may be prescribed can improve energy and nutritional intake, body weight and have a variety of clinical and functional benefits in a number of patient groups. Meta-analyses have repeatedly shown that oral nutritional supplements produce significant reductions in complications (e.g. infections) and mortality, and a recent meta-analysis shows a reduction in hospital admissions (OR 0.56 (95% CI 0.41, 0.77), six randomised controlled trials). Such benefits suggest that the appropriate use of oral nutritional supplements should form an integral part of the management of malnutrition, particularly as there is currently a lack of evidence for alternative oral nutrition strategies (e.g. food fortification and counselling). As with all therapies, compliance to oral nutritional supplements needs to be maximised and the use monitored. To make sure that those at risk of malnutrition are identified and treated appropriately, there is a need to embed national and local policies into routine clinical practice. In doing so, the economic burden of this costly condition can be curtailed. As recently suggested by the National Institute for Health and Clinical Excellence, substantial cost savings could be made if screening and treatment of malnourished patients was undertaken.

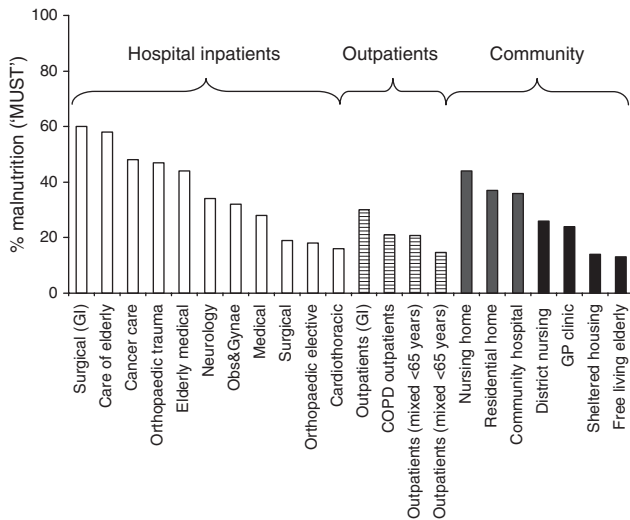
#### Malnutrition: Nutrition: Oral: Enteral: Supplement: Diet

Healthcare systems with budgetary constraints focus on the use of cost-effective evidence-based treatments, particularly during economic downturns. Therefore, in the current economic climate, it is becoming increasingly important to identify conditions promptly and to treat them in the most clinically and cost-effective way. This applies to the treatment of disease-related malnutrition, a condition that is prevalent in hospital inpatients (10–60% of hospital admissions are at risk of malnutrition), outpatients (15–30%) and in individuals living in the community (including free-living older people (aged 65 years and

over), those visiting general practice and those living in care homes or sheltered housing, 14–44%) (see Fig. 1 for prevalence of disease-related malnutrition identified with the ‘Malnutrition Universal Screening Tool’ (‘MUST’), see [www.bapen.org.uk](http://www.bapen.org.uk) for screening criteria)<sup>(1–10)</sup>. At any given point in time, more than 3 million people in the UK are malnourished with most (approximately 93%) living in the community<sup>(11)</sup>. Disease-related malnutrition is detrimental physiologically and clinically, impairing the quality of life and delaying recovery from illness<sup>(12)</sup>. Data suggest that disease-related malnutrition doubles the risk of

**Abbreviations:** ESPEN, European Society for Clinical Nutrition and Metabolism; ‘MUST’, ‘Malnutrition Universal Screening Tool’; NICE, National Institute for Health and Clinical Excellence; ONS, oral nutritional supplement; RCT, randomised controlled trial.

\*Corresponding author: Dr Rebecca J. Stratton, fax +44 2380 794945, email R.J.Stratton@soton.ac.uk

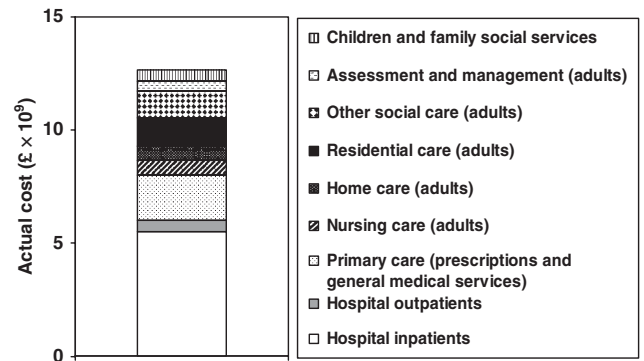


**Fig. 1.** Prevalence of disease-related malnutrition (using 'Malnutrition Universal Screening Tool' ('MUST')) in patients in hospital and community settings in the UK. GI, gastrointestinal; Obs & Gynae, obstetrics and gynaecology; COPD, chronic obstructive pulmonary disease; GP, general practitioner.

mortality in hospital patients and triples mortality in older patients (aged 65 years and above) in hospital and after discharge<sup>(5,13)</sup>. Disease-related malnutrition increases the use of health care (hospitalisations, General Practitioner visits and support required after hospital discharge)<sup>(1,3,12–16)</sup> and latest estimates suggest that this condition costs the UK more than £13 × 10<sup>9</sup> annually (2007 data; Fig. 2)<sup>(17)</sup>.

Despite the enormous public expenditure on malnutrition, the expenditure on treatments which may be prescribed for the management of this condition remains low. In 2007, the total cost of prescriptions in England was £8.372 × 10<sup>9</sup> (£8372.7 × 10<sup>6</sup>). Of this, 1.88% (£157 × 10<sup>6</sup>) was for nutrition (British National Formulary Section 9.4.2), a category including adult and paediatric oral and tube feeds, specialised infant and other formulae and fibre supplements. Specifically, about £99 × 10<sup>6</sup> (about 1.2%) was for oral nutritional supplements (ONS) and approximately £56 × 10<sup>6</sup> (approximately 0.7%) was for enteral tube feeds<sup>(18)</sup>. The costs of other forms of nutritional support, including the costs of dietetic time to manage malnourished patients and the costs of other interventions (food snacks, food fortification) remain unclear and need to be elucidated.

Considering the enormous costs of disease-related malnutrition, a condition that is largely treatable, prompt identification with screening, followed by the most appropriate, effective, evidence-based treatment is recommended<sup>(1,19,20)</sup>. The National Institute for Health and Clinical Excellence (NICE), recently released cost saving guidance, within the top four of which was nutrition support (in the form of oral nutrition support, tube feeding and parenteral nutrition). Specifically, NICE suggested that improving the systematic screening, assessment and treatment of malnourished patients (NICE CG32 guideline) could lead to an estimated cost saving of £28 472 per 100 000. NICE suggests that 'If this guidance (CG32) was fully implemented and resulted in better nourished patients



**Fig. 2.** Estimated costs of disease-related malnutrition in the UK<sup>(17)</sup>.

then this would lead to reduced complications such as secondary chest infections, pressure ulcers, wound abscesses and cardiac failure. Conservative estimates of reduced admissions and reduced length of stay for admitted patients, as well as reduced demand for General Practitioner and outpatient appointments indicate that significant savings are possible<sup>(21)</sup>.

A pragmatic programme of screening implementation (using 'MUST') in care homes in Peterborough Primary Care Trust highlights some such benefits<sup>(22)</sup>. A programme involving education and training on malnutrition, screening and treatment using the framework of 'MUST', locally agreed care plans and monitoring, improved the documentation of nutritional status, the proportion of residents screened and the use of appropriate care plans. After the implementation of the screening programme, significant reductions in the number and duration of hospital admissions were observed, associated with a significant cost saving of about £600 per resident over 3 months<sup>(22)</sup>. This could be equivalent to approximately £1 × 10<sup>9</sup> annually if extrapolated to the entire population of care home residents in the UK, although the costs of training and screening would need to be taken into account in order to estimate the overall net cost saving. Similar improvements of nutritional care and outcome have been observed in other settings where screening has been implemented. Rypkema *et al.*<sup>(23)</sup> showed improvements in nutritional status and fewer complications in older (>65 years) inpatients with a multi-disciplinary intervention involving a screening programme and Stratton and coworkers found an increase in the documentation of nutritional information, use of care plans and shorter hospital stay in neurology wards after 'MUST' implementation (RJ Stratton, M Collins and M Elia, unpublished results). In another study, early nutritional screening and the treatment of malnourished patients reduced the length of hospital stay in malnourished patients who had low handgrip strength (i.e. frail patients). The authors concluded that to shorten the mean length of hospital stay by 1 d for all malnourished patients, a mean investment of 76 euros (£69) in nutritional screening and treatment would be needed (only about one-quarter of the cost of one bed day)<sup>(24)</sup>.

Implementing a screening programme is an effective way to identify those who do and do not need nutritional support, such as help with meals, feeding or shopping or artificial nutrition. Most patients who are malnourished or

at risk of malnutrition can be managed using the oral route, often with a variety of dietary approaches including dietary modification (fortification, extra snacks, etc.), counselling by a dietitian and/or ONS<sup>(25)</sup>. However, with the rise of evidence-based practice, there is a need to demonstrate the effectiveness of these different strategies while making sure that they are used appropriately and their efficacy is maximised.

Although the focus of this review is the use of ONS, it is important to note that there is little formal evidence to support many of the other strategies used in the management of malnutrition, such as food snacks, fortification and dietary counselling<sup>(26)</sup>. Although the clinical and cost effectiveness of such strategies appear to be undocumented, they are widely advocated across health care settings, especially in primary care, in an attempt to reduce the use and costs of products which may be prescribed. Policies that focus only on reducing costs by withholding or stopping treatments are considered unsatisfactory, since they do not assess the clinical and economic consequences of this reduction and do not represent cost effectiveness<sup>(27)</sup>. Malnutrition that is untreated or ineffectively treated is likely to lead to a poorer quality of life, more complications, greater health care use and greater total health care expenditure. There is an additional financial implication for patients if prescribed forms of nutritional support are withdrawn or withheld, as the individual becomes responsible for acquiring and paying for the extra food or over the counter products that are recommended. An additional risk is that patients may then seek unsuitable or unsafe alternative forms of over the counter supplements, some of which may be unbalanced and potentially dangerous for their condition. In such patients, the end result could be increased costs to deal with unforeseen complications. Therefore, the implementation of such policies needs to be carefully considered and the effects monitored frequently to assess their clinical and cost effectiveness in both the short and long term.

#### *Oral nutritional supplements*

Many individuals while acutely or chronically ill are unable to consume the energy and/or nutrients they need from food alone, for a wide variety of reasons<sup>(12)</sup>. These are broadly divided into two main causes: a variety of disease-related factors and the inadequate availability and quality of food. Disease-related factors are many and include anorexia, nausea and vomiting, changes in taste and smell, painful or dry mouth, disorders of swallowing, breathlessness, difficulties in chewing, fatigue and other specific side-effects of surgery, drugs or inflammatory conditions. Disease-related psychosocial problems may also impair food intake, including depression, anxiety, social isolation and unappealing meal environments. For individuals at home, inadequate availability of food may be due to inadequate resources (finances and cooking facilities), poor access to shops or physical difficulties affecting food preparation. Within institutions, the quality, timing and presentation of food may limit intake. ONS offer a useful and effective strategy to meet this deficit in nutrient intake. ONS are typically multi-nutrient containing a mix

of macronutrients (protein, carbohydrate and fat) and micronutrients (vitamins, minerals and trace elements). Ready-made, nutritionally complete supplements are also energy dense (mostly containing 6.3 kJ (1.5 kcal)/ml to 10.1 kJ (2.4 kcal)/ml, 1.26 MJ (about 300 kcal) per serving (125–220 ml)) and provide a good source of protein (10–20 g per 1.26 MJ (about 300 kcal) serving) and a balance of micronutrients. Most are liquids that are available ready-made and so are convenient for individuals to use at home when ill and for health care professionals to administer in busy community and hospital settings, such as care homes and hospital wards. Powder supplements (to be reconstituted with whole milk before consumption) are also available on prescription or over the counter, although currently there is limited evidence to support their use<sup>(12,20)</sup>. The current evidence base supporting supplements is almost entirely restricted to ready-made types<sup>(12,20)</sup> and highlights their effectiveness for use in patients with or at a risk of malnutrition, particularly older individuals, those who are acutely ill and peri-operative patients. In the UK, there are a number of prescribed indications for the use of ONS which extend beyond disease-related malnutrition (and vary according to the supplement type; see Table 1 for a full list).

#### *Evidence-base for oral nutritional supplements*

A systematic review, which may or may not include a meta-analysis, has traditionally been considered as the best way of assessing the evidence-base for an intervention, such as ONS (type I in the hierarchy of evidence<sup>(28)</sup>). This is particularly so when the review is undertaken by those with a good understanding of the clinical use of the treatment, in combination with statistical expertise. In the last decade, an increasing number of systematic reviews have been undertaken to examine the effectiveness of oral nutrition support strategies in the management of malnutrition. The majority of these systematic reviews have focused on the use of ONS, the strategy for which there is the greatest number of individual trials available, usually in comparison with routine care (no nutritional support)<sup>(12,20)</sup>. Such reviews have had a major influence on the guideline development by national and international organisations, including non-governmental and governmental bodies. Indeed, there are already a substantial number of guidelines and standards referring to the use of ONS. Within Europe, these include guidelines from British organisations, such as the British Association for Parenteral and Enteral Nutrition, NICE and the Scottish Intercollegiate Guidelines Network (SIGN) as well as the European Society for Clinical Nutrition and Metabolism (ESPEN) (summarised in Table 2).

*Clinical outcomes and oral nutritional supplements.* Systematic reviews and meta-analyses<sup>(12,20,29–31)</sup> consistently suggest that ONS produce a range of clinical benefits including reduced mortality and fewer complications, such as wound and chest infections, pressure and leg ulcers. These are described in more detail in a 'review of reviews'<sup>(32)</sup> and a summary of these meta-analyses is shown in Table 3. In most trials, the daily reported intake of ONS was typically between 1.05 and 2.52 MJ

**Table 1.** Recommendations for use of oral nutritional supplements in clinical practice<sup>(32)</sup>

Use oral nutritional supplements (ONS) as part of the management of disease-related malnutrition and for the other listed prescribed indications (pre-operative preparation of malnourished patient, inflammatory bowel diseases, short bowel syndrome, intractable malabsorption, post-total gastrectomy, dysphagia, bowel fistulae, growth failure and hypoproteinaemia) (varies according to supplement, see British National Formulary). For disease-related malnutrition, routine screening can be used to identify at-risk individuals across health care settings. A valid, evidence-based tool such as 'MUST' should be used. Implement appropriate nutritional treatment as part of a care plan as soon as possible. Consider ONS as part of the care plan for the treatment of malnutrition:

- Liquid ONS can be used if improvements in energy, protein and micronutrient intakes are required. Liquid supplements tend not to suppress appetite or voluntary food intake and in some patient groups may stimulate food intake. A supplement containing a mix of macronutrients and micronutrients is important. Supplements with higher energy density may improve compliance and nutritional intake.
- For patients requiring longer term oral nutritional support, often in the community, it is likely that a variety of types of ONS and concomitant use of other dietary strategies would be beneficial to maintain improvements in nutritional intake.
- Liquid 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.
- High-protein ONS may be beneficial in preventing pressure ulcers in high risk groups and in improving clinical outcome in fractured neck of femur patients.
- Liquid, ready-made, multi-nutrient supplements (about 250–600 kcal (1.05–2.52 MJ) daily) can improve clinical outcome, reducing mortality and complications (infections and pressure ulcers), and health care use (reducing hospital admissions and length of stays).

Other oral nutritional support strategies that can form part of the care plan for the management of malnutrition include food snacks, food fortification and dietary counselling (although there is currently little evidence to support their efficacy).

Although dietetic support may be ideal for all patients identified with malnutrition, limited resources in many countries mean that this is an impractical strategy. However, if time and resources permit, or if there is clinical concern and specialised food or artificial nutritional support may be required, referral should be made to a dietitian, or nutrition support team for detailed nutritional assessment. This should consider intakes and requirements for energy, protein and micronutrients. Any specific identifiable nutrient deficiencies (trace elements, minerals and vitamins) should be corrected where possible.

The goal of any nutritional treatment, including ONS, should be identified for an individual patient at the onset of treatment. Regular and frequent monitoring is essential to assess the effectiveness of ONS, including the acceptability and compliance with ONS, changes in clinical and nutritional status, whether ONS are still required and need for other forms of nutritional support (e.g. changes to diet, tube feeding, etc.).

(250–600 kcal), with one review<sup>(31)</sup> suggesting that patients offered 1.68 MJ (>400 kcal)/d were more likely to benefit. The duration of supplementation varied depending on the patient group, from short periods in hospital (1 week) to much longer periods in the community (up to 2 years). The NICE<sup>(20)</sup> review suggested that the significant reduction in mortality and other improvements in clinical outcome seen with proprietary ONS in malnourished patients could not be demonstrated for other forms of oral nutritional support (e.g. food fortification and dietary advice), due to a lack of data. Similarly, a Cochrane review also highlighted the lack of data on the effects of dietary advice on clinical outcomes in both community and hospital settings<sup>(26)</sup>.

Systematic reviews and meta-analyses have highlighted significantly reduced mortality with ONS v. routine care (Table 3) in patients with a range of acute and chronic conditions, especially older patients<sup>(12,20,30–33)</sup>. One meta-analysis of studies across health care settings indicated that ONS produced a 30% reduction in mortality, predominantly due to effects in acutely ill, hospitalised patients<sup>(12,31,33)</sup>. The effect of ONS on mortality may vary according to the nutritional status of patients. The NICE reviews only considered trials in malnourished patients, but both Stratton *et al.*<sup>(12)</sup> and Milne *et al.*<sup>(31)</sup> indicated that ONS were more likely to reduce mortality in underweight/undernourished patients. One review indicated that the greatest reduction in mortality was observed in studies in which the mean BMI was <20 kg/m<sup>2</sup><sup>(12)</sup>. Meta-analyses of trials in the acute setting indicated significant reductions in mortality with ONS use in the undernourished (OR 0.66 (95% CI 0.49, 0.90), nine randomised controlled trials

(RCT)) with less effect in the well-nourished (OR 0.99 (95% CI 0.81, 1.21), five RCT), although the results from one single trial of stroke patients, >90% of whom were well-nourished (FOOD trial<sup>(34)</sup>), dominated this analysis<sup>(31)</sup>. However, it is difficult to interpret these results fully as individual studies defined malnutrition in different ways and some studies included a range of malnourished and well-nourished individuals. In addition, significant reductions in mortality have been reported in patients classified as well-nourished, for example by Stratton *et al.*<sup>(12)</sup> and by a small, specific meta-analysis of patients receiving ONS in long-term care (OR 0.46 (95% CI 0.25, 0.86), two RCT)<sup>(31)</sup>. Irrespective of nutritional status, the strongest and most consistent evidence for an effect of ONS on mortality is in older people and in the acutely ill<sup>(32)</sup>, where mortality is the highest. There was little evidence of an effect of ONS on mortality in free living individuals, where mortality rates are low. Studies with very large sample sizes and a prolonged duration of supplementation are needed to examine the existence of such effects as sufficiently powered trials are lacking. There is also a need to undertake high-quality studies to obtain a better understanding of the mechanisms by which ONS improve patient outcome, which may enable a more targeted use of ONS in specific health care settings and patient types. Although the methodology of individual trials (assessed in all reviews) was often judged to be poor, usually due to a lack of blinding, the effect of bias on unambiguous outcome measures, such as mortality, may be limited.

Systematic reviews of trials across different patient groups have highlighted substantial reductions in a range

of complications with ONS<sup>(12,20,29–31,33,35)</sup>, including infections (wound, chest, urinary, etc.), incomplete wound healing, pressure ulcers and total complications (see Table 3 for meta-analysis results). One systematic review showed a significant reduction in the development of one specific complication (pressure ulcers) with ONS *v.* routine care (OR 0.75 (95% CI 0.62, 0.89), four RCT, *n* 1224) (Table 3)<sup>(29)</sup>. In this meta-analysis, most studies used a liquid, high protein ONS for between 2 and 26 weeks, across hospital and long-term care. The other systematic reviews and meta-analyses mostly reported significant reductions in a range of complications with ONS use in hospital, community or combinations of health care settings<sup>(12,20,31,33,36)</sup>. In most cases, liquid, ready-made, multi-nutrient ONS were used, with reported intakes of 250–600 kcal (1.05–2.52 MJ)/d. In one systematic review including only high-protein ONS (containing >20% energy from protein), marked reductions in complications were also observed<sup>(36)</sup>. Systematic reviews of trials in patients in the peri-operative period have consistently indicated fewer complications with ONS use before, during and after hospitalisation, including total complications, infectious complications, major complications and intra-abdominal/thoracic complications<sup>(12,32,33,37)</sup>. Similarly, in hip fracture patients, a Cochrane review<sup>(38)</sup> suggests significantly fewer patients with an unfavourable outcome (mortality and complications) (relative risk 0.52 (95% CI 0.32, 0.84), three RCT, *n* 139) with ONS *v.* routine care.

The reduction in complications with ONS does not appear to differ between studies in which the mean BMI was <20 from those in which it is >20 kg/m<sup>2</sup>.<sup>(12)</sup> Indeed, reductions in complications are observed in surgical patients (e.g. gastrointestinal surgery<sup>(32,33,37)</sup>), who are not obviously thin but in whom poor nutritional intake in the post-operative period may have contributed to the development of complications.

*Functional outcomes and oral nutritional supplements.* Due to the wide range of functional outcomes measured in trials of ONS across different patient groups, it can be difficult to synthesise the evidence into a single meta-analysis of RCT. One systematic review that considered the impact of ONS on function in detail was Stratton *et al.*<sup>(12)</sup>. Within this systematic review, a number of individual studies in both hospital and community patients were found to show significant improvements in functional measures with ONS in groups such as older people, patients with liver disease and those undergoing surgery. The functional improvements included muscle strength, quality of life, immune function, walking distances and activities of daily life. This review also reported that in chronically ill patients in the community, functional benefits were more likely to occur in underweight individuals (BMI <20 kg/m<sup>2</sup>) who gained weight (>2 kg) with ONS. Another review that attempted to integrate a functional outcome (muscle strength) from only five trials in older people into a meta-analysis reported no significant effects of ONS<sup>(31)</sup>. Further research is warranted to determine the effects of ONS on important functional measures, especially quality of life, and other 'Patient reported outcome measures', which are now incorporated into policies within the National Health Service in England.

### *Nutritional outcomes and oral nutritional supplements*

*Nutritional status.* Systematic reviews and meta-analyses that assess nutritional status consistently indicate significant improvements with ONS<sup>(12,31,39)</sup>. The most common indicator of nutritional status assessed has been body weight. All meta-analyses that examined this outcome appeared to report a significant improvement with ONS relative to routine care in all settings (hospital, long-term care and community)<sup>(12,31)</sup>. Meta-analyses by Milne *et al.*<sup>(31)</sup> indicated significant improvements in the percentage weight change with ONS relative to routine care in older patients in long-term care (weighted mean difference 2.51 (95% CI 1.73, 3.20)%), in the community (2.25 (95% CI 1.72, 2.70)%) and in the hospital (1.75 (95% CI 1.12, 2.30)%) with a wide range of conditions, although it was unclear whether they were malnourished or not<sup>(31)</sup>. Another meta-analysis indicated a significant improvement in weight with ONS relative to dietary advice (weighted mean difference 1.09 (95% CI 0.29, 1.90) kg)<sup>(39)</sup>. In general, ONS use aided weight gain in chronically ill patients in the community setting and attenuated weight loss in studies in acutely ill patients in the hospital<sup>(12)</sup>. Improvements in weight with ONS were seen more frequently in community trials in which the mean BMI was <20 kg/m<sup>2</sup> (*v.* >20 kg/m<sup>2</sup>), but it was not possible to analyse the impact of ONS on patients who were losing weight, irrespective of BMI<sup>(12)</sup>. The composition of weight gain achieved with ONS (e.g. lean tissue and fat mass) was either not assessed or unclear in many studies, although a few RCT indicated significant improvements in lean tissue or body fat. In most trials, upper-arm anthropometry was used, possibly as an easier and more practical method to use clinically than other more sophisticated body composition techniques<sup>(40)</sup>. The review by Milne *et al.*<sup>(31)</sup> showed a significant increase in the mid-arm muscle circumference with ONS use in older hospital patients (weighted mean difference 1.41% (95% CI 0.46, 2.35%), six RCT). Irrespective of the composition of weight change, the increases in weight observed with ONS were linked to functional benefits, particularly in older people and in patients with chronic obstructive pulmonary disease<sup>(12)</sup>. In studies in the acute setting, improvements in clinical outcome were often associated with very small changes in body weight (<1–2 kg) as the periods of supplementation were sometimes as brief as 1 week. It is possible that the improvements in outcome observed with ONS, particularly in the acutely ill, occur via mechanisms that are largely independent of changes in body mass. One or more nutrients (macronutrients or micronutrients) provided by liquid, multi-nutrient ONS, could influence immune/inflammatory responses, and hence clinical outcome irrespective of changes in body weight or lean tissue mass<sup>(12,40)</sup>.

*Nutritional intake.* Systematic reviews that address the impact of ONS on nutritional intake consistently show improvements in total energy intakes in acutely and chronically ill patients in hospital and community settings<sup>(12,20,29,39)</sup>. Some indicate significant improvements in the intakes of protein and micronutrients<sup>(12,20,29)</sup>. Although often not assessed in trials, it is likely that total nutrient intakes (including micronutrient intakes)

**Table 2.** A summary of guidelines from British Association for Parenteral and Enteral Nutrition, National Institute for Health and Clinical Excellence, Scottish Intercollegiate Guidelines Network and European Society for Clinical Nutrition and Metabolism referring to oral nutritional supplement (ONS) use

Body	Patient group	Title	Guideline or standard*†
British Association for Parenteral and Enteral Nutrition			
Malnutrition Advisory Group <sup>(14)</sup>	Patients in the community	Guidelines for detection and management of malnutrition November 2000	5.3.2. Treatment typically begins with food, but may progress to the use of supplements. In some patients it may begin with both food and supplements. 5.3.2.2. If ordinary food is ineffective in improving nutritional status and ineffective in achieving the goals set at the beginning of treatment, nutritional supplements (mixed micronutrient 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)
Malnutrition Advisory Group <sup>(1)</sup>	All	The 'MUST' report. Nutritional screening of adults: a multidisciplinary responsibility. Development and use of the MUST for adults	B.6 There is substantial evidence of the beneficial clinical effects of nutritional supplements containing a mixture of macronutrients and micronutrients in particular groups of patients in the hospital and community, and of greater benefit in individuals with a BMI <20 kg/m <sup>2</sup> than >20 kg/m <sup>2</sup> , particularly patients in the community (A)
National Institute for Health and Clinical Excellence (NICE)			
NICE (CG32) <sup>(20)</sup>	All patients in hospital and in the community	Nutrition Support for Adults Oral Nutrition Support, Enteral Tube feeding and Parenteral Nutrition	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 <sup>†</sup> offered contains a balanced mixture of protein, energy, fibre, electrolytes, vitamins and minerals. (D(GPP)) Oral nutrition support <sup>†</sup> should be stopped when the patient is established on adequate oral intake from normal food. (D(GPP)) Peri-operative oral nutrition support* should be considered for surgical patients who can swallow safely and are malnourished. (B)
NICE and Royal College of Nursing <sup>(57)</sup>	Patients with pressure ulcers (primary and secondary care)	The management of pressure ulcers in primary and secondary care. A clinical practice guideline. September 2005	Nutritional support/supplementation for the treatment of patients with pressure ulcers should be based on – nutritional assessment (using a recognised tool e.g. 'MUST') – general health status – patient preference – expert input supporting decision making (dietician or specialists) (D)
NICE <sup>(58)</sup>	Chronic obstructive pulmonary disease	Chronic obstructive pulmonary disease. Management of chronic obstructive pulmonary disease in adults in primary and secondary care. Clinical guideline 12	If the BMI is low, patients should also be given nutritional supplements to increase their total energy intake, and be encouraged to take exercise to augment the effects of nutritional supplementation. (D)
NICE <sup>(59)</sup>	Stroke patients	National Clinical Guideline for Diagnosis and Initial Management of Acute Stroke and Transient Ischaemic Attack	Nutritional support should be initiated for people with stroke who are at risk of malnutrition. This may include ONS, specialist dietary advice and/or tube feeding
Scottish Intercollegiate Guidelines Network (SIGN)			
SIGN <sup>(60)</sup>	Older people – hip fractures	No. 111 Management of hip fracture in older people	Supplementing the diet of hip fracture patients in rehabilitation with high energy protein preparations containing minerals and vitamins should be considered (A) Oral multi-nutrient feeds provide protein, energy, some vitamins and minerals, and may reduce complications while in hospital, although they have no effect on mortality. The presence of protein in an oral feed may reduce the number of days spent in rehabilitation (1 + +)
SIGN <sup>(61)</sup>	Stroke and dysphagia	No. 78 Management of patients with stroke: identification and management of dysphagia. A national clinical guideline. September 2004	One randomised trial observing stroke patients . . . showed that oral nutrition supplementation is an effective method of improving nutritional status and clinical outcome (1 +)
SIGN <sup>(62)</sup>	Post-operative	No. 77 Postoperative management in adults. A practical guide to postoperative care for clinical staff. August 2004	Patients who are malnourished either at the time of, or shortly following major abdominal or vascular surgery have a more rapid recovery of nutritional status, physical function and quality of life, if given nutritional advice and prescribed routine oral supplements in the immediate postoperative period and following two months (1 +)

Table 2 (Continued)

Body	Patient group	Title	Guideline or standard*†
European Society for Clinical Nutrition and Metabolism (ESPEN)			
Meier <i>et al.</i> <sup>(63)</sup>	Pancreatic disease	ESPEN guidelines on enteral nutrition: pancreas	1.10 (Acute pancreatitis) Oral feeding (normal food and/or ONS) can be progressively attempted once gastric outlet obstruction has resolved, provided it does not result in pain and complications are under control (C). 2.4 (Chronic pancreatitis) 10–15% of all patients require ONS (C)
Lochs <i>et al.</i> <sup>(64)</sup>	Gastrointestinal diseases (Crohn's disease, ulcerative colitis, and short bowel syndrome)	ESPEN guidelines on enteral nutrition: gastroenterology	3.6 (Crohn's disease) In case of persistent intestinal inflammation (e.g. steroid dependent patients) use ONS (B) 3.1/3.2 Use ONS in addition to normal food to improve nutritional status and to eliminate consequences of undernutrition such as growth retardation (A) 4.1 Using ONS, a supplementary intake of up to 600 kcal (2.52 MJ)/d can be achieved in addition to normal food (A) 17.3 (Short bowel syndrome) Use ONS or tube feeding if normal nutritional status cannot be maintained by normal food alone (C)
Ockenga <i>et al.</i> <sup>(65)</sup>	HIV and other chronic infectious diseases	ESPEN guidelines on enteral nutrition: wasting in HIV and other chronic infectious diseases	2.4 (HIV) Diarrhoea does not prevent a positive effect of ONS on nutritional status (A) 2.2 (HIV) Nutritional counselling with ONS, or counselling alone, are equally effective at the beginning of nutritional support and/or for preserving nutritional status (B) 2.2 (HIV) 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) 4.0 (Infectious diseases) Nutritional support should be given to patients with undernutrition resulting from infectious diseases – prefer ONS (B)
Weimann <i>et al.</i> <sup>(66)</sup>	Surgery	ESPEN guidelines on enteral nutrition: surgery including organ transplantation	4.1 Encourage patients who do not meet their energy needs from normal food to take ONS during the pre-operative period (C) 6.0 Before transplantation, in undernutrition, use additional ONS (C)
Anker <i>et al.</i> <sup>(67)</sup>	Chronic heart failure and chronic obstructive pulmonary disease	ESPEN guidelines on enteral nutrition: cardiology and pulmonology	1.3 (Heart failure) Enteral nutrition (by means of ONS or tube feeding) is recommended in cardiac cachexia to stop or reverse weight loss (C) 2.5 (Chronic obstructive pulmonary disease) Frequent small amounts of ONS are preferred to avoid postprandial dyspnoea and satiety and to improve compliance (B)
Volkert <i>et al.</i> <sup>(68)</sup>	Geriatrics	ESPEN guidelines on enteral nutrition: geriatrics	2.1 In patients who are undernourished or at risk of undernutrition use oral nutritional supplementation to increase energy, protein and micronutrient intake, maintain or improve nutritional status and improve survival (A) 2.2 In the frail elderly use ONS to improve or maintain nutritional status (A) 2.4 In geriatric patients after hip fracture and orthopaedic surgery use ONS to reduce complications (A) 2.7 In demented patients ONS or tube feeding may lead to an improvement of nutritional status 2.7 In early and moderate dementia consider ONS – and occasionally tube feeding – to ensure adequate energy and nutrient supply and to prevent undernutrition (C) 2.10 Oral nutritional supplements, particularly with high protein content, can reduce the risk of developing pressure ulcers (A)

\*Levels of evidence: 1 + +, high-quality meta-analyses, systematic reviews of randomised controlled trial (RCT) or RCT with a very low risk of bias; 1 +, well-conducted meta-analyses, systematic reviews or RCT with a low 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 bias; 2 +, well-conducted case-control or cohort studies with a low risk of confounding bias. 3, case reports; 4, expert opinion.

†Grades of recommendations: 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 an overall consistency of results; B, a body of evidence including studies rated as 2 + +, directly applicable to the target population and demonstrating good overall consistency of results or extrapolated evidence from studies rated as 1 + + or 1 +; C, a body of evidence including studies rated as 2 +, directly applicable with consistent results or extrapolated from studies rated as 2 + +; D, evidence level 3 or 4, extrapolated evidence from studies rated as 2 + or formal consensus; D (GPP), a good practice point, a recommendation for best practice based on experience. For more information, refer to [www.nice.org.uk](http://www.nice.org.uk) or [www.sign.ac.uk](http://www.sign.ac.uk).

‡Oral nutritional support; includes ONS, dietary advice, food fortification, etc.

**Table 3.** Effect of oral nutritional supplements (ONS) on mortality and complication rates (analyses of trials in a mix of patient groups; adapted from Stratton & Elia<sup>(32)</sup>)

Systematic review	Intervention v. routine care	Mortality*	Complication*
Stratton <i>et al.</i> <sup>(12)</sup> (studies in a wider range of patient groups, hospital and community settings)	Mostly multi-nutrient, liquid ONS, 250–600 kcal (1.05–2.52 MJ)/d for <1 week to 2 years	OR 0.62 (95% CI 0.49, 0.76), 17 RCT, <i>n</i> 2096	OR 0.29 (95% CI 0.18, 0.47), 10 RCT, <i>n</i> 494
NICE <sup>(20)</sup> (studies in malnourished patients with a wide range of conditions in hospital and community settings)	Multi-nutrient proprietary ONS	RR 0.81 (95% CI 0.68, 0.97), 18 RCT, <i>n</i> 2564	RR 0.71 (95% CI 0.61, 0.82), 7 RCT, <i>n</i> 1001
Milne <i>et al.</i> <sup>(31)</sup> (all studies with a mean age >65 years, individuals with a wide range of conditions)	Mostly multi-nutrient, liquid ONS, some powders, 175–1000 kcal (0.74–4.2 MJ)/d for 10 d to 18 months	OR 0.86 (95% CI 0.74, 1.00), 25 RCT, <i>n</i> 6852 Unwell OR 0.86 (95% CI 0.74, 1.00), 22 RCT, <i>n</i> 6630 Aged >75 years OR 0.64 (95% CI 0.49, 0.85), 18 RCT, <i>n</i> 1611	OR 0.82 (95% CI 0.65, 1.03), 19 RCT, <i>n</i> 5508
Stratton <i>et al.</i> <sup>(29)</sup> (studies in all patients at risk of developing pressure ulcers, hospital and community settings)	All multi-nutrient, liquid ONS, mostly high protein, 250–600 kcal (1.05–2.52 MJ)/d for 2 to 26 weeks	–	OR 0.79 (95% CI 0.62, 0.89) <sup>†</sup> , 4 RCT, <i>n</i> 1224
Koretz <i>et al.</i> <sup>(33)</sup> ‡ (studies in geriatrics and in perioperative patients – variety of conditions and both hospital and community settings)	Mostly multi-nutrient, liquid ONS	Geriatrics <sup>§</sup> –4% (95% CI –7% to –1%), 14 RCT, <i>n</i> 1733 Peri-operative <sup>§</sup> 0 (95% CI –2, 2)%, 8 RCT, <i>n</i> 792	Geriatrics <sup>§</sup> Infectious complications only –5 (95% CI –13, 3)%, 3 RCT, <i>n</i> 503 Peri-operative <sup>§</sup> Total complication rate –13 (95% CI –23, –3)%, 9 RCT, <i>n</i> 789 Infectious complication rate –10 (95% CI –18, –1)%, 8 RCT, <i>n</i> 637 Major complications –11 (95% CI –20, –2)%, 6 RCT, <i>n</i> 568
Cawood <i>et al.</i> <sup>(36)</sup> ‡ (studies in patients with a wide range of conditions and in both hospital and community settings)	Ready-made, multi-nutrient ONS. High protein (>20% energy from protein)	–	OR 0.68 (95% CI 0.54, 0.86), 7 RCT, <i>n</i> 1543

RR, relative risk; RCT, randomised controlled trials.

\*An OR or RR < 1 indicates a lower incidence of mortality or complications in the supplemented patients than control patients. If the confidence interval does not pass 1.00, the result is statistically significant.

†In this meta-analysis the only complication assessed was pressure ulcers. In all other trials, a variety of complications were assessed (including wound infections, chest infections, pressure ulcers, etc.).

‡Added since publication of the 'review of reviews'<sup>(32)</sup>.

§Data presented as absolute risk difference.

are improved with ONS. This is partly because liquid supplements contain a range of macronutrients and micronutrients and also because liquid ONS do not appear to substantially suppress voluntary food intake or appetite<sup>(12,41)</sup>. This may be particularly important in older patients and those suffering from anorexia, in whom liquid ONS have been shown to improve energy, protein and micronutrient intakes to a greater degree than isoenergetic food snacks in both the hospital and community environment<sup>(42,43)</sup>. Similarly, the Cochrane review of Baldwin *et al.* found significantly greater energy intakes were achieved with ONS than dietary advice (weighted mean difference 91 (95% CI 23, 159) kcal) (0.38 MJ (95% CI 0.10, 0.67 MJ)), four RCT (*n* 138)<sup>(39)</sup>.

See Stratton *et al.*<sup>(12)</sup> and Stratton<sup>(44)</sup> for a more detailed review.

*Health care use and costs with oral nutritional supplements.* There has been an increasing interest in the effects of ONS on health care use and costs. In the acute setting, reductions in the length of hospital stay and complications and a reduction in associated costs with ONS have been well documented<sup>(3)</sup>. The British Association for Parenteral and Enteral Nutrition's health economic report found that the average net cost saving associated with ONS use in specific groups of hospitalised patients was about £850 per patient (2003 prices) and concluded that 'ONS can produce a net cost saving and be cost-effective in selected patient groups (such as patients undergoing gastrointestinal or

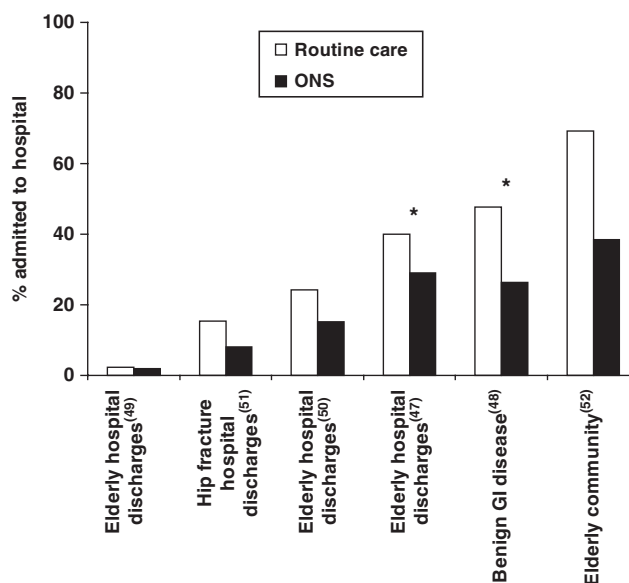


orthopaedic surgery'. The evidence-base for the use of nutritional support (ONS and tube feeding) to prevent pressure ulcers has been systematically examined<sup>(29)</sup>. This review found that nutritional support had important clinical and statistically significant effects on reducing the development of pressure ulcers in at-risk populations. Based on this systematic review, a simple cost analysis indicated a reduction in costs with the use of ONS to prevent pressure ulcers<sup>(45)</sup>. For all stages of pressure ulcers, there was a net cost saving in favour of ONS, which was significant for stage III (effect size 0.12 (95% CI 0.00, 0.11;  $P = 0.04$ )) and stage IV ulcers (0.12 (95% CI 0.01, 0.11;  $P = 0.04$ )). This corresponded to a net cost saving of £5 (stage I) to £460 per patient (stage IV) (2004 prices)<sup>(45)</sup>.

**Hospital admissions/readmissions.** Studies are now starting to assess the effects of ONS use, either entirely in the community or partly in the community following initiation in hospitals, on hospital admissions and readmissions. Recently, two large RCT have highlighted significant reductions in hospital readmissions following the use of ONS in community settings, in older people with a wide range of conditions and in individuals with benign gastrointestinal disease<sup>(46,47)</sup>. Other trials have also shown lower (not significantly so) hospital admissions/readmissions with the use of ONS v. routine care<sup>(48–51)</sup> (Fig. 3). When combined in a meta-analysis, the results highlight a highly significant reduction in hospital admissions with ONS (OR 0.56 (95% CI 0.41, 0.77), six RCT). The cost savings associated with such reduction in health care use are important, and the associated improvements to the patients' quality of life are also likely to be hugely beneficial, but require verification.

#### Encouraging appropriate use and maximising compliance

ONS, like any type of treatment, need to be used appropriately, and as effectively as possible. In addition to using ONS for their prescribed indications (Table 1) and in line with the evidence-base for their use, there are other matters to consider. Nutrition support should be tailored to the individual as much as is feasible and an individual's preference for the type of treatment they require should be taken into account, including the type of supplement they prefer, the time and way in which they receive and consume it (or other interventions that they may prefer). Of course, ensuring compliance to supplements is vital if improvements in nutritional intake and outcomes are required. Maximising the acceptability of supplements to patients may include using a variety of flavours, textures, temperatures, serving formats and consistencies. However, other patients are happy consuming the same supplement (type and flavour) for long periods of time. The energy density, volume and macronutrient profile of the supplement, the time and way in which it is administered and the duration of supplementation are factors that may affect compliance<sup>(12,52)</sup>. Recently, studies have suggested that increasing the energy density of liquid feeds improves both nutritional intake and compliance with supplementation, over the use of standard energy dense feeds in hospital and community patients<sup>(53–55)</sup>. Increasing the energy density of ONS minimises the volume needed to be consumed by a



**Fig. 3.** Reduction in hospital admissions/readmissions with the use of oral nutritional supplements (ONS). \*Significant reduction,  $P < 0.05$  (individual study references:<sup>(46–51)</sup>).

malnourished patient, and so encourages compliance and nutritional intake<sup>(53–55)</sup>. It is also likely that encouragement and education about the reasons for taking supplements would be beneficial. Overall, a greater understanding is still needed to maximise compliance with supplementation, especially over long periods of time, so that benefits can be achieved and sustained.

Like other treatments in clinical practice, it is recommended that the use of ONS (and other forms of nutritional support, such as dietary counselling) is appropriate and monitored. This typically involves reviewing the indications for the use of ONS, setting appropriate goals at the onset and reviewing these goals at intervals (the goals may include improvements in nutritional intake, weight and clinical/functional outcomes). The optimal dose and timing of supplementation for a patient is also important and should be reviewed regularly. It is necessary to review whether the termination of ONS is needed and whether the addition of other forms of nutritional support is needed. A recent publication supported by a number of national organisations (British Association for Parenteral and Enteral Nutrition, Parenteral and Enteral Nutrition Group, British Dietetic Association and National Nurses Nutrition Group) has highlighted some examples of good practice for the appropriate use of ONS in older people, while also summarising the evidence to support their use<sup>(56)</sup>. The NICE guidelines also highlight the importance of monitoring the use of all forms of nutritional support<sup>(20)</sup>.

#### Conclusion

Appropriate, evidence-based use of ONS should be an essential part of the management of disease-related malnutrition, particularly in the current economic environment we are facing. Malnutrition needs to be identified and treated effectively, since failure to do so can lead to disease complications and delay recovery from illness, at

enormous cost to the healthcare service. Prompt identification and treatment is required to attenuate the detrimental impact of malnutrition on health and the quality of life. The appropriate use of ONS should be an integral part of the management of disease-related malnutrition. Perhaps surprisingly, the use of ONS (mainly ready-made, multi-nutrient ONS) is the only form of oral nutritional support with a substantial evidence-base supporting its use. The evidence from systematic reviews and meta-analyses supports the use of ONS in a wide variety of conditions, but the evidence is strongest in the acutely ill, in older patients and in malnourished patients, in whom a range of clinical benefits, including a significant reduction in mortality and complications, such as infections and pressure ulcers, have been demonstrated. Appropriate use of ONS is likely to lead to economic benefits associated with reduced health care use, including a reduction in the number of hospital admissions and duration of hospital stay.

### Acknowledgements

Both R. S. and M. E. contributed to the writing of the manuscript and both authors read and approved the final manuscript. R. S. is also an employee of Nutricia Ltd. M. E. has no conflict of interest.

### References

- Elia M (2003) *Screening for Malnutrition: A Multi-disciplinary Responsibility. Development and Use of the Malnutrition Universal Screening Tool ('MUST') for Adults*. Redditch, Wores: BAPEN.
- Elia M & Stratton RJ (2005) Geographical inequalities in nutrient status and risk of malnutrition among English people aged 65 years and over. *Nutrition* **21**, 1100–1106.
- Elia M, Stratton RJ, Russell C *et al.* (2005) *The Cost of Disease-Related Malnutrition in the UK and Economic Considerations for the Use of Oral Nutritional Supplements (ONS) in Adults*. Redditch, Wores: BAPEN.
- Stratton RJ, King CL, Stroud MA *et al.* (2006) 'Malnutrition Universal Screening Tool' predicts mortality and length of hospital stay in acutely ill elderly. *Br J Nutr* **95**, 325–330.
- Stratton RJ & Elia M (2006) Deprivation linked to malnutrition risk and mortality in hospital. *Br J Nutr* **96**, 870–876.
- Cawood AL, Smith A, Dalrymple-Smith J *et al.* (2008) Prevalence of malnutrition and use of nutritional support in Peterborough Primary Care Trust. *J Hum Nutr Diet* **21**, 384.
- Parsons EL, Cawood AL, Warwick H *et al.* (2009) Prevalence of malnutrition risk in care homes in Hampshire. *J Nutr Health Aging* **13**, Suppl. 1, 159.
- Ralph A, Cawood AL, Hubbard GP *et al.* (2010) Prevalence of malnutrition in sheltered housing schemes in Wiltshire and Somerset. *Proc Nutr Soc* (In the Press).
- Collins PF, Stratton RJ, Kurukulaaratchy R *et al.* (2010) Prevalence of malnutrition in outpatients with chronic obstructive pulmonary disease. *Proc Nutr Soc* (In the Press).
- Rust S, Cawood AL, Walters E *et al.* (2010) Prevalence of malnutrition in hospital outpatients. *Proc Nutr Soc* (In the Press).
- Elia M & Russell CA (2009) *Combating Malnutrition: Recommendations for Action*. Redditch, Wores: BAPEN.
- Stratton RJ, Green CJ & Elia M (2003) *Disease-Related Malnutrition: An Evidence Based Approach to Treatment*. Oxford: CABI Publishing.
- Stratton RJ, King CL, Stroud MA *et al.* (2006) 'Malnutrition Universal Screening Tool' ('MUST') predicts mortality and length of hospital stay in acutely ill elderly. *Br J Nutr* **95**, 325–330.
- Elia M (2000) *Guidelines for Detection and Management of Malnutrition*. Maidenhead: Malnutrition Advisory Group (MAG), Standing Committee of BAPEN.
- Green CJ (1999) Existence, causes and consequences of disease-related malnutrition in the hospital and the community, and clinical and financial benefits of nutritional intervention. *Clin Nutr* **18**, Suppl. 2, 3–28.
- Elia M (2006) Nutrition and health economics. *Nutrition* **22**, 576–578.
- Elia M & Stratton RJ (2009) Calculating the cost of disease-related malnutrition in the UK. In *Combating Malnutrition: Recommendations for Action* [M Elia and CA Russell, editors]. Redditch, Wores: BAPEN.
- NHS Information Centre (2007) *Prescription Cost Analysis: England 2007. Based on British National Formulary (BNF)*. London: The Information Centre, Prescribing Support Unit.
- Elia M, Zellipour L & Stratton RJ (2005) To screen or not to screen for adult malnutrition. *Clin Nutr* **24**, 867–884.
- National Institute for Health and Clinical Excellence (NICE) (2006) *Nutrition Support in Adults: Oral Nutrition Support, Enteral Tube Feeding and Parenteral Nutrition (Clinical Guideline 32)*. London: National Institute for Health and Clinical Excellence (NICE).
- National Institute for Health and Clinical Excellence (NICE) (2009) *Cost Saving Guidance*. London: NICE; available at <http://www.nice.org.uk/usingguidance/benefitsofimplementation/costsavingsguidance.jsp>
- Cawood AL, Smith A, Pickles S *et al.* (2009) Effectiveness of implementing MUST into care homes within Peterborough Primary Care Trust England. *Clin Nutr* **4**, Suppl. 2, 81.
- Rypkema G, Adang E, Dicke H *et al.* (2003) Cost-effectiveness of an interdisciplinary intervention in geriatric inpatients to prevent malnutrition. *J Nutr Health Aging* **8**, 122–127.
- Kruizenga HM, Van Tulder MW, Seidell JC *et al.* (2005) Effectiveness and cost-effectiveness of early screening and treatment of malnourished patients. *Am J Clin Nutr* **82**, 1082–1089.
- Stratton RJ (2007). *Malnutrition*. In *Manual of Dietetic Practice*, 3rd ed. [B Thomas and J Bishop, editors], Oxford: Blackwell Publishing.
- Baldwin C & Weekes CE (2008) Dietary advice for illness-related malnutrition in adults. *Cochrane Database Syst Rev* (1), Issue 1, Article no. CD002008.
- Silk DBA, Russell CA & Stratton RJ (2008) Managing malnutrition in primary care: Letter to the editor. *Complete Nutr* **8**, 4.
- Higgins JPT & Green S (2006) *Cochrane Handbook for Systematic Reviews of Interventions*, 4.2.6. [updated September 2006]. In: *The Cochrane Library*. Chichester, UK: John Wiley & Sons Ltd.
- Stratton RJ, Ek A-C, Engfer M *et al.* (2005) Enteral nutritional support in prevention and treatment of pressure ulcers: a systematic review and meta-analysis. *Ageing Res Rev* **4**, 422–450.
- Potter J, Langhorne P & Roberts M (1998) Routine protein energy supplementation in adults: systematic review. *Br Med J* **317**, 495–501.
- Milne AC, Avenell A & Potter J (2006) Meta-analysis: protein and energy supplementation in older people. *Ann Intern Med* **144**, 37–48.

32. Stratton RJ & Elia M (2007) A review of reviews: a new look at the evidence for oral nutritional supplements in clinical practice. *Clin Nutr* **26**, 5–23.
33. Koretz RL, Avenell A, Lipman TO *et al.* (2007) Does enteral nutrition affect clinical outcome? A systematic review of the randomized trials. *Am J Gastroenterol* **102**, 412–429; quiz 468.
34. Dennis MS, Lewis SC & Warlow C (2005) Routine oral nutritional supplementation for stroke patients in hospital (FOOD): a multicentre randomised controlled trial. *Lancet* **365**, 755–763.
35. Cawood AL, Elia M, Freeman R *et al.* (2008) Systematic review and meta-analysis of the effects of high-protein oral nutritional supplements on healthcare use. *Proc Nutr Soc* **67**(OCE), E118.
36. Cawood AL, Elia M, Freeman R *et al.* (2007) Systematic review and meta-analysis of the effects of high protein oral nutritional supplements on complications. *Clin Nutr* **2**, Suppl. 2, 97–98.
37. Stratton RJ & Elia M (2007) Who benefits from nutritional support: what is the evidence? *Eur J Gastroenterol Hepatol* **19**, 353–358.
38. Avenell A & Handoll HH (2005) Nutritional supplementation for hip fracture aftercare in older people. *Cochrane Database Syst Rev* (2), CD001880.
39. Baldwin C, Parsons T & Logan S (2003) *Dietary Advice for Illness-Related Malnutrition in Adults (Cochrane Review)*. Oxford: Update Software.
40. Stratton RJ (2006) Are body composition measurements of value in the management of undernutrition? *Int J Body Compos Res* **4**, 45–50.
41. Stratton RJ & Elia M (1999) A critical, systematic analysis of the use of oral nutritional supplements in the community. *Clin Nutr* **18**, Suppl. 2, 29–84.
42. Stratton RJ, Bowyer G & Elia M (2006) Food snacks or liquid oral nutritional supplements as a first line treatment for malnutrition in post-operative patients? *Proc Nutr Soc* **65**, 4A.
43. Turic A, Gordon KL, Craig LD *et al.* (1999) Nutrition supplementation enables elderly residents of long-term-care facilities to meet or exceed RDAs without displacing energy or nutrient intakes from meals. *J Am Diet Assoc* **98**, 1457–1459.
44. Stratton RJ (2005) Elucidating effective ways to identify and treat malnutrition. *Proc Nutr Soc* **64**, 305–311.
45. Elia M & Stratton RJ (2005) A cost-benefit analysis of oral nutritional supplements in preventing pressure ulcers in hospital. *Clin Nutr* **24**, 640–641.
46. Gariballa S, Forster S, Walters S *et al.* (2006) A randomized, double-blind, placebo-controlled trial of nutritional supplementation during acute illness. *Am J Med* **119**, 693–699.
47. Norman K, Kirchner H, Freudenreich M *et al.* (2008) Three month intervention with protein and energy rich supplements improve muscle function and quality of life in malnourished patients with non-neoplastic gastrointestinal disease – a randomized controlled trial. *Clin Nutr* **27**, 48–56.
48. Edington J, Barnes R, Bryan F *et al.* (2004) A prospective randomised controlled trial of nutritional supplementation in malnourished elderly in the community: clinical and health economic outcomes. *Clin Nutr* **23**, 195–204.
49. Price R, Daly F, Pennington CR *et al.* (2005) Nutritional supplementation of very old people at hospital discharge increases muscle strength: a randomised controlled trial. *Gerontology* **51**, 179–185.
50. Miller MD, Crotty M, Whitehead C *et al.* (2006) Nutritional supplementation and resistance training in nutritionally at risk older adults following lower limb fracture: a randomized controlled trial. *Clin Rehabil* **20**, 311–323.
51. Chapman IM, Visvanathan R, Hammond AJ *et al.* (2009) Effect of testosterone and a nutritional supplement, alone and in combination, on hospital admissions in undernourished older men and women. *Am J Clin Nutr* **89**, 880–889.
52. Nieuwenhuizen WF, Weenen H, Rigby P *et al.* (2010) Older adults and patients in need of nutritional support: Review of current treatment options and factors influencing nutritional intake. *Clin Nutr* **29**, 160–169.
53. Hubbard GP, Holdoway A, Kerr A *et al.* (2009) A randomised, controlled trial comparing the use of energy dense nutritional supplement with dietary advice in malnourished community-based elderly patients. *Clin Nutr* **4**, Suppl. 2, 121.
54. Hubbard GP, Holdoway A & Stratton RJ (2009) A pilot study investigating compliance and efficacy of a novel low volume energy dense multi-nutrient supplement in malnourished community patients. *Clin Nutr* **4**, Suppl. 2, 41.
55. Hubbard GP, Buchan B, Sanders K *et al.* (2010) Improved compliance and increased intake of energy and protein with a high energy density, low volume multi-nutrient supplement. *Proc Nutr Soc* (In the Press).
56. Beck S, Church S, Duncan D *et al.* (2009) Appropriate use of oral nutritional supplements in older people. Good practice examples and recommendations for practical implementation.
57. National Institute for Health and Clinical Excellence (NICE) and Royal College of Nursing (2005) *The Management of Pressure Ulcers in Primary and Secondary Care. A Clinical Practice Guideline*. London: National Institute for Health and Clinical Excellence (NICE).
58. National Institute for Health and Clinical Excellence (NICE) (2004) *Chronic Obstructive Pulmonary Disease. Management of Chronic Obstructive Pulmonary Disease in Adults in Primary and Secondary Care. Clinical Guideline 12*. London: National Institute for Health and Clinical Excellence.
59. National Institute for Health and Clinical Excellence (NICE) (2008) *National Clinical Guideline for Diagnosis and Initial Management of Acute Stroke and Transient Ischaemic Attack (TIA)*. London: NICE.
60. Scottish Intercollegiate Guidelines Network (SIGN) (2009) *Management of Hip Fracture in Older People. A National Clinical Guideline. No. 111*. Edinburgh: NHS Quality Improvement Scotland.
61. Scottish Intercollegiate Guidelines Network (SIGN) (2004) *Management of Patients with Stroke. Identification and Management of Dysphagia*. Edinburgh: NHS Quality Improvement Scotland.
62. Scottish Intercollegiate Guidelines Network (SIGN) (2004) *Guideline No. 77 Postoperative Management in Adults. A Practical Guide to Postoperative Care for Clinical Staff*. Edinburgh: Scottish Intercollegiate Guidelines Network (SIGN).
63. Meier R, Ockenga J, Pertkiewicz M *et al.* (2006) ESPEN guidelines on enteral nutrition: pancreas. *Clin Nutr* **25**, 275–284.
64. Lochs H, Dejong C, Hammarqvist F *et al.* (2006) ESPEN guidelines on enteral nutrition: gastroenterology. *Clin Nutr* **25**, 260–274.
65. Ockenga J, Grimble R, Jonkers-Schuitema C *et al.* (2006) ESPEN guidelines on enteral nutrition: wasting in HIV and other chronic infectious diseases. *Clin Nutr* **25**, 319–329.
66. Weimann A, Braga M, Harsanyi L *et al.* (2006) ESPEN guidelines on enteral nutrition: surgery including organ transplantation. *Clin Nutr* **25**, 224–244.
67. Anker SD, John M, Pedersen PU *et al.* (2006) ESPEN guidelines on enteral nutrition: cardiology and pulmonology. *Clin Nutr* **25**, 311–318.
68. Volkert D, Berner YN, Berry E *et al.* (2006) ESPEN guidelines on enteral nutrition: geriatrics. *Clin Nutr* **25**, 330–360.