Health Council of the Netherlands

Undernutrition in the elderly

Gezondheidsraad
Health Council of the Netherlands

To the Minister of Health, Welfare and Sport

Subject : presentation of advisory report *Undernutrition in the elderly*
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Dear Minister,

On 18 August 2009, the Minister of Health, Welfare and Sport at the time asked for advice from the Health Council concerning energy-protein undernutrition. I would hereby like to present the advisory report *Ondervoeding bij ouderen* (Undernutrition in the elderly). I will also send this to the Minister of Economic Affairs, Agriculture and Innovation today.

In order to advise you, an appointed committee of experts has analysed the results of the available research. The Standing Committee on Nutrition, the Standing Committee on Medicine and the Advisory Committee on Health Research have reviewed the findings.

The requests for advice were connected with the memorandum *Gezonde voeding, van begin tot eind* (Health Nutrition, from beginning to end), which the Government sent to the House of Representatives in July 2008. A lot is being done in hospitals, care facilities and in primary care and home care to recognise and treat undernutrition. The questions posed to the Health Council were aimed at improving the policy in this field with a scientific foundation of the diagnostics and treatment of undernutrition.

However, the Committee has concluded that the scientific foundation of this problem is inadequate. We often do not know whether elderly people are ill and undernourished as a result, or whether the undernourishment actually contributes to the occurrence or exacerbation of an illness. The advice has raised more questions than answers. The uncertainties relate to the manner in which undernutrition can be diagnosed and the benefits

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gained by treating undernutrition. As undernutrition is a potentially serious problem, I think that it is essential to provide a powerful impulse in this field of nutritional research. That research should focus on determining the efficacy of supplementation. This advisory report provides a guide in this.

Yours sincerely,
(signed)
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Vice President

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to:

the Minister of Health, Welfare and Sport

No. 2011/32E, The Hague, November 29, 2011

The Health Council of the Netherlands, established in 1902, is an independent scientific advisory body. Its remit is "to advise the government and Parliament on the current level of knowledge with respect to public health issues and health (services) research..." (Section 22, Health Act).

The Health Council receives most requests for advice from the Ministers of Health, Welfare & Sport, Infrastructure & the Environment, Social Affairs & Employment, Economic Affairs, Agriculture & Innovation, and Education, Culture & Science. The Council can publish advisory reports on its own initiative. It usually does this in order to ask attention for developments or trends that are thought to be relevant to government policy.

Most Health Council reports are prepared by multidisciplinary committees of Dutch or, sometimes, foreign experts, appointed in a personal capacity. The reports are available to the public.

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Part 1

Undernutrition in the elderly

Executive summary

In recent years, there has been an increasing focus on the issue of undernutrition in the elderly. Hospitals and care institutions are alert to the risk of protein and energy deficiency in the elderly and provide nutritional supplementation where this is deemed to be necessary. This is considered to be a necessary step to improve the health of elderly people. The Minister of Health, Welfare and Sport has asked the Health Council of the Netherlands to provide a scientific basis for the way undernutrition is dealt with. What is the exact scope of the problem, what is the best way of identifying cases of undernutrition, and how can this condition best be treated? The Health Council has now collated the available data on this issue.

Over the long term, inadequate protein and energy intake is known to be harmful to health. However, it is not clear exactly where the boundary lies. When can someone be said to be undernourished? In practice, a range of methods is used to measure undernutrition (such as recent weight loss, and a low Body Mass Index). There is no “gold standard” (i.e. a reliable method). While various studies have demonstrated the existence of a link between undernutrition and mortality rate, for example, it is not known whether a causal connection exists. In other words, are elderly people at greater risk of dying as a result of undernutrition, or is their higher mortality risk mainly due to other factors, such as disease? As long as there is no clarity on this issue, there will be no reliable data on the severity and scope of the problem of undernutrition in the elderly.

Furthermore, many questions still remain to be answered concerning the effectiveness of dietary interventions in the elderly. While a great deal of research has been published in this area, the quality of the research in question is substandard. According to the Health Council, nutritional supplementation with extra protein and energy should produce clear health gains, such as shorter hospital stays or a lower mortality risk. However, it is impossible to identify those cases to which this would apply.

The current approach to undernutrition in the elderly is based on the view that the treatment of this condition is always worthwhile. However, this view is very much open to debate. Given the lack of a reliable method of measurement, too many elderly people may be classified as being undernourished. Accordingly, for some of these individuals, nutritional supplementation with extra protein and energy may not actually help to improve their health. Part of the elderly people who have experienced weight loss due to illness may also recover by receiving proper medical treatment, without a contributing effect of nutritional supplementation. There is another category of undernourished elderly people, however, for whom nutritional supplementation is essential to their health. As yet, there are no exact details concerning the cases to which this would apply. A better understanding of this issue is needed if undernutrition is to be dealt with effectively.

Undernutrition can be harmful to health, so it is vital to ensure that elderly people enjoy a good nutritional status. However, solid scientific research is needed to identify the magnitude of the problem, and the most effective way of dealing with it. According to the Health Council, collaboration between care providers is needed to achieve studies of good quality and sufficient scope.

Chapter 1

Introduction

Request for advisory report

There is much attention in society to protein-energy undernutrition in hospitals, care institutions and in home care. It appears from investigations and signals that a quarter of clients in health care are undernourished and that elderly people and the chronically ill form an important risk group. Hospitals, care institutions and home care therefore do a great deal to recognise and treat protein-energy undernutrition early. In 2005, the Steering Group *'Wie beter eet wordt sneller beter'* ('Whoever eats better gets better quicker'), otherwise known as the Malnutrition Steering Group, was formed, which focuses on optimal care concerning prevention, detection and treatment of undernutrition.[1] A National Primary health care Collaboration Covenant (in Dutch, LESA) was published in 2010 for the purposes of primary health care in the field of undernutrition; this contained agreements about screening for (district) nursing care, diagnosis, referral by the GP, treatment by the dietician, and the times when consultation is necessary.[2] Sections were targeted at combating undernutrition in the elderly in two – now completed – ZonMw (Netherlands Organisation for Health Research and Development) programmes: the project *'Sneller Beter'* ('Better Quicker') was directed at elderly people in hospitals and the improvement track 'Eating and drinking' in the programme *'Zorg voor Beter'* ('Take Better Care') at the non-independently-living elderly. In all these activities, the emphasis was and is on a purposeful approach in practice.

In the data from 2008 about nutrition and health, *'Gezonde Voeding, van begin tot eind'* ('Healthy Nutrition, from start to finish'), the Government put the problem of undernutrition in care on the agenda. From the wish to reinforce the approach to this problem with a scientific justification of the diagnosis and treatment, the Minister asked the Health Council for an advisory report. This concerns a scientific opinion on:

- the extent and impact of the problem of protein-energy undernutrition
- the methods of screening for protein-energy undernutrition
- the possible intervention points for reducing undernutrition and the percentage of the current prevalence of undernutrition that is avoidable
- the gain that is directly or indirectly possible through treatment of people with protein-energy undernutrition, for the perception of clients, for care provision as well as from a financial viewpoint.

The Minister has requested the Health Council, in responding to the request for advice, to take account of the different parts of the care chain and the various care professionals who are involved with (the solution of) the problem. The complete advisory report request may be found in Annex A.

To prepare the said report, the Council set up a Committee. The composition of the Committee is given in Annex B. The advisory report was evaluated in the Standing Committee on Nutrition, and in the Advisory Committee on Health Research.

Delineation

Based on the advice questions, this advisory report is specifically targeted at undernutrition as a result of inadequate intake of protein and energy (referred to hereafter as 'undernutrition'). Shortages of vitamins and minerals can also have undesirable consequences for health, but fall outside the scope of this report.*

The Committee opts for a demarcation to undernutrition in the elderly (over 65 years old). The prevalence in care institutions would appear to increase gradually with age from 65 years, while prevalence figures in younger patients are more or less stable.[3] The causes of the higher prevalence of undernutrition in the elderly are various. As elderly people of increasing age become less

* In the research available, deficiencies of micronutrients may well be present; a proportion of the people with protein-energy undernutrition also in fact have deficiencies of certain vitamins or minerals.

physically active, their energy demand decreases, and so generally does their energy intake. The energy intake can also reduce due to a reduction in appetite. This may be caused in the elderly by a reduced appreciation of food as a result of changes in the perception of tastes and smells, by psychosocial factors like loneliness, grief and depression, or by illness or infections. There are therefore many reasons why elderly people start to eat less. In order nevertheless to fulfil the need for protein, vitamins and minerals while eating and drinking less, qualitatively higher grade nutrition is required.

In the evaluation of the clinical utility of nutritional intervention, the Committee directs itself towards clinically relevant effects of the provision of extra protein and energy via foodstuffs, liquid foods or supplements. These interventions link up best with the increased broad approach to protein and energy undernutrition in care. Foods and supplements that are employed for serious or more specific problems are excluded from consideration; examples here are nutrition given via a tube or infusion, and supplementation with vitamins or minerals or with substances that can affect the immune system.

Lack of clarity on definition and assessment of undernutrition

There is no consensus either nationally or internationally about what undernutrition is exactly, or how it can be established. The consequence is that the concept of undernutrition is put into practice in different ways in the available research. The Committee describes from the available research not only the results but also the way in which undernutrition is established and discusses where necessary the implications of the diversity of definitions employed.

Structure of the advisory report

The Committee has made an inventory of the data available about undernutrition in the elderly and then assessed the scientific justification of this. Although a large number of studies into undernutrition have been published, only a small part of them are qualitatively good enough to serve as basis for this advisory report. The Committee does discuss all this research, but has opted for the sake of readability to present the methodological evaluation of the studies in a Background document. This advisory report therefore comprises two parts: a main text with the results of the analyses, the line of argument and a reaction to the advice questions, and a Background document in which the complete data are discussed. In the advisory report, the Committee refers to the relevant passages in the Background document.

In Chapter 2, the Committee discusses figures about undernutrition in elderly Dutch people and evaluates the scientific basis of the criteria with which undernutrition is established. Then, in Chapter 3, the instruments for screening come into consideration, including the data on the quality of these instruments. Chapter 4 considers the effectiveness of treatment with nutritional supplements. It contains an analysis of the research that has been published on this and an evaluation of its results. In Chapter 5, the Committee formulates its conclusions and recommendations.

Chapter 2

Prevalence of undernutrition in the elderly

There is no consensus either nationally or internationally about the definition of undernutrition. Studies that have been published on the subject each define in their own way what undernutrition is. The definition chosen of course affects the results of the study. This is also the case in the Dutch investigations into the prevalence of undernutrition.

Dutch figures

In the Netherlands, the prevalence of undernutrition has been determined annually since 2004 in the National Prevalence Survey on Health Care Problems (LPZ).[4] Because this contains little information specifically on the elderly, the LPZ also carried out additional analyses on the Health Council's request.* The LPZ provides data about undernutrition in hospitals, nursing and care homes, and home care. The prevalence of undernutrition in the Dutch elderly living independently at home is determined in the Longitudinal Aging Study Amsterdam (LASA**).[5] These data are also considered.

* For these analyses, the data about the elderly from the LPZ surveys of 2008, 2009 and 2010 were combined. The analyses were carried out by Dr. J.M.M. Meijers in consultation with Committee member Prof. J.M.G.A. Schols and the project leader of the LPZ, Dr. R.J.G. Halfens (MUMC Maastricht).

** These LASA data were collected in the years 2005 and 2006.

In the LPZ study, undernutrition in the elderly is established on the basis of three criteria: a body mass index (BMI) of less than 20.0 kg/m^2, recent unintentional weight loss or recent reduction in food consumption.[4] The criterion for unintentional weight loss is a reduction of at least 3 kilos in the last month or 6 kilos in the last 6 months. If a person has not eaten or has only eaten little for three days, or has eaten less than normal for a week, then there is considered to be a reduction in food consumption. Within the LPZ, reduced food consumption is only considered to be a criterion for undernutrition if the elderly person concerned has a BMI between 20.1 and 23.0 kg/m^2.

In the LASA study, undernutrition is established based on two criteria: a BMI less than 20.0 or an unintentional weight loss of at least 5 per cent in the last six months.[5]

Table 1 gives an overview of the prevalence estimates. To gain insight into the effect of the differences in the criteria on the prevalence data, both definitions are applied to the LPZ data. The LASA result for the independently-living elderly without home care is set out alongside. The table clearly shows that the difference in the criteria used to establish undernutrition leads to seriously divergent prevalence estimates. The largest difference occurred for the two figures on undernutrition in hospitals: depending on the criteria, these were 18 or 33 per cent. The differences in the other care settings were smaller. In nursing and care homes, around 20 per cent of the elderly were considered to be

Table 1 Prevalence of the separate criteria for undernutrition.[a]

	Nature of data		Prevalentieschattingen			
	Data set	Criteria employed[b]	Hospitals	Nursing and care homes	Home care	Independent without home care
Undernutrition	LPZ	LPZ	33%	21%	16%	
	LPZ	LASA	18%	18%	12%	
	LASA	LASA				7%
A low BMI	LPZ	LPZ	11%	15%	8%	
	LPZ	LASA	10%	15%	8%	
	LASA	LASA				3%
Unintentional weight loss	LPZ	LPZ	24%	9%	10%	
	LPZ	LASA	12%	5%	5%	
	LASA	LASA				5%
Reduced intake with BMI 21-23	LPZ	LPZ	7%	2%	2%	

[a] The sum of the prevalences of the separate criteria is higher than the prevalence of undernutrition, because a proportion of the elderly people meets multiple criteria.

[b] A description of the criteria used in the LPZ and in the LASA study may be found on the previous page.

undernourished. For the elderly people living independently without home care this was around 7 per cent. Because the great majority of the Dutch elderly (94 per cent in 2003) lives independently, this setting supplies the greatest proportion in an absolute sense of the total number of Dutch elderly considered to be undernourished.

In those elderly people living independently and in hospitals considered to be undernourished, the main issue was unintentional weight loss; this was the case in around 70 per cent of these undernourished elderly people. In nursing and care homes, that percentage was substantially lower (30-40 per cent), but 70 to 80 per cent of the elderly people considered as undernourished had a low BMI. The prevalence data are described in detail in Sections A1.1 and A1.2 of the Background document.

Justification of criteria to establish undernutrition: the relationship with a negative prognosis

In order to establish the extent and impact of the problem of undernutrition, a dependable definition is vital. For this reason, the Committee put the scientific justification of the factors that often play a role in establishing undernutrition under the microscope: a low BMI, unintentional weight loss and reduced food consumption. Are these factors associated with a negative prognosis, and if so, is it possible to make pronouncements about causality? In the scientific literature, the justification of these characteristics of undernutrition is based on the associations with the mortality risk. The Committee observes that other outcome measures may also be relevant, but that the scientific knowledge about associations of characteristics of undernutrition with outcome measures other than mortality is extremely limited.

Research reveals that a low BMI is associated with increased mortality. Recently, two large meta-analyses on this subject were published in prominent journals.[6,7] Smoking habits play an important role in the association between a low BMI and an increased mortality risk. According to some publications, there are indications that the BMI range within which the mortality risk is lowest lies at a higher BMI level in the elderly that in young adults[6,8-10], but this is not consistently found in all publications.[7] The shift could be partly due to the reduction in stature with time. According to the Committee, the available research is not sufficient in order to specify a limit value for the elderly, below which the BMI is considered too low (in relation to increased mortality). It is equally impossible to make out from the data whether a life-long stable but low

BMI increases the mortality risk. There is more information on this in the Background document: A1.3.1.

Weight loss is also associated with an increased mortality risk. Two studies provide indications that this mainly applies when the weight loss is unintentional.[11,12] In one study in which the association with mobility restrictions was investigated, associations were reported for subgroups with unintentional or intentional weight loss.[13] Six other studies make no distinction between unintentional and intentional weight loss.[14-19] It was found in two studies that the association between weight loss and mortality does not only exist at a low BMI, but also at a normal or high BMI.[13,17] The research is described in the Background document: A1.3.2.

Insufficient justification exists for reduced food consumption as an indicator of undernutrition: it was found in one study that reduced food consumption is associated with an increased mortality risk in the short term.[20] In that study, it was not investigated whether the said association is dependent on the BMI (see Background document A1.3.3).

The relationship among the three factors listed and mortality was investigated in observational research and therefore concerns associations. An association does not in fact provide any evidence that these characteristics of undernutrition increase the risk of death. Illness is potentially an important interfering variable in the connection between undernutrition and prognosis. Illness may be the cause of a low BMI, unintentional weight loss and reduced food consumption on the one hand, and on the other of a poor prognosis. In this way, in observational research, illness can lead to an association between these characteristics of undernutrition and a poor prognosis, even if the poor prognosis is the consequence of illness and not of the said characteristics of undernutrition.

Conclusion

A low BMI, weight loss and reduced food consumption are associated with a higher mortality risk. Due to the absence of trials, it is unclear whether causality exists in these associations. The cut-off points are equally poorly scientifically justified. For this reason, the meaning of these characteristics for establishing undernutrition is uncertain. In order to achieve certainty, research into the causality of the relationship between the characteristics of undernutrition and the prognosis is necessary. Questions that remain open include:

- Is someone with a life-long stable yet low BMI actually undernourished? If undernutrition arises through a gradual reduction in body weight over a

period of years, is a low BMI then the best indicator or would it be better to assess the weight loss over longer periods? Do nutritional interventions through which a low BMI is corrected to a target value lead to a better prognosis?

- Weight loss and reduced food consumption often occur in ill people and in people with psychosocial problems like loneliness, grief and depression. Is the association of these characteristics with a poor prognosis caused by the characteristics of undernutrition (the weight loss or the reduced consumption) or by the underlying illnesses or problems? Are elderly people better off when the weight loss or reduced consumption is combated or corrected via nutritional intervention?

According to the available research data, undernutrition in the elderly would appear to be a substantial problem, but the state of science is inadequate to assess the value of these prevalence data. Only when clarity is achieved about the questions of causality and there is a golden standard for establishing undernutrition can certainty be gained about the extent and seriousness of the problem.

Chapter 3

Methods of screening for undernutrition

On the Minister's request, the Committee presents a scientific opinion about the instruments for identifying undernutrition.

Instruments

Five instruments are the most relevant for the Netherlands:

- the Subjective Global Assessment (SGA)
- the Mini Nutritional Assessment (MNA)
- the Short Nutritional Assessment Questionnaires for hospitals (SNAQ), nursing and care homes ($SNAQ^{RC}$) and the elderly in first-line and home care ($SNAQ^{65+}$)
- the Malnutrition Universal Screening Tool (MUST) and
- the Nutrition Risk Screening 2002 (NRS-2002).

The instruments are presented, described and discussed in the Background document: A2.2 to A2.6. They take the form of a questionnaire, sometimes supplemented with some measurement values. The three characteristics of undernutrition sketched out above – weight loss, a low BMI and reduced food consumption – often play a major role. Besides these, the more complex instruments are based on information about factors such as illnesses that increase the probability that weight loss, a low BMI and reduced food consumption will occur.

The names of the instruments appear to make clear which instruments are intended for screening and which for assessment. According to the usual distinction, screening is rapid and simple to implement, and makes clear whether an assessment is necessary. An assessment is more complex and time-consuming and provides an answer to whether treatment is needed. The Committee points out that this usual distinction between screening and assessment cannot be recognised in the instruments in the undernutrition field.

Conclusion

The reproducibility (inter-observer variability)* appears usually to be adequate; moderate reproducibility has only been reported for application of the MNA in a hospital. No certainty can be given about the validity** of the instruments. Research has indeed been done into this, but because there is no golden standard to establish undernutrition, this research does not tell us much. The method evaluated is in fact always compared to a reference method of which it is not known whether it gives the correct picture either. This makes it unclear what value should be attributed to the estimates of the sensitivity and specificity of the instruments that arise from the studies.

The instruments are not founded on interventional research. Research is available for some instruments that specifies a connection between the results from the instrument and the prognosis, but those studies give no information about causality. Here too*** illness is an important potentially-interfering variable. It is unclear whether the group that is indicated as undernourished by the instrument would actually benefit from an intervention.

* The reproducibility is the extent to which repeated measurements with the same instrument yield the same results. Research into reproducibility in the field of undernutrition has mostly concerned inter-observer variability: the extent to which different care providers achieve the same result with the said instrument.

** The validity is the extent to which the results obtained with the instrument correspond to reality. To establish the actual value, a golden standard is needed: a method of which it is known that it presents a true picture of reality.

*** This was considered earlier on pages 22 and 23.

Chapter 4

Effectiveness of treatment with extra protein and energy

One of the Minister's advice questions concerns the gain that is possible through treatment of protein-energy undernutrition: does the health of undernourished elderly improve when these elderly people receive extra protein and energy? In the Committee's opinion, the answer to this question ought to play a central role in the choice of whether someone should or should not be treated with a nutritional supplement. Ideally, a nutritional intervention would only be instigated if a beneficial effect could be expected from it. This does not concern the effects on food consumption or on body weight, which in themselves have no clinical relevance, but rather on effects on for example mortality, the occurrence of complications, the admission duration, function and the quality of life.

Approach

In order to answer this question, the Committee has evaluated the state of science about the effectiveness of the provision of extra protein and energy via foodstuffs or liquid nutrition, hereafter called food supplementation (for the complete evaluation, see Chapter A3 in the Background document). Because the advice questions address the scientific justification of the current efforts of hospitals, care homes, and primary health care and home care to recognise and treat protein-energy undernutrition earlier, the Committee restricted itself to trials:

- in which the intervention concerned the intake of both protein and energy
- in which the supplement contained no specific amino acids, nor other specific nutrients that possibly have effects on the immune system
- in elderly people who consumed food normally and were not fed or supplemented via a tube or infusion
- in which the nutritional intervention was given orally (via the mouth, and not via tube or infusion).

Trials were only taken into consideration if clinically relevant effects were investigated within them (outcome measures like mortality, complications, quality of life and functional status, including muscle strength and mobility). Trials in which effects on body weight or intake of protein and energy were indeed reported, but no clinically relevant effects, therefore remained out of consideration.

State of science

The relevant publications up to December 2007 were identified via the meta-analysis by Milne and colleagues from 2009, entitled *Protein and energy supplementation in elderly people at risk from malnutrition.*[21] Further study of the intervention studies included in this meta-analysis revealed that a large part of them suffer from serious methodological limitations (Background document A3.2.2). These concern for example non-randomised allocation to treatment, non-use of placebos, small numbers of participants in many studies, and limited length of intervention. Additionally, only some of the trials were conducted in people considered to be undernourished, while it is plausible that elderly people who are indeed undernourished benefit from food supplementation. For this reason, the findings (Background document A3.2.3) are inadequately justified. Moreover, side-effects were not studied systematically.

Next, the Committee looked at the picture that arises from a selection of the six qualitatively-better *randomised controlled trials* (RCTs) in undernourished elderly people in the meta-analysis from Milne and coauthors[22-27], supplemented with six relevant publications of more recent date.[28-33] Even with regard to these RCTs, critical remarks could be made; the RCTs took place in a wide variety of settings, and undernutrition was established in divergent ways (Background document A3.3.2). The following picture emerges from this selection of twelve RCTs (Background document A3.3.3):

- the results concerning mortality do not give a consistent picture
- there are insufficient indications that food supplementation of the undernourished elderly reduces the risk of complications
- there are no indications for an effect of food supplementation on the admission duration in care institutions
- no conclusions may be reached about the other clinically relevant outcome measures: the number of RCTs and their size are too small for this.

Conclusion

In conclusion the Committee states that the state of science about the effect of treatment of protein-energy undernutrition in elderly people is very limited. The question of whether, and if so, what health gain is achievable if extra protein and energy is provided to undernourished elderly people cannot be answered, because too little qualitatively good research is available. Sensible conclusions about cost-effectiveness are equally impossible; this first demands clarity about the effects of food supplementation. Research of good quality and adequate extent is necessary for all settings (hospital, care institutions and elderly people living at home).

Chapter 5

Conclusions and recommendations

Conclusions

It was described in the introductory chapter that much effort is expended in hospitals, care institutions, and primary health care and home care to recognise and treat undernutrition in the elderly earlier. Undernutrition in the elderly is potentially an important problem. Attention to it is therefore valuable and should not be lost, in the Committee's opinion. From this advisory report, it proves however that a responsible approach requires a scientific knowledge base broader than what is currently available. The advice questions about the extent and the impact of undernutrition, methods for screening for undernutrition and the clinical utility of nutritional intervention cannot be answered based on the available research. The state of science is also inadequate to be able to conclude whether recent initiatives for a better detection of undernutrition and an increase in the energy and protein intake in the elderly are better than the usual nutritional policy in institutions and primary health care. These initiatives have indeed caused more attention to the problem.

The Committee only evaluated the state of science on the effect of food supplementation with extra protein and energy, because this type of intervention links up best with the current approach in practice; other possible intervention points for reducing undernutrition were left out of consideration.

The most important problems in the research available are the following:

- No golden standard exists to establish undernutrition. As a result of this, available estimates of the prevalence suffer from great uncertainties and the validity of screening instruments cannot be specified. The absence of a golden standard also works through into research into the effects of the provision of extra protein and energy to the undernourished elderly: undernutrition is established in diverse ways in the available interventional studies.
- Because characteristics of undernutrition (low body weight, weight loss) are often heavily interwoven with illness, it is difficult to determine to what extent an increased risk of illness and mortality is caused by undernutrition. If elderly people lose much weight in a short time, something is the matter. It is in fact unclear whether this problem can be solved by extra protein and energy intake. The Committee is of the opinion that protein-energy undernutrition is only clinically relevant is when a shortage of protein or energy is the *cause* of mortality, morbidity or delayed recovery. There is no doubt that insufficient intake of protein and energy can have clinical consequences in due course (famines provide harrowing evidence of this), but it is not clear for mild forms of undernutrition whether the link with a poorer prognosis is causal. The evidence for causality can only be supplied by qualitatively high-grade interventional research into the effect of food supplementation on the prognosis.
- The available interventional research into the effect of extra protein and energy on undernourished elderly people suffers from serious methodological limitations and shortcomings. As a result of this, this research gives insufficient insight into the clinical utility of interventions.

Recommendations

The close interrelationship between undernutrition and illness means that observational research (research into the associations between undernutrition and prognosis) only provides restricted insight into this problem. It is certain that it is damaging to health if someone obtains too little energy and protein in the long term. It is not clear where exactly the limit lies: when is someone undernourished? It is also unclear which elderly people would benefit from nutritional intervention. This last question can easily be answered by research. Research into this question is of importance due to its direct relevance for patients, care providers, health care insurers and the government.

The interventional research that is necessary for this must be randomised, be of sufficient scope and have an adequate intervention period. The intake of protein and energy must increase sufficiently due to the intervention to allow a clinically relevant effect to be distinguished. The research should be conducted in groups of (supposedly) undernourished elderly people, which are as homogeneous as possible as regards clinical picture, care setting and psychosocial characteristics (loneliness, grief and depression). The primary outcome measures of the research are clinically relevant effects (mortality, disease and function). Perception and quality of life may be included as secondary outcome measures.

Screening methods should in the future be directed at identification of treatable forms of undernutrition. For the purposes of improving the screening, the extent of the intended interventional research should be adequate for subgroup analyses to categories of BMI and weight loss.

The Committee notes that a multi-centre approach will generally be necessary in this field to allow qualitatively high-grade research of sufficient extent to be realised.

Finally

This advisory report and the Committee's recommendations are targeted at the clinical relevance of protein-energy undernutrition and of food supplementation with extra protein and energy, in elderly who do not receive (par)enteral nutrition. There are many other important aspects of the nutrition of the elderly that deserve attention in health care but which fall outside the scope of this advisory report. Examples are the need for extra vitamins and minerals, enteral/parenteral nutrition, nutritional quality, taste preferences, the presentation of meals and the ambience within which meals are enjoyed. Besides effects on health and prognosis, social, psychological, financial and ethical considerations are of importance.

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A	Request for advice
B	The Committee

Annexes

Annex **A**

Request for advice

Letter dated August 18, 2009 from the Minister of Health, Welfare and Sport to the President of the Health Council of the Netherlands.

In July 2008, I sent the Memorandum on Nutrition and Health to the Lower House. In this, nutritional policy is further described, as elaboration of my Cabinet's prevention vision.
In this memorandum I indicate, among other things, that I wish to reinforce the connection between prevention and care. More attention to healthy nutrition within the health services is an example of this. A healthy nutritional pattern in combination with a healthy lifestyle can reduce the risk of various (chronic) illnesses. In the phase when someone is ill or requires care also, a healthy nutritional pattern can contribute to a patient's health and the quality of his life.

In the memorandum, I mention undernutrition as a serious problem in hospitals and care institutions. The results of various studies and signals from different bodies that 25% of clients in health care are undernourished justify this supposition.

The elderly and the chronically ill are an important risk group for undernutrition. From a preventive viewpoint, attention to recognising and treating undernutrition in independently-living elderly people is also of particular importance.

In hospitals, care institutions and in primary health care and home care, much is already done to recognise and treat undernutrition earlier. In this, the emphasis is on a purposeful approach in the practical situation. Results within the *Sneller Beter* ('Better Quicker') project and in the improvement

tracks *Zorg voor Beter* ('Take Better Care') have demonstrated in practice that improvement is possible.

I should like to reinforce the approach to this problem with a scientific justification of the diagnosis and treatment of undernutrition. This could lead for example to simpler screening which would be to the benefit to the comparability of institutions, groups of the population or parts of integrated care. I wish to request the Health Council to employ its expertise in this matter.

Request for advisory report

Based on consultation with representatives involved from the field and discussions that took place at official level between the Health Council and the Ministry of Health, Welfare and Sport, I request you to prepare an advisory report about undernutrition in the elderly and the (chronically) ill.

In this, I request you to state a scientific opinion on:

- the extent and impact of the problem of energy-protein undernutrition;
- the methods of screening for energy-protein undernutrition;
- the possible intervention points for reducing undernutrition and the percentage of the current prevalence of undernutrition that is avoidable;
- the gain that is directly or indirectly possible through treatment of energy-protein undernutrition, for the perception of clients, for care provision as well as from a financial viewpoint.

In this, I request you to take account of the different parts of the care chain and the various care professionals who are involved with (the solution of) the problem.

In April this year I received from you the advisory report *Prevention in the Elderly: Focus on Self-sufficiency.* The advisory report request detailed above links up with this. I consider that more insight into the approach to undernutrition can contribute to both illness-related and function-related prevention, as you have stated in your advisory report on prevention in the elderly.

I wish you every success in the preparation of the report and await it with confidence.

Yours faithfully,
The Minister for Public Health, Welfare and Sport,
(signed)
Dr. A. Klink

Annex **B**

The Committee

- Prof. D. Kromhout, *Chairman*
  Vice-President of the Health Council of the Netherlands
- Prof. J.J. van Binsbergen
  Endowed Chair: Professor of Nutrition and Family Medicine, St. Radboud University Medical Centre, Nijmegen
- Prof. H. Boersma
  Professor of Clinical Epidemiology of Cardiovascular Disease, Erasmus Medical Center, Rotterdam
- Dr. M.A.E. van Bokhorst-de van der Schueren
  Senior Nutrition Scientist, Nutrition and Dietetics, VU University Medical Center, Amsterdam
- Prof. R.J. Brummer
  Professor of Gastroenterology and Clinical Nutrition, University of Örebrö, Sweden; Professor of Medical Nutrition and Clinical Dietetics, Maastricht University Medical Center, Maastricht
- Prof. C.P.G.M. de Groot
  Personal chair Nutrition and ageing, with due attention for nutrition later in life, Wageningen University
- Dr. J.A. Iestra
  Assistant Professor, Department of Dietetics and Nutritional Sciences, Utrecht University Medical Center, Utrecht

- Prof. L. van Loon
  Special Professor of Physiology of Exercise, Maastricht University Medical Centre, Maastricht
- Prof. B.W.J.H. Penninx
  Professor of Psychiatric Epidemiology, VU University Medical Center, Amsterdam
- Prof. H. Pijl
  Professor of Diabetology, Leiden University Medical Center, Leiden
- Prof. J.M.G.A. Schols
  Professor of Old Age Medicine, Maastricht University Medical Center, Maastricht
- Prof. M. Visser
  Professor of Healthy Aging, VU University Medical Center and VU University, Amsterdam
- R.J. Metaal, *Observer*
  Ministry for Public Health, Welfare and Sport, The Hague
- Dr. C.J.K. Spaaij, *Scientific secretary*
  Netherlands Health Council, The Hague

The Health Council and interests

Members of Health Council Committees are appointed in a personal capacity because of their special expertise in the matters to be addressed. Nonetheless, it is precisely because of this expertise that they may also have interests. This in itself does not necessarily present an obstacle for membership of a Health Council Committee. Transparency regarding possible conflicts of interest is nonetheless important, both for the chairperson and members of a Committee and for the President of the Health Council. On being invited to join a Committee, members are asked to submit a form detailing the functions they hold and any other material and immaterial interests which could be relevant for the Committee's work. It is the responsibility of the President of the Health Council to assess whether the interests indicated constitute grounds for non-appointment. An advisorship will then sometimes make it possible to exploit the expertise of the specialist involved. During the inaugural meeting the declarations issued are discussed, so that all members of the Committee are aware of each other's possible interests.

Part 2

Background document Undernutrition in the elderly

Chapter **A1**

Prevalence of undernutrition

One of the advice questions concerns the extent of the problem of protein-energy undernutrition. This chapter evaluates and discusses the data available on the matter. This concerns the results of new analyses from the Dutch National Prevalence Surveys of Care Problems (LPZ), which are conducted to properly map out the prevalence of undernutrition in the elderly in care, and figures from the Longitudinal Aging Study Amsterdam (LASA).[4,5] In the second part of this chapter, the Chapter considers the justification of the criteria that are used to establish undernutrition.

A1.1 The data sets on which the prevalence data are based: LPZ and LASA

The LPZ supplies the most important Dutch figures about the prevalence of undernutrition in health care.[4] The LPZ reports annually. According to the reports, over a quarter of clients in Dutch health care are undernourished. It may be read in the LPZ reports that from 65 years old there is a gradual increase in the prevalence as age increases[3], but they further contain little specific information about elderly people. Due to this, the LPZ carried out new analyses for this advisory report on the Committee's request. The analyses were carried out by Dr. J.M.M. Meijers, in discussion with Committee member Prof. J.M.G.A. Schols and the LPZ project leader Dr. R.J.G. Halfens (MUMC Maastricht).

For the new analyses, the data about the elderly from the LPZ surveys of 2008, 2009 and 2010 were combined, so that the prevalence estimates could be based on larger numbers of elderly people. Some of the care institutions participate repeatedly. It is unfortunately not possible within the LPZ data to recognise for which participants data from multiple years are collected, so that it was not possible to filter for duplication. The consequence is that certain people in the combined data set will occur multiple times. Because repeated observations of the same people are not independent, this is an undesirable situation. The Committee estimates however that the number of duplications will be limited.*

The LPZ provides no information about elderly people who live independently without home care (nursing or care). The prevalence of undernutrition in elderly people living independently at home is determined in the LASA study.[5] This is a longitudinal study: the results presented were the most recent when the report concerned was prepared.

A1.1.1 Way in which undernutrition is established in the LPZ and LASA studies

There is no consensus either nationally or internationally about the definition of undernutrition. No golden standard exists either to establish undernutrition. This is also apparent in the two Dutch studies in which the prevalence of undernutrition in the elderly is determined: LPZ and LASA use different criteria to establish undernutrition (see Table A1). The LPZ criteria are partly based on the results of a study concerning the definition and the operationalisation of undernutrition.[35] The greatest differences between the LPZ and LASA are in the elaboration of the criterion for unintentional weight loss and in the fact that reduced food intake is indeed included in the LPZ as criterion, but not in the LASA study. Further, in the LPZ, reduced intake is only considered to be a criterion for undernutrition if the elderly person concerned has a BMI between 20.1 and 23.0. In neither the LPZ nor the LASA study can people outside this BMI range be considered as undernourished on the basis of reduced food intake.

* The number of admissions per nursing home bed per year in nursing homes is between 0.96 and 1, which means that the length of stay for the entire nursing home population is approximately 1 year on average. There are on average 1.4 admissions per bed per year to somatic departments, and the average length of stay is around 8 months. There are on average 0.6 admissions per bed per year to psycho-geriatric departments, and the average length of stay is around 20 months.[34] These data concern 2001. No more recent report is available. Committee members estimate that the length of stay has decreased in the last decade.

Table A1 Criteria for establishing undernutrition in the LPZ and the LASA studies.

	LPZ	LASA
Low BMI	A BMI (Body Mass Index[a]) less than or equal to 20.0.[b]	A BMI less than 20.0.
Unintentional weight loss	To have unintentionally lost more than 6 kg in the last 6 months, or more than 3 kg in the last month	Undesired weight loss was 5% or more in the last 6 months.[c]
Reduced food intake	A BMI between 20.1 and 23.0 in combination with three days of eating little or nothing, or with eating less than normal for more than a week.[d]	-

[a] The Body Mass Index is calculated as the weight in kilograms divided by the square of the height in metres.

[b] This is the LPZ definition for people of 65 years or older; clients younger than 64 years are undernourished if their BMI is 18.5 kg/m^2 or less.

[c] In the LASA study, the number of kg of weight change in the last 6 months is enquired of the participants. The current weight is measured in a standardised way during the LASA home visits. The percentage weight loss is calculated based on these two values and is thus established via a combination of self-reporting by participant, measurement by investigator and calculation.

[d] This is the LPZ definition for people of 65 years or older; clients younger than 65 years old are undernourished in the LPZ for a BMI between 18.6 and 20.0 in combination with three days of eating little or nothing, or with eating less than normal for more than a week.

The criteria with respect to unintentional weight loss differ both as regards the period of the weight loss (in both studies, a period of 6 months is used, but in the LPZ additionally a period of one month) and as regards the threshold value and the unit used. Finally, there is a minor difference between these studies in the criterion for the BMI: in the LPZ, people with a BMI of exactly 20.0 are indeed classified as undernourished, while this did not happen in the LASA.

Both in the LPZ and the LASA study, weight loss is considered as 'intentional' when it happens while following a slimming diet. If this is not the case, 'unintentional weight loss' is referred to.

A1.1.2 The elderly in the LPZ and LASA studies

Table A2 outlines the characteristics of the elderly people in both datasets. The great majority of elderly people in the LPZ study (72 per cent) are residents of nursing and care homes; around 20 per cent of the participating elderly people were in-patients in hospitals, and only 8 per cent made use of professional home care (nursing and care). Due to the differences in the numbers of elderly people in the different care settings, the LPZ results that concern data from all participating elderly people are dominated by the findings in nursing and care homes, and the Committee prefers the results per care setting. Of the elderly in the LASA study, 5 per cent make use of home care (personal care); this study therefore mainly concerns elderly people living at home without home care.

Table A2 Characteristics of the elderly people on whom the prevalence data in this Section A1.2 are based.

	LPZ: elderly in health care 2008-2010			LASA: elderly living at home 2005-2006	
	hospital	nursing and care homes	home care	home care	no home care
N	11,609	41,911	4,848	48	895
Average age (yrs)	77 (SD 7)	84 (SD 7)	81 (SD 7)	85 (SD 7)	77 (SD 6)
% women	54%	76%	70%	25%	45%
Average weight (SD)	73 (17)	68 (15)	74 (16)	*not available*	*not available*
Average BMI	*not available*	*not available*	*not available*	28 (SD 5)	27 (SD 4)
BMI < 20	9%	13%	7%	6%	3%
BMI 20-25	38%	39%	35%	25%	33%
BMI 25-30	36%	32%	36%	38%	44%
BMI ≥ 30	17%	16%	23%	31%	21%
No. of institutions	68	315	25	not available	not available
Cancer primary indication	18%	7%	10%	not available	not available
Intensive care	5%	*not applicable*	*not applicable*	*not applicable*	*not applicable*

A1.2 Prevalence of undernutrition in the elderly

The prevalence estimates are presented in Table A3. To gain insight into the effect of the differences in the criteria between the LPZ and LASA on the prevalence data, both definitions are applied to the LPZ data. The LASA result for the independently-living elderly without home care is set out alongside.

The differences between the criteria for establishing undernutrition prove to have a great effect on the prevalence estimate, particularly in the hospital setting: in comparison with the LPZ criteria, the LASA criteria result in the prevalence estimate for undernutrition in hospitals almost being halved. Although the LASA definition also gives lower prevalence estimates than the LPZ definition for both other care settings, the difference there is smaller. The result is that, using the LPZ definition, a large difference is observed between the prevalence of undernutrition in hospitals and that in nursing and care homes, while using the LASA definition the prevalence of undernutrition in hospitals and in nursing and care homes is at the same level. With both definitions, the prevalence in home care is around 5-6 per cent less than in nursing and care homes. In the elderly who live independently without home care, the prevalence is least. Nevertheless, this group represents by far the greatest proportion of the total prevalence of

undernutrition in the Netherlands, because the great majority of the elderly (94 per cent in 2003*) live independently.[36]

Because the different definitions lead to significant differences in results, the prevalence based on the separate criteria for undernutrition is calculated and presented in Table A3.

It proves from the data that the major effect of the criteria used (LPZ or LASA criteria) on the prevalence estimate for undernutrition in hospitals is mainly the consequence of the different definition of unintentional weight loss. The LPZ criteria that are based on weight loss in kilograms (at least 3 kilograms of weight loss in the last month or at least 6 kilograms in the last 6 months) yield a significantly greater prevalence than the LASA criterion of 5 per cent weight loss or more in the last 6 months. The use or non-use of a criterion for reduced intake also plays a role to a lesser extent. This corresponds to the fact that elderly people in hospitals are on average sicker or suffer more stress (such as operations) than the elderly in other settings: in these people, acute weight loss and reduced appetite occur more often.

A low BMI occurs more in nursing and care homes than in hospitals and home care.

Table A3 Prevalence of the separate criteria for undernutrition.[a]

	Nature of data		Prevalentieschattingen			
	Data set	Criteria employed	Hospitals	Nursing and care homes	Home care	Independent without home care
Undernutrition	LPZ	LPZ	33%	21%	16%	
	LPZ	LASA	18%	18%	12%	
	LASA	LASA				7%
A low BMI	LPZ	LPZ	11%	15%	8%	
	LPZ	LASA	10%	15%	8%	
	LASA	LASA				3%
Unintentional weight loss	LPZ	LPZ	24%	9%	10%	
	LPZ	LASA	12%	5%	5%	
	LASA	LASA				5%
Reduced intake with BMI 21-23	LPZ	LPZ	7%	2%	2%	

[a] The sum of the prevalences of the separate criteria is higher than the prevalence of undernutrition, because a proportion of the elderly people meets multiple criteria.

* Recent data are not available, because Statistics Netherlands no longer collects them.

A1.3 Scientific justification for the criteria

In the LPZ and LASA studies, a low BMI and unintentional weight loss are used as indicators of undernutrition, and in the LPZ there was a third indicator: reduced intake with a BMI of 20.1-23.0. In this Section, the Committee discusses the scientific justification for these indicators. In this the Committee considered the relationship between the indicator and the mortality risk.

A1.3.1 Low Body Mass Index

Considerations with respect to research methodology, confounding and bias

There are various factors that may blur the relationship between the BMI and the mortality risk. When assessing the research into the relationship between BMI and mortality, the following considerations about research methodology and possible forms of confounding and bias must be kept in mind.

It is important that height and weight are actually measured by the investigators. In the meta-analysis by Janssen and Mark, the studies based on measured values for height and weight led to conclusions about the relationship between high BMI and mortality that differ substantially from the conclusions from those studies in which height and weight were reported by the participants.[37]

The BMI is an index with which body weight is judged in relation to the height of the person concerned, but the BMI gives no insight into the body composition. The muscle mass may be low in thin people, in people with a normal BMI and even in those who are overweight or obese. The last case is referred to as sarcopenic obesity. The research available into the risk-increasing effect of a low muscle mass for functional problems, fall frequency and mortality however fails to give a consistent picture. Due to this it is not entirely clear how problematic it is if people have a relatively low muscle mass. The picture is clearer with respect to the function or strength of the muscles: if this is at a low level (dynapenia), stronger and more consistent relationships are found with the risks of functional problems, fall frequency and mortality.[38, 39]

Research into the relationship between a low BMI and the mortality risk may lead to erroneous conclusions as a result of confounding by illness. In participants suffering from illnesses at the time when the BMI is determined, the body weight (and thus the BMI) may have been reduced by the illness. If these

are illnesses that lead to early mortality, then the probability that an association is found between a low BMI and mortality increases, while the mortality is not really caused by the low BMI, but by the illness.[40,41] In order to reduce this form of confounding, some researchers leave the mortality in the first years of follow-up out of consideration. People who, at the start of the study, have an illness that leads to death in the relatively short term are excluded from the analyses in this way. Even then residual confounding by illness remains possible: some illnesses due to which the body weight is reduced have an effect on the mortality in the longer term; one example is COPD*. The risk of confounding by illness in research on the elderly is greater than in research on young adults, because the probability that someone has one or more chronic or non-chronic illnesses increases with age.

Smoking is associated on the one hand with the development of conditions such as cardiovascular diseases and cancer, and on the other hand with a reduced body weight. Smoking therefore reinforces the relationship between low BMI and mortality, even if at the time the BMI was determined there was not yet any illness. In some studies, this problem of confounding by smoking is accommodated by limiting the analyses to people who have never smoked.

In the elderly, account must further be taken of selection bias: very elderly people are survivors. Due to this, the relationship between BMI and mortality in this age cohort may be different from younger age cohorts.

People's height reduces as they age. If the body weight remains unchanged, the BMI increases automatically. This could partly explain why the BMI range in which the mortality risk is lowest gradually shifts up to higher BMI values as age increases. In the Longitudinal Aging Study Amsterdam, the effect of the reduction in height on the BMI is determined by calculating the BMI during the 9-year follow-up, based, on the one hand, on the height at follow-up, and on the other, on the height at the start of the study, while for the body weight, the value at follow-up is used.[42] By combining together the results from the different age cohorts in this study (a reservation is appropriate here in connection with possible cohort effects), the cumulative reduction in height for the entire life period from 65 to 90 years appears to be 3 cm (men) and 5 cm (women), and it appears to lead to a cumulative increase in the BMI of around 1½ kg/m^2 (women) and around 1 kg/m^2 (men).

* COPD stands for chronic obstructive pulmonary disease.

The relationship between a low BMI and increased mortality

The World Health Organization (WHO) uses a threshold BMI value of 18.5 kg/m^2 for underweight. Worked out in more detail: for a BMI of between 18.5 and 17.0 kg/m^2, WHO refers to slight underweight; for a BMI of between 17 and 16 kg/m^2, to moderate underweight; and for a BMI of under 16 kg/m^2, to severe underweight.[43] The threshold value of 18.5 kg/m^2 is supported by research findings from which it proves that a BMI of between 19 and 20 kg/m^2 at young adult age is associated with the lowest mortality risk.[6,44]

For the elderly – as in the LPZ and LASA studies – a somewhat higher threshold value is often used. How powerful is the scientific justification that the BMI range in which the mortality risk is lowest gradually shifts up to higher values as age increases? Two meta-analyses of prospective cohort studies and three prospective cohort studies in elderly people provide information about this; characteristics of these studies are listed in Table A4 and described briefly in the text.

The meta-analyses of prospective cohort research reveal the following picture:

- In the Prospective Studies Collaboration[7], analyses of the relationship between BMI and mortality are also split up by age group (35-59, 60-69 and 70-79 years) and sex (Figure 1 in the web appendix). In the groups between 35 and 69 years and for men from 70 to 79, the relationship was U-shaped, in which the lowest mortality risk was found for a BMI between 22.5 and 25 kg/m^2. For women of 70-79 and 80-89 years and for men of 80-89 years, the curve levelled out: there was no clear difference in mortality risk within the BMI range from 20 to 27.5 kg/m^2. These analyses fail to provide any clear support for the theory that the BMI at which the mortality risk is lowest may shift up to higher values with increasing age. Further, the analyses indicated that the higher mortality in people with a low BMI in this study may mainly be ascribed to illnesses related to smoking habits.
- In never-smokers with a study entry age between 20 and 49 years, Berrington de Gonzalez et al.[6] found that a BMI of less than 18.5 kg/m^2 was associated with a higher mortality risk than a BMI of 22.5 to 24.9 kg/m^2 (the reference group). In all older age groups, the threshold value was higher, namely 20 kg/m^2, and the *hazard ratio* for a BMI of between 18.5 and 19.9 kg/m^2 was increased statistically significantly compared with the reference group. Further, with increasing entry age, the mortality risk in never-smokers with a BMI of 18.5 to 19.9 kg/m^2 gradually increased.[6]

Table A4 Characteristics of the prospective cohort studies and meta-analyses of prospective cohort studies that provide information about the relationship between BMI and mortality in different age groups and in the elderly.

	Publication	No. of studies	No. of participants	Entry age	Manner of dealing with confounders		Follow-up
					Illness	Smoking	
Meta-analysis:							
Prospective Studies Collaboration[7]	Lancet 2009	57	900,000	Average 46 years	Any death in first 5 years of follow-up was excluded from the analyses	Analysis of non-smokers[a]	8 years
Berrington de Gonzalez et al.[6]	NEJM 2010	19	1,500,000	Median 58 years	Exclusion of people who at start of study had diagnosis of cancer or heart disease	Analysis of non-smokers[a]	10 years
Prospective cohort study in the elderly:							
Adams et al.[8]	2006	1	527,000	50-71 years	Any death in first 5 years of follow-up was excluded from the analyses		10 years
de Hollander et al.[9]	2011	1	1,980	70-75 years	Any death in first 2 years of follow-up, or elderly people who had chronic illnesses at start, were excluded in extra analyses	Analysis of non-smokers[a]	10 years
Flicker et al.[45]	2010	1	9,000	70-75 years	Any death in first year of follow-up was excluded from analyses		10 years
Wijnhoven et al.[10]	2010	1	1,700	55-85 years	Any death in first 3 years of follow-up was excluded from the analyses	Analysis of non-smokers[a]	15 years

[a] In these publications, in addition to the analyses of the data of both smokers and non-smokers, extra analyses were carried out that only concern the data for non-smokers.

The following emerges from the four recent prospective cohort studies in the elderly:

- Adams et al. found for a BMI between 18.5 and 20.9 kg/m^2 a higher mortality risk than for a BMI between 23.5 and 24.9 kg/m^2. The BMI in this study was calculated on the basis of data on height and weight reported by the participants.[8]
- De Hollander et al. found the lowest total mortality for a BMI of 27.1 kg/m^2 (95% confidence interval 24.1 to 29.3 kg/m^2). The mortality was statistically significantly higher for a BMI lower than 21.1 kg/m^2 and for a BMI higher than 31.4 kg/m^2. In the analysis for non-smokers, there was no clear risk-increasing effect of a low BMI. The BMI in this study was calculated on the basis of data on height and weight measured by the researchers.[9]
- Flicker et al. found a higher mortality risk for a BMI between 18.5 and 24.9 kg/m^2 than for a BMI between 25.0 and 29.9 kg/m^2. The BMI categories were not subdivided further, so that it is unclear whether the mortality was

increased in the entire BMI range from 18.5 to 24.9 kg/m^2, or only in part of this range. The BMI in this study was calculated on the basis of data on height and weight reported by the participants.[45]
- Wijnhoven et al. found the lowest mortality for a BMI of around 24 to 25 kg/m^2, but when smokers and ex-smokers and participants with COPD and cancer were excluded, the association between BMI and mortality disappeared. The BMI in this study was calculated on the basis of data on height and weight measured by the researchers.[10]

The Committee finds that there are indications that the BMI range in which the mortality risk is lowest gradually shifts up to higher values as age increases, but that this hypothesis is not supported by all the relevant studies. The Committee does not consider the available research to be sufficient in order to present a threshold value for the elderly, below which there is considered to be underweight – based on increased mortality.

A1.3.2 Unintentional weight loss

In this Section, the state of science is described which serves as justification for the use of unintentional weight loss as a measure of undernutrition. Nine relevant publications are listed in Table A5. The first two of these concern the same cohort; this therefore covers eight studies in all.

Considerations with respect to confounding by illness and bias

In part of the research into the relationship between BMI and mortality, mortality in the initial years of follow-up is not included in the analyses, in order to reduce confounding by illness (see Section A3.1). This procedure is not applied in the research into the relationship between weight loss and mortality: in all the prospective studies described, the mortality during the entire follow-up period is included in the analyses. This means that serious account must be taken of the possibility of confounding by illness that was already present at the start of the study. Some multivariate analyses adjust for relevant diagnoses or health status. This approach reduces the confounding by illness, but residual confounding remains possible.

In the first five publications (four studies) in the table, the weight loss is established based on measurements of the body weight. In the last four publications, the weight progression is (partly) established based on values reported by the participants. This order was chosen because measured values

Tabel A5 Characteristics of and results from the prospective cohort studies of elderly people which give information about the relationship between weight loss and mortality and other outcome measures.

Study	n	Setting and age of participants at start of study	Weightloss					Follow-up	Result
			Period	Distinction intentional/ unintentional	Threshold	Classification of weight progression	Measured or self-reported		
Newman et al. (Cardiovascular Health Study)[17]	4,700 Cohort 1: n=4.255; cohort 2: 459 African Americans.	Living at home ≥65 jaar	3 years	no	5%	Stable, loss or gain	Measured	Cohort 1: 4 years; cohort 2: 1 year.	5% weight loss during 3 years was associated with increased mortality, even after adjusting for age, sex and other potential confounders which demonstrated an independent association with mortality: HR = 1.67 (95% confidence interval 1.29 to 2.15). Hazard ratios were in the same order of magnitude in the three tertiles of body weight.
Arnold et al. (Cardiovascular Health Study)[14]	3,300	Ditto	1 year and also comparison with start meas't	no	5%	Stable, loss, gain or fluctuating	Measured	7 years	5% weight loss in 1 year was associated with new problems in carrying out the *Activities of Daily Living* (ADL) and also with increased mortality, also in multivariate analysis. Unstable weight (both increases and decreases in the 7-year follow-up) was associated with a greater increase in these risks and with an increased risk of mobility problems.
De Groot et al. (SENECA) [15]	2,000	Representative random sample of 9 European cities 70-75 years	4 years	no	5 kg	Stable, loss or gain	Measured	10 years	5 kg weight loss in 4 years was associated in men with increased mortality (RR = 2.2; $p < 0.0001$). In women, this effect was not clear (RR = 1.3; $p = 0.35$).
Sullivan et al. (Geriatric Anorexia Nutrition [GAIN] Registry)[18]	900	Nursing home	1 month and 3 months	no	5% and 10%	Stable, loss or gain	Measured	7 months	With ≥5% weight loss in 1 month, mortality was greatly increased: adjusted RR = 10.6 (95% confidence interval 3.2 to 35.5). The mortality was also increased with 5-10% weight loss in 3 months (adjusted RR = 5.0; 95% confidence interval 1.5 to 17.0) and for ≥10% weight loss in 3 months (adjusted RR = 8.1; 95% confidence interval 2.3 to 29.0).

Study	n	Setting and age of participants at start of study	Weightloss					Follow-up	Result
			Period	Distinction intentional/ unintentional	Threshold	Classification of weight progression	Measured or self-reported		
Wallace et al.[12]	250	Living at home >65 years	1 year	Yes	4%	Unintentional weight loss versus stable weight	Measured	2 years	Elderly people with 4% unintentional weight loss in 1 year had a greater mortality than those without weight loss (n=175) (adjusted RR = 2.83; 95% confidence interval 1.38 to 5.81; *p*=0.004). The number of elderly people with intentional weight loss was lower (n=30) and their mortality was not significant greater than for those without weight loss (unadjusted RR = 3.45; 95% confidence interval 0.75 to 15.90; *p*=0.16).
Locher et al. 2007 (Univ. of Alabama at Birmingham [UAB] study of aging)[11]	1,000	Living at home ≥65 years	1 year	Yes	10 Lbs (4.6 kg)	Unintentional, intentional or no weight loss	Self-reported	3 years	>4.6 kg unintentional weight loss in 1 year was associated with increased mortality in the 3 years' follow-up compared with the group without weight loss: multivariate HR = 1.67; 95% confidence interval 1.14 to 2.45; *p* = 0.008. Intentional weight loss was not associated with increased mortality: multivariate HR = 0.62; 95% confidence interval 0.27 to 1.42; *p* = 0.3.
Lee et al. 2005 (Health Aging and Body Composition [Health ABC] Study)[13]	2,932	Living at home 70-79 years	12 months	Yes	5 Lbs (= 2.3 kg)	Stable, loss, gain or both	Self-reported	2.5 years	*Unintentional* weight loss during 1 year was associated with an increased risk of mobility restrictions: • In subgroup with BMI ? 35 (HR = 3.79; 95% confidence interval 1.84 to 7.79), • In subgroup with BMI<25 (HR = 2.55; 95% confidence interval 1.80 to 3.60). *Intentional* weight loss during 1 year was associated with an increased risk of mobility restrictions: • In subgroup with BMI 25-29.9 (HR = 1.59; 95% confidence interval 1.12 to 2.25).

Study	n	Setting and age of participants at start of study	Weightloss					Follow-up	Result
			Period	Distinction intentional/unintentional	Threshold	Classification of weight progression	Measured or self-reported		
									Intentional weight fluctuation during 1 year was associated with an increased risk of mobility restrictions: • In subgroup with BMI 25-29.9 (HR = 1.59; 95% confidence interval 1.10 to 2.28). In this cohort, the effect of weight loss and weight fluctuation was dependent on the distinction intentional/unintentional and current BMI.
Ingram et al. 2010 (NHANES-3)[16]	6,117	Living at home ≥50 years	Life-long [a)]	no	<5%; 5-15%; ≥15%	Loss versus stable	Both[a]	6-12 years	In men with obesity and in women in all BMI classes, ≥15% weight loss was associated with an increased mortality risk in comparison with the same BMI-sex group with <5% weight loss. 5-15% weight loss was associated with increased mortality risk in certain groups: • In women with obesity: increased total mortality • In obese men: increased CVD mortality. Analyses were adjusted for age, race, smoking habits, health status and illness present at start.
Van Bokhorst et al.[19]	64	Hospital (cancer) 61 (SD 10) years	6 months	no	5%, 10% and 15%	Weight loss	Both[b]	Length of stay in hospital	With logistic regression, >5%, >10% and >15% weight loss were all significantly associated with the occurrence of serious complications. The correlation was strongest for >10% weight loss.

a In NHANES-3[16], in the initial determinations, weight was measured and the participants were asked what was the highest body weight they had had to date. The percentage weight loss was calculated as: (highest weight ever – measured weight) / highest weight ever.

b In the study of Van Bokhorst et al.[19], the current weight was measured while the usual weight (the weight from 6 months previously) was reported by the participants.

give a more reliable picture of weight progression than do recalled values (see Section A3.1).

The relationship between weight loss and a poorer prognosis

Intentional weight loss is the result of deliberate efforts to slim; for unintentional weight loss, this is not the case. In three studies, a distinction was made between intentional and unintentional weight loss. In two publications, unintentional weight loss was significantly associated with increased mortality, but intentional weight loss was not.[11, 12] In the third publication, both unintentional and intentional weight loss were associated with a significantly increased risk of mobility restrictions, but in different BMI classes.[13]

In six publications, the analyses were based on the percentage weight loss. In the other three publications, that departure point was the weight loss in kilograms. For both measures of weight loss, associations with the prognosis were found.

The period during which the weight loss was calculated varied greatly among the studies:

- In one study of nursing home residents, it was investigated whether acute weight loss (five per cent weight loss in one month) was associated with increased mortality; the results indicate a powerful risk-increasing effect. Five per cent or more weight loss in 3 months was also associated with increased mortality in this study.
- In one publication, the weight loss during a period of 6 months was determined and it was found that 5 per cent weight loss was associated with an increased risk of serious complications.
- In four publications, weight loss during a year was determined. Four or five per cent weight loss and also 2.3 and 5 kilograms of weight loss during one year were associated with a poorer prognosis.
- Two other publications concerned the weight loss during 3 and 4 years respectively. In these studies too, an association with increased mortality was found, but in one of the studies, the link was only statistically significant in men.
- Finally, there was one publication in which it was investigated whether the current body weight was less that the reported maximum weight at any moment in the past. This analysis is less relevant for the Committee's issue.

In three studies, it was investigated whether weight loss is also associated with a poor prognosis for people with obesity. In the Cardiovascular Health Study, the

participants were split up into tertiles based on body weight. It proved that in each of the three tertiles, the association between ≥ 5 per cent weight loss and mortality was statistically significant.[17] In the Health ABC study, an association between unintentional weight loss and mobility restrictions was found in two BMI classes (BMI<25 and BMI≥35) and within a third BMI class (BMI 25-35), an association was found between intentional weight loss and mobility restrictions.[13] Wallace et al. found an association between ≥5 per cent weight loss and mortality in the subgroup with a BMI of 24 or less, but not in the subgroup with higher BMI. This cohort was however very limited in extent and the absence of an association in the subgroup with greater BMI may therefore be the result of insufficient statistical discriminatory power.[12]

The Committee finds that weight loss in the elderly is associated with a poorer prognosis. This is observed from around 5 per cent and 5 kilograms of weight loss. The indications are most powerful for weight loss during a period of one year. So far, only one study for each of the periods has been published about weight loss during a period of 1, 3 and 6 months. The associations were found in people with both a low and a high BMI. In the associations observed, serious account must be taken of confounding by illness. No research into the causative relationship between weight loss and a poor prognosis is available.

A1.3.3 Reduced food intake

In the establishment of undernutrition, reduced food intake is often one of the criteria considered. In fact, little research into the relationship between food intake and mortality has been published. The only prospective study that specifically considers this association is what is called the *Nutrition Day Survey 2006*.[20] In over 16,000 hospital patients of 18 years or older, originating from 256 hospitals in 25 countries, the food intake during one hospital day was estimated using a semi-quantitative method. It was also enquired how the patient had eaten in the previous week (normally, somewhat less than normal, less than half or less than a quarter of the normal amount). The mortality in the subsequent 30 hospital days was defined as outcome measure. The food intake proved to be strongly associated with the mortality: the risk increased steadily the less the patient had eaten on the measurement day. Hiesmayr et al. adjusted for illness in their multivariate survival analysis.

The Committee observes that the scientific justification for reduced food intake as indicator of undernutrition is meagre. There is only one study available, with a

very brief follow-up period. In that study, no distinction was made between people in different BMI classes.

A1.4 Summary and consideration

The prevalence figures for undernutrition in the Dutch elderly are based on two or three factors: a low BMI, unintentional weight loss and reduced food intake.

A low BMI is associated with increased mortality. Smoking habits play an important role in the association between a low BMI and an increased mortality risk. There are indications that the BMI range in which the mortality risk is lowest gradually shifts up to higher BMI values as age increases, but this was not found in all relevant publications. The shift could be partly due to the reduction in height with age. The Committee does not consider the available research to be sufficient in order to present a threshold value for the elderly, below which – based on increased mortality – the BMI is considered to be too low. It is equally impossible to make out from the data whether a life-long stable but low BMI increases the mortality risk.

Weight loss is associated with an increased mortality risk. This has been found in thin people, people of normal weight as well as in overweight and obese people. Some investigations have yielded indications that this may mainly be the case when the weight loss is unintentional, but in most publications, no distinction is made between unintentional and intentional weight loss. The indications are most powerful for a 5 per cent or 5 kilogram weight loss during a period of one year.

The support for reduced food intake as an indicator of undernutrition is slender: it was found in one study that reduced food intake is associated with an increased mortality risk in the short term. In that study, it was not investigated whether the presence of the said association is dependent on the BMI. There does not seem to be any scientific justification for the choice in the LPZ only to include reduced food intake as criterion when the BMI is between 20.1 and 23.0. This indicator in fact only provides a limited contribution to the estimated prevalence of undernutrition.

The scientific basis for all the factors described rests on observational research, that is on associations. An association is not in fact convincing evidence that the measure of undernutrition concerned increases the risk of death. Illness is potentially an important confounding variable in the relationship between undernutrition and prognosis, because illness may be the cause of a low BMI, unintentional weight loss and reduced food intake on the one hand, and on the

other of a poor prognosis. In this way, in observational research, illness can lead to an association between these characteristics of undernutrition and a poor prognosis, even if the poor prognosis is the consequence of illness and not of the said characteristics of undernutrition.

The association between a low BMI and an increased mortality risk has also been found in analyses in which mortality in the initial years of follow-up was excluded. This means that a low BMI is also associated with increased mortality, even in the absence of acute illness. Residual confounding by illness remains possible, but with this approach, the effects of existing illness on mortality are reduced. This means of analysis was not applied with regard to the connection of unintentional weight loss and reduced food intake with increased mortality. In some studies, adjustments are made in multivariate analyses for illness or health status; even then, residual confounding by illness remains possible.

A1.5 Conclusion

Due to the lack of a golden standard to establish undernutrition, and the impact of the criteria chosen on prevalence estimates, there is no certainty about the prevalence of undernutrition. The uncertainty is greatest for the hospital setting: depending on the criteria chosen, the prevalence in hospitals may be estimated at 33 or 18 per cent. In nursing and care homes, around 20 per cent of the elderly are considered to be undernourished. For the elderly people living independently without home care this is around 7 per cent. Because the great majority of the Dutch elderly (94 per cent in 2003) lives independently, this setting contributes by far the greatest proportion in an absolute sense to the prevalence of undernutrition.

The indications that reduced food intake is associated with an increased mortality risk are very limited, but there is ample scientific justification for the claim that both a low BMI and unintentional weight loss are associated with an increased mortality risk. The research available however provides no scientific evidence that these factors cause the poorer prognosis; confounding and residual confounding by illness cannot be excluded.

Chapter **A2**

Evaluation of screening instruments

One of the advice questions concerns a scientific opinion about the methods for screening for protein-energy undernutrition. This chapter describes and evaluates the most relevant instruments for the elderly Dutch. It is indicated for each instrument what elements play a role in the assessment, split up by the indicators discussed in the previous chapter (low BMI, unintentional weight loss and/or reduced intake) and other elements that the instrument also takes account of. The Committee describes what is known for each instrument about its reproducibility and validity.

A2.1 Evaluation of five instruments

In the following Sections, the Committee describes five instruments that are employed to identify the undernourished elderly:

- the Subjective Global Assessment (SGA)
- the Mini Nutritional Assessment (MNA)
- the Short Nutritional Assessment Questionnaires (SNAQ, SNAQ^{RC} and SNAQ^{65+})
- the Malnutrition Universal Screening Tool (MUST) and
- the Nutrition Risk Screening 2002 (NRS-2002).

These are the most relevant instruments for the Dutch elderly. The instruments take the form of a questionnaire, sometimes supplemented with some measured values.

A2.1.1 Screening or assessment

All instruments have the term ‘screening’ or ‘assessment’ in the name. The general impression of the distinction between screening and assessment is that a screening method identifies those people for whom it is sensible to carry out an assessment and that the assessment then leads to a diagnosis and treatment plan. Screening instruments are simple and relatively quick to carry out by a wide range of care providers and give an initial impression. An assessment is generally based on different examinations or measurements from the prior screening, may be more complex in its implementation and provides sufficient information for choices with regard to treatment. In the closing Section of this chapter, the Committee discusses the extent to which the terminological choice links up with the usual distinction between screening and assessment.

A2.1.2 Reproducibility and inter-observer variability

The reproducibility is the extent to which repeated measurements yield the same results. Research into reproducibility in the field of undernutrition has mostly concerned the question of whether different care providers achieve the same estimate of the nutritional status with the said instrument; a more accurate term is then ‘inter-observer variability’. This is determined by having different care providers evaluate the same patients with the instrument.

The inter-observer variability is generally expressed as a kappa value (Table A6). This describes the extent to which the scores agreed more than could be attributed to chance. An example: a kappa value of 0.83 means that there is 83 per cent more agreement than could be attributed to chance.

Table A6 Overview of the meaning of kappa values by Landis and Koch.[46]

Kappa ≤0	Less agreement than could be expected as a result of chance; there is a possible systematic lack of agreement
Kappa 0.01-0.20	Fair agreement
Kappa 0.21-0.40	Slight agreement
Kappa 0.41-0.60	Moderate agreement
Kappa 0.61-0.80	Substantial agreement
Kappa 0.81-0.99	Almost perfect agreement

A2.1.3 Validity

Validity research is about the question whether the instrument indeed measures what it ought to measure. To what degree do the results obtained with this instrument agree with reality? To establish the actual situation, a golden standard is needed: a method of which it is known that it presents a true picture of reality. The method to be investigated must be compared to the golden standard in order to be able to establish the validity.

The validity is described by means of sensitivity and specificity:

- The sensitivity is the probability that people who are considered to be undernourished based on the reference method are also undernourished according to the instrument under investigation (in Table A7: A/[A+C]).
- The specificity is the probability that people who are not considered to be undernourished based on the reference method are not undernourished according to the instrument under investigation either (in Table A7: D/[B+D]).

Table A7 Cross-table for the purposes of explaining the measures of validity.

		Result from the golden standard method	
		Undernourished	Not undernourished
Result with the instrument investigated	Undernourished	A	B
	Not undernourished	C	D

The purpose for which the instrument is employed (screening or assessment) determines what results for sensitivity and specificity are considered acceptable. In practice, 70 per cent is often used as threshold value for both measures.

In the case of undernutrition, the great problem is the lack of a golden standard. The validity of the instruments therefore cannot be established. Research does exist in which results about sensitivity and specificity are presented, but in this the instruments are compared with methods of which the validity has not been established any better. The value of these results is unclear.

An additional problem is that the reference method in most cases is partially based on the same parameters as the methods investigated: for instance, weight loss is often a criterion in both the method investigated and the reference method. This has the effect that a too-favourable picture of the validity is obtained.

A2.2 Subjective Global Assessment (SGA)

The Subjective Global Assessment (SGA) was developed in 1982. The SGA leads to classification of patients into one of the following three categories: 'well-fed' (A), 'moderately (or suspected of being) malnourished' (B) and 'severely malnourished' (C).

Table A8 Evaluation with the SGA is based on the following aspects.[47]

Indicators that are used to estimate the prevalence of undernutrition in the Netherlands (Chapter A1)	Other aspects
• weight loss during 6 months 5-10% or >10% and weight course over the last 2 weeks, • reduced food intake	• two skinfold thicknesses, • muscle circumference and tone via palpating two muscles • oedema formation at three places in the body • reduced functional capacity • gastro-intestinal complaints (nausea, vomiting and anorexia) • presence of illnesses that increase the demand for protein and/or energy

No information is included in the SGA questionnaire about the way in which the SGA score can lead to decision-making about the nutritional policy.

The SGA questionnaire on the next page was obtained from the Nutritional Guidelines of the Dutch Federation for Nephrology (NFN).[48]

Name of patient: _____ Number: _____ Date: ____-_____-_____
See also the points for consideration in the practical manual

Part A: Anamnesis

Weight change

Total change in the last 6 months: _____ kg
Percentage change:
- □ Increase or < 5% decrease
- □ 5% - 10% decrease
- □ > 10% decrease

Change in the last 2 weeks:
- □ Increase
- □ No change
- □ Decrease

SGAweight change score						
Severely undernourished		Moderately-slightly undernourished			Normally nourished	
1	2	3	4	5	6	7

Food intake

Current nutrition
- □ Increase
- □ No change

Food intake issues
- □ Little solid food
- □ Liquid
- □ Nutritional supplements
- □ Taking very little of anything

Duur: ____ weeks

Gastro intestinal symptoms

- □ Loss of appetite
- □ Nausea
- □ Vomiting
- □ Diarrhoea

SGA food intake and Gastro-intestinal symptoms score						
Severely undernourished		Moderately-slightly undernourished			Normally nourished	
1	2	3	4	5	6	7

Duration: ____ weeks

Part B: Physical examination

Signs of:

- □ Decrease in subcutaneous fat tissue
- □ Muscle atrophy

Physical examination SGA score						
Severely undernourished		Moderately-slightly undernourished			Normally nourished	
1	2	3	4	5	6	7

Part C: SGA Classification

Classification of SGA score						
Severely undernourished		Moderately-slightly undernourished			Normally nourished	
1	2	3	4	5	6	7

The SGA is carried out by a professional (doctor, dietician, nurse). There are subjective elements in the assessment. The researchers who developed this method argue in fact that a purely mathematical approach is not always optimal and that a subjective weighting of data is necessary to be able to assess a patient's nutritional status properly.[47]

An example of a subjective element in the evaluation with the SGA is the evaluation of the unintentional weight loss. The basic idea is that a net weight loss of less than five per cent has little clinical relevance, five to ten per cent is potentially clinically relevant, and more than ten per cent has clear clinical relevance. According to these researchers, the net weight loss during six months however gives insufficient information for a final verdict; the weight progression during the last two weeks should also be involved in the evaluation. Weight loss can come into being gradually and progressively, but it is also possible that the weight was seriously reduced initially and is increasing again towards the initial weight. If at least ten per cent of progressive weight loss is present along with serious loss of subcutaneous tissue and muscle mass and different symptoms or problems in the other elements of the case history, the person comes into category C (severely undernourished). With five to ten per cent of progressive weight loss with reduced food intake and signs of slight subcutaneous tissue loss, the person comes into category B (not well-nourished or suspicion of undernutrition). If however the weight has risen in the last two weeks and there are other improvements in the case history without signs of oedema formation, the person is assigned to category A (well-nourished).

There are more aspects that make a subjective weighing up of findings necessary according to these researchers. In the case of oedema formation, a different view of weight changes is needed. In the assessment of muscle mass and muscle tone via palpation, it must be borne in mind that neurological problems may affect muscle tone. In certain illnesses, such as heart failure, a different weighting must be assigned to findings with respect to oedema.

All these examples underline the fact that for a proper diagnosis, a broader case history is needed than the questionnaire alone. Due to the subjective elements described, the SGA is a relatively complex method, and care providers must be trained to be able to apply this instrument well.

A2.2.1 Reproducibility

The inter-observer variability of the SGA was determined from paired comparisons between doctors and nurses who were trained to use the SGA. The kappa values between pairs of nurses and/or doctors varied between 0.6 and

1.0.[47] This means there is substantial to almost perfect agreement between the assessments of the same people by different investigators.

A2.2.2 Validity

The quality of the SGA was investigated in 48 patients who had to have an operation.[49] The study was carried out on a group of patients who were selected based on the fact that they were relatively easy to score using the SGA*; the Committee notes that this selection of participants will contribute to an overestimation of the validity. The results of this study were as follows:

- The SGA score was significantly associated with preoperative values of the following parameters: the serum concentrations of albumin and transferrin, the body weight as a percentage of the ideal weight, the fat-free mass as percentage of the ideal fat-free mass, the creatinine-height index, the amount of body fat as percentage of body weight and the total quantities of nitrogen and potassium in the body.[49] According to the Committee, the meaning of these findings is unclear, because the validity of the reference method is unclear.
- The patients with a less-favourable SGA score had more postoperative infections, took more antibiotics during their stay in hospital and remained longer in hospital.[49]

It was investigated in 705 patients in an academic hospital to what extent the SGA score – determined within 48 hours of admission to the hospital – was associated with a very long length of stay and the occurrence of complications and mortality.[50] Almost 40 per cent of the patients studied were considered to be undernourished based on the SGA (SGA score B or C); these groups had an increased risk of remaining in hospital for a long time and an increased risk of developing a complication.

According to the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.), the SGA has a good predictive value in gastro-intestinal surgery, liver transplantation and kidney dialysis with regard to the development of complications, though the usability for seriously ill patients was not investigated.[51]

* Two clinicians determined the SGA score of 59 patients, independently of each other. The validity of the SGA was investigated in the subgroup of 48 patients to which both clinicians assigned the same score. The other 11 patients (who were apparently more difficult to score) were excluded from the validity investigation.

Table A9 Results from the study of Raslan et al.[50]

Outcome measure	SGA score	Odds Ratio	95% confidence interval	*p* value
Complications	B	2.0	1.1 to 3.4	0.02
	C	2.9	1.4 to 5.8	0.003
Very long length of stay	B	1.9	1.2 to 3,2	0.008
	C	3.8	2.0 to 7.2	<0.0001
Mortality	B	3.5	0.9 to 13.3	0.06
	C	3.9	0.9 to 17.0	0.07

A2.3 Mini Nutritional Assessment (MNA)

In 1994, the Mini Nutritional Assessment (MNA) was developed as an instrument with which not only doctors, but also other care providers could establish undernutrition in the elderly. The instrument was developed based on research on 155 elderly people of average age 78 years.[52, 53] A maximum of 30 points can be scored in the MNA. People who score less than 17 points are considered to be undernourished; people with 17 to 23.5 points are considered being at risk of undernutrition and the nutritional status is seen as adequate at 23.5 points and over. In the MNA questionnaire, no information is included about the way in which the MNA score can lead to decision-making about the nutritional policy.

Based on the original – relatively extensive – version, an abbreviated version was developed in 2001: the MNA-SF, where SF stands for *short form.*[54] The MNA-SF is used to investigate whether it is necessary to complete the full MNA.

In the MNA, no information is included in the questionnaire about the way in which the MNA score can lead to decision-making about the nutritional policy.

The MNA on pages 74 and 75 was obtained from the Nestlé Nutrition Institute website.[55]

A2.3.1 Reproducibility

The inter-observer variability of MNA values is reasonable: kappa values are reported of 0.51 (moderate agreement) for elderly people in hospitals and of 0.78 (substantial agreement) for institutionalised elderly people.[56]

Table A10 Evaluations with the MNA-SF and MNA are based on the following aspects.

	Indicators that are used to estimate the prevalence of undernutrition in the Netherlands (Chapter I)	Other aspects
MNA-SF	• weight loss during recent months 1-3 kg or >3 kg • less food intake in the last 3 months • body mass index <19, 19-21, 21-23 or ≥23 kg/m^2	• mobility status • mental stress or serious illness in the last 3 months • neuropsychological problems
MNA comprehensive	As the MNA-SF.	• As the MNA-SF, supplemented with: • mid-arm circumference • calf circumference • number of full meals daily • intake of protein • intake of fruit and vegetables • fluid intake • ability to eat independently • living situation • >3 medicines/day • bedsores or skin infections • the opinion of the patient about their own nutritional situation • the opinion of the patient about their own health situation

A2.3.2 Validity

In 2006, the researcher who developed this instrument, Guigoz, described the results of thirteen publications on research into the validity of the MNA.[56] The reference methods are presented in this publication in a table and are very varied. Guigoz concludes that the sensitivity of the MNA is good, because it was above 70* per cent in eleven of the thirteen studies, but states that the specificity of the MNA leaves something to be desired, because this varied widely and was only over 70 per cent in six of the thirteen studies. This means that the MNA classifies more people as undernourished that the methods that were used as reference methods. The meaning of this is in fact unclear, because the validity of the reference methods is unknown.

* The chosen threshold value of 70 per cent is arbitrary.

Nestlé Nutrition Institute

Mini Nutritional Assessment
MNA®

Last name: First name:

Sex: Age: Weight, kg: Height, cm: Date:

Complete the screen by filling in the boxes with the appropriate numbers. Add the numbers for the screen. If score is 11 or less, continue with the assessment to gain a Malnutrition Indicator Score.

Screening

A Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?
0 = severe decrease in food intake
1 = moderate decrease in food intake
2 = no decrease in food intake ☐

B Weight loss during the last 3 months
0 = weight loss greater than 3kg (6.6lbs)
1 = does not know
2 = weight loss between 1 and 3kg (2.2 and 6.6 lbs)
3 = no weight loss ☐

C Mobility
0 = bed or chair bound
1 = able to get out of bed / chair but does not go out
2 = goes out ☐

D Has suffered psychological stress or acute disease in the past 3 months?
0 = yes 2 = no ☐

J How many full meals does the patient eat daily?
0 = 1 meal
1 = 2 meals
2 = 3 meals ☐

K Selected consumption markers for protein intake
- At least one serving of dairy products (milk, cheese, yoghurt) per day yes ☐ no ☐
- Two or more servings of legumes or eggs per week yes ☐ no ☐
- Meat, fish or poultry every day yes ☐ no ☐

0.0 = if 0 or 1 yes
0.5 = if 2 yes
1.0 = if 3 yes ☐.☐

L Consumes two or more servings of fruit or vegetables per day?
0 = no 1 = yes ☐

M How much fluid (water, juice, coffee, tea, milk...) is consumed per day?
0.0 = less than 3 cups
0.5 = 3 to 5 cups
1.0 = more than 5 cups ☐.☐

E Neuropsychological problems
0 = severe dementia or depression
1 = mild dementia
2 = no psychological problems ☐

F Body Mass Index (BMI) (weight in kg) / (height in m^2)
0 = BMI less than 19
1 = BMI 19 to less than 21
2 = BMI 21 to less than 23
3 = BMI 23 or greater ☐

Screening score ☐☐
(subtotal max. 14 points)

12-14 points:	Normal nutritional status
8-11 points:	At risk of malnutrition
0-7 points:	Malnourished

For a more in-depth assessment, continue with questions G-R

Assessment

G Lives independently (not in nursing home or hospital)
1 = yes 0 = no ☐

H Takes more than 3 prescription drugs per day
0 = yes 1 = no ☐

I Pressure sores or skin ulcers
0 = yes 1 = no ☐

N Mode of feeding
0 = unable to eat without assistance
1 = self-fed with some difficulty
2 = self-fed without any problem ☐

O Self view of nutritional status
0 = views self as being malnourished
1 = is uncertain of nutritional state
2 = views self as having no nutritional problem ☐

P In comparison with other people of the same age, how does the patient consider his / her health status?
0.0 = not as good
0.5 = does not know
1.0 = as good
2.0 = better ☐.☐

Q Mid-arm circumference (MAC) in cm
0.0 = MAC less than 21
0.5 = MAC 21 to 22
1.0 = MAC 22 or greater ☐.☐

R Calf circumference (CC) in cm
0 = CC less than 31
1 = CC 31 or greater ☐

Assessment (max. 16 points) ☐☐.☐

Screening score ☐☐.☐

Total Assessment (max. 30 points) ☐☐.☐

Malnutrition Indicator Score

24 to 30 points	☐	normal nutritional status
17 to 23.5 points	☐	at risk of malnutrition
Less than 17 points	☐	malnourished

Ref. Vellas B, Villars H, Abellan G, et al. *Overview of MNA® - Its History and Challenges.* J Nut Health Aging 2006; 10: 456-465.
Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. Screening for Undernutrition in Geriatric Practice: *Developing the Short-Form Mini Nutritional Assessment (MNA-SF).* J. Geront 2001; 56A: M366-377.
Guigoz Y. The Mini-Nutritional Assessment (MNA®) *Review of the Literature – What does it tell us?* J Nutr Health Aging 2006; 10: 466-487.

For more information: www.mna-elderly.com

A2.3.3 Validity of the Mini Nutritional Assessment Short Form (MNA-SF)

Guigoz describes the validity of the MNA-SF based on eight studies described in six publications.[56] In five cases, a comparison is made with the full MNA, in two cases with a detailed diagnosis of undernutrition, and in one case as reference method it is ascertained whether the BMI was lower than 23. In using the full MNA as reference method, there is undesirable dependence of the scores, so that an overoptimistic picture of the validity is obtained. The sensitivity varied between 64 and 100 per cent and was above 86 per cent in six of the eight cases. When using of the full MNA as reference method, the specificity was between 89 and 100 per cent, but in comparison to a detailed diagnosis of the nutritional status, the specificity was below 40 per cent.

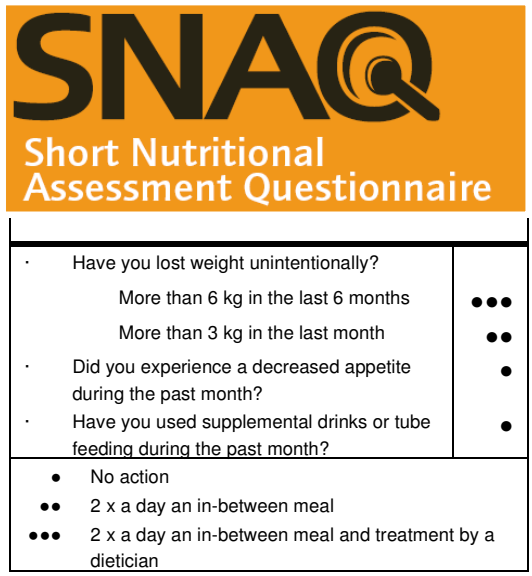
In the validity study described, the problem that no golden standard exists to establish undernutrition also plays a role of course.

A2.4 Short Nutritional Assessment Questionnaires (SNAQ, SNAQ^{RC} and SNAQ^{65+})

In the Netherlands, the Short Nutritional Assessment Questionnaire (SNAQ) was developed for early detection and treatment of undernutrition in hospital patients.[58] The SNAQ may be applied in less than five minutes by nurses and is linked directly to a treatment plan. This instrument includes questions about unintentional weight loss, reduced appetite en and the use of liquid nutrition or tube feeding. The questionnaire was obtained from the Dutch Undernutrition Steering Group website.[59]

A modified version[60] was then developed for nursing and care homes: the Short Nutritional Assessment Questionnaire for Residential Care (SNAQ^{RC}). The questions in the SNAQ^{RC} about unintentional weight loss and reduced appetite correspond with the SNAQ. The question about tube feeding and liquid nutrition in the SNAQ is replaced in the SNAQ^{RC} with the question of whether the person concerned does or does not need help in eating. Further, the SNAQ^{RC} also evaluates the BMI; this is calculated based on body weight and knee height, where the knee height is extrapolated to the person's total height using Chumlea's formula. The choice of knee height rather than total height was prompted by the many practical problems in measuring the height of patients in nursing and care homes.[61] The researchers assume that a BMI of 20 kg/m^2 or less corresponds to severe undernutrition and that a BMI of 20 to 22 kg/m^2

corresponds to moderate undernutrition. Although it is indicated in the SNAQ^{RC} that obesity exists at a BMI above 28 kg/m^2, this has no effect on the score. The questionnaire was obtained from the Dutch Undernutrition Steering Group website.[59]



Finally, the SNAQ^{65+} was developed for elderly people in first-line and home care.[62] Instead of the BMI, the mid-arm circumference is determined. This choice was prompted by both practical and scientific arguments: the circumference of the upper arm is simpler to determine than height and weight, and there are indications that this is a better predictor of mortality in the elderly than the BMI.[10] The questionnaire was obtained from the Dutch Undernutrition Steering Group website.[59]

It is indicated in the SNAQ, SNAQ^{RC} and SNAQ^{65+} questionnaires what the implication of the result is for the nutrition policy.

Ask these questions	
Have you lost weight unintentionally?	
• More than 6 kg in the recent months	Red
• More than 3 kg in the last month	Red
Do you need assistance with eating?	Orange
Have you experienced a decreased appetite over the last month?	Orange
Measure BMI	
• BMI below 20 • BMI 20 to 22 • BMI 22 to 28 • BMI above 28 equals overweight	Red Orange Green -
Total score of questions + BMI	
Red + red Orange + red Orange + orange Green + red	Red Red Red Red

SNAQ RC

Screening and treatment plan

Screen and weigh* on admission and before each MDO make notes in care (life) plan

Green	Orange	Red
No action	• 2-3x per day supplies in-between meals • Motivate, poss. leaflet • Overall monitoring of intake	• 2-3x per day supplies in-between meals + fortified main meals + overall monitoring of intake • Notify doctor to engage dietician • ≤3 working days after screening, consultation with dietician • Evaluation 5 working days after start of treatment

* Weigh		www.stuurgroepondervoeding.nl
Green Orange Red	1 x every 1-3 months 1 x a month 1 x a month	

SNAQ 65+

		green	orange	red
1	Weight loss	less than 4 kg		4 kg or more
2	Mid-upper arm circumference	25 cm or more		less than 25 cm
3	Appetite and functionality	good appetite and/ or well functioning	poor appetite and poor functioning	
4	Treatment plan	not undernourished	at risk of undernutrition	undernourished

Table A11 The evaluations with the SNAQ, SNAQ^{RC} and SNAQ^{65+} are based on the following aspects.

Type of SNAQ	Indicators that are used to estimate the prevalence of undernutrition in the Netherlands (Chapter I)	Other aspects
SNAQ (for hospitals)	• Weight loss >6 kg in the last 6 months or >3 kg in the last month	• Reduced appetite for 1 month • Use of supplemental drinks or tube feeding during the past month
SNAQ^{RC} (for nursing and care homes)	• Weight loss >6 kg in last 6 months or >3 kg in last month • BMI < 20 or BMI 20-22	• Reduced appetite for 1 month • Assistance needed in eating
SNAQ^{65+} (for elderly people in first-line and home care)	• Weight loss ≥4 kg	• Mid-upper arm circumference <25 cm

A2.4.1 Reproducibility

The inter-observer variability was indeed determined for the SNAQ, but for neither the SNAQ^{RC} nor the SNAQ^{65+}. The inter-observer variability of the SNAQ was determined in a study on a group of 47 patients who were screened with the SNAQ upon admission to hospital. It was investigated to what extent different nurses and dieticians arrived at the same score with the SNAQ. The nurses' scores corresponded in 40 of the 47 patients; the kappa value was thus 0.69 (substantial agreement). Between nurses and dieticians, the scores corresponded in 44 of the 47 patients; the kappa value was thus 0.91 (almost perfect agreement).[58]

A2.4.2 Validity

The validity of the SNAQ was determined in a study of almost 300 hospital patients (the same study as that in which the inter-observer variability was determined).[58] The patients were screened with the SNAQ upon admission to hospital. The reference method to establish severe undernutrition was: a BMI < 18.5, unintentional weight loss of more than 5 per cent in the last month or more than 10 per cent in the last six months. The reference method to establish moderate undernutrition was: unintentional weight loss of 5 to 10 per cent in the last six months. Both the SNAQ and the reference method are partly based on weight loss. In this validity study, the weight loss was determined twice at different times. Nonetheless, dependence cannot be excluded: it is conceivable that the participants remembered their answering of the first questionnaire while completing the second. And regardless of anything else, both observations of the weight loss are correlated and therefore contribute to an overoptimistic picture of the validity. The outcome of this validation study is summarised in Table A12.

Table A12 Outcome of the SNAQ validation study.[58]

Quality indicator for the SNAQ	Reference with which the outcome of the SNAQ was compared	
	Moderate undernutrition, defined as 5-10% unintentional weight loss in the last six months	Severe undernutrition, defined as BMI < 18.5 or unintentional weight loss 5% in the last month or ≥10% in the last six months
Sensitivity	79	76
Specificity	83	83

For the determination of the validity of the SNAQ^{RC}, a study was carried out on almost 500 nursing home residents and almost 250 care home residents (in total twelve locations, spread over a large part of the Netherlands).[60] The reference method to establish severe undernutrition was: a BMI ≤20 kg/m^2 and/or unintentional weight loss of at least 5 per cent in the last month or at least 10 per cent in the last six months. The reference method to establish moderate undernutrition was: a BMI between 20.1 and 22 kg/m^2 and/or unintentional weight loss of 5 to 10 per cent in the last six months. Because it proved that the sensitivity and specificity differed little between the two settings, the results were pooled. The sensitivity was estimated at 87 per cent and the specificity at 82 per cent. The fact that the outcome of both the SNAQ^{RC} and the reference method are determined by BMI and weight loss contributes to a high sensitivity and specificity. It further applies that the meaning of the findings with respect to the validity is unclear, due to the lack of a golden standard for establishing undernutrition.

A2.5 Nutritional risk screening 2002 (NRS-2002)

The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends the use of Nutritional Risk Screening 2002 (NRS-2002)[63] when screening for undernutrition in hospitals. The NRS-2002 instrument can be applied by nurses, dieticians or doctors.

The NRS-2002 is gone through in two steps. Firstly, it is enquired generally whether the BMI is under 20.5, there is weight loss, reduced intake or serious illness. If one of these aspects applies, the same subjects are worked out in more detail to arrive at an estimate of the risk of undernutrition. The evaluation is based on the following aspects:

The *Nutritional Risk Screening* (NRS-2002) questionnaire below was obtained from the publication about the ESPEN guidelines for nutrition screening 2002.[63]

Part 1	Initial screening		
		Yes	No
1	Is BMI <20.5?		
2	Has the patient lost weight within the last 3 months?		
3	Has the patient had a reduced dietary intake in the last week?		
4	Is the patient severely ill? (e.g. in intensive therapy)		
Yes: **No**:	If the answer is 'Yes' to any question, the screening in Table 2 is performed. If the answer is 'No' to all questions, the patient is re-screened at weekly intervals. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.		

Part 2	Final screening		
Impaired nutritional status		Severity of disease (increase in requirements)	
Absent *Score 0*	Normal nutritional status	Absent **Score 0**	Normal nutritional requirements
Mild **Score 1**	Weight loss > 5% in 3 months or food intake below 50-75% of normal requirement in preceding week	Mild **Score 1**	Hip fracture* Chronic patients, in particular with acute complications: cirrhosis*. COPD*. *Chronic haemodialysis, diabetes, oncology*
Moderate **Score 2**	Weight loss > 5% in 2 months or BMI 18.5-20.5 + impaired general condition or food intake 25-60% of normal requirement in preceding week	Moderate **Score 2**	Major abdominal surgery* Stroke* *Severe pneumonia, hematologic malignancy*
Severe **Score 3**	Weight loss > 5% in 1 month (>15% in 3 months) or BMI < 18.5 + impaired general condition or food intake 0-25% of normal requirement in preceding week	Severe **Score 3**	Head injury* Bone marrow transplantation* *Intensive care patients (APACHE > 10)*
Score:	+	**Score**:	= Total score
Age	if ≥70 years: add 1 to total score above	= age-adjusted total score	
Score > 3: **Score < 3**:	the patient is nutritionally at-risk and a nutritional care plan is initiatedweekly rescreening of the patient. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status		

NRS-2002 is based on an interpretation of available randomized clinical trials.
* indicates that a trial directly supports the categorization for patients with that diagnosis. Diagnoses shown in *italics* are based on the prototypes given below.
Nutritional risk is defined by the present **nutritional status** and risk of impairment of present status, due to **increased requirements** caused by stress metabolism of the clinical condition.
A nutritional care plan is indicated in all patients who are (1) severely undernourished (score = 3), or (2) severely ill (score = 3) or (3) Moderately undernourished + mildly ill (score 2 + 1), or (4) mildly undernourished + moderately ill (score 1 + 2)
Prototypes for severity of disease
Score = 1: a patient with chronic disease, admitted to hospital due to complications. The patient is weak but out of bed regularly. Protein requirement is increased, but can be covered by oral diet or supplements in most cases.
Score = 2: a patient confined to bed due to illness, e.g. following major abdominal surgery. Protein requirement is substantially increased, but can be covered, although artificial feeding is required in many cases.
Score = 3: a patient in intensive care with assisted ventilation etc. Protein requirement is increased and cannot be covered even by artificial feeding. Protein breakdown and nitrogen loss can be significantly attenuated.

Table A13 Evaluation with the NRS-2002 is based on the following aspects.

Indicators that are used to estimate the prevalence of undernutrition in the Netherlands (Chapter I)	Other aspects
• BMI <18.5 or 18.5-20.5 kg/m^2 • Weight loss >5% during the last 3, 2 or 1 month(s) • Intake in the last week 50-75%, 25-60% or 0-25% of normal requirement	• Reduced general fitness • Presence of specific clinical pictures (see Annex C)

It is indicated in the NRS-2002 questionnaire what the implication of the result is for the nutrition policy.

A2.5.1 Reproducibility

Kondrup et al. investigated the inter-observer variability of the NRS-2002: the kappa value for the variation in the outcome of the NRS-2002 for questionnaires gone through by nurses, dietician and doctors was estimated at 0.67 (substantial agreement).[64]

A2.5.2 Validity

Kyle and colleagues determined the validity of the NRS-2002 by using the SGA as reference method.[65] The study took place in a Swiss hospital and included almost 1000 adult patients. The sensitivity was estimated at 62 per cent and the specificity at 93 per cent. The meaning of the findings with respect to the validity is unclear.

In the study that was also described in Section A2.2.2, it was investigated in 705 patients in an academic hospital to what extent the outcome of the NRS-2002 – determined within 48 hours of admission to the hospital – was associated with a very long length of stay and the occurrence of complications and mortality.[50] Almost 30 per cent of the patients investigated had a risk of undernutrition according to the NRS-2002. This outcome was associated with an increased risk of both complications ($p = 0.03$) and death ($p = 0.03$). The effect on the length of stay was not statistically significant.

Table A14 Results from the study of Raslan et al.[50]

Outcome measure	Prognosis in people with an NRS-2002 score of 3 or more compared with people with a lower score		
	Odds Ratio	95% confidence interval	*p* value
Complications	1.9	1.1 to 3.5	0.03
Very long length of stay	1.9	0.8 to 2.5	0.19
Mortality	3.9	1.2 to 13.1	0.03

A2.6 Malnutrition Universal Screening Tool (MUST)

It is indicated in the MUST questionnaire what the implication of the result is for the nutrition policy. The version below was obtained from the Academic Hospital Maastricht's website.[57]

MUST (The Malnutrition Universal Screening Tool)

1. BMI:
   - >20 : 0
   - 18.5-20 : 1
   - <18 : 2

2. Unintentional weight loss in 3-6 months
   - <5% : 0
   - 5 - 10% : 1
   - >10% : 2

(>5% in 1 month or 10% in 1 year)

3. Acute disease and
   no or little food intake happened/expected during >5 days : 2

____ sum

General risk of undernutrition:

0 = low	Routine clinical care: repeat screening in hospital every week
1 = moderate	Observe: maintain nutrition and fluid list
2 or over = high	Treat: refer to dietician. First encourage with ordinary food, thereafter supplements.

Reference: Stratton R.J., Green C.J., Elia M. Disease-related undernutrition: an evidence-based approach to treatment. CABI publishing, USA, 2003.

The Malnutrition Universal Screening Tool (MUST) was developed in 2000 by the Malnutrition Advisory Group of the British Association for Parenteral and Enteral Nutrition (BAPEN).[66] The instrument is intended for all health services settings and all patient groups. The risk of undernutrition is estimated based on BMI, weight loss and acute disease effect. The MUST is simple, can be carried out by any care worker in three to five minutes, and is directly linked to a treatment plan.[67]

Table A15 Evaluation with the MUST is based on the following aspects.

Indicators that are used to estimate the prevalence of undernutrition in the Netherlands (Chapter I)	Other aspects
• BMI below 18 or between 18.5 and 20 kg/m^2 • 5-10% or >10% weight loss during 3-6 months • Little or no food intake for more than 5 days through acute illness	None

A2.6.1 Reproducibility

The inter-observer variability of the MUST was evaluated by Stratton et al. Kappa values were between 0.8 and 1.0 (near-perfect agreement).[67]

A2.6.2 Validity

The validity of the MUST was determined by comparison with different reference methods; the reference methods and outcomes are specified in the publication on this.[67] The degree of agreement with other instruments was expressed as a kappa value and varied greatly. It was also calculated what percentage of the participants were categorised identically with the MUST and with the reference method. Starting from the cross-table A7, this percentage was calculated as (A+D)/(A+B+C+D). The values varied between 62 and 96 per cent; there was therefore substantial to near-perfect agreement between the MUST and the reference methods.

After the publication by Stratton et al. described above, two more studies were published with data about the MUST's validity.

In a study of 100 elderly people of average age 80 years, a dietician determined whether the participant was or was not at risk of undernutrition based on average food intake, questions about health and illness, body weight and BMI. This reference method is not further specified in the publication. The MUST score determined by a doctor was compared to the reference method. The sensitivity was estimated at 100 per cent and the specificity at 98 per cent.[68]

The other study involved 275 patients, of whom 171 were elderly (60 years and older). Serious risk of undernutrition for elderly people was defined as a BMI <20.0 and unintentional weight loss of >5 per cent during the last month or >10 per cent during the last six months; a moderate risk of undernutrition was defined as unintentional weight loss of 5-10 per cent during the last six months, regardless of BMI (the reference method). For the distinction between serious risk of undernutrition as against no or moderate risk of undernutrition, the sensitivity was estimated at 67% and the specificity at 82%. For the distinction between moderate or serious risk of undernutrition as against no risk of undernutrition, the sensitivity was estimated at 97% and the specificity at 79%.

The meaning of the estimates of sensitivity and specificity is unclear, because these are not based on comparison to a golden standard method.

A2.7 Summary and consideration

The findings in this chapter are summarised in Table A16.

A2.7.1 Elements that are assessed

Each of the screening instruments studied investigates whether weight loss has occurred. Almost all instruments – the SNAQ is the only exception – include an anthropometric measure in the evaluation (BMI, arm or calf circumference). Many instruments include in the evaluation whether the person has been eating less than normal recently; the SNAQ, the SNAQ^{RC} or the SNAQ^{65+} do not include this factor, though it is asked whether appetite is reduced.

In some instruments, the presence of illnesses or symptoms plays a role in the evaluation (SGA, MNA and NRS-2002). In one instrument, the MNA, besides illness, enquiry is also made about other factors that may increase the risk that undernutrition develops, such as restricted mobility, mental stress and use of medicines.

Table A16 Overview of findings in this chapter.

	Instrument for establishing undernutrition							
	SGA	MNA-SF	MNA	SNAQ	SNAQ^{RC}	SNAQ^{65+}	NRS-2002	MUST
Name of instrument includes:								
• The term assessment	+	+	+	+	+	+	-	-
• The term screening	-	-	-	-	-	-	+	+
Elements that are assessed with this instrument:								
• BMI	-[a]	+	+[a]	-	+	-[a]	+	+
• Unintentional weight loss	+	+	+	+	+	+	+	+
• Reduced intake	+[b]	+	+	-[b]	-[b]	-[b]	+	+
• Illnesses and/or physical symptoms	+	+	+	-	-	-	+	-
• Reduced functional capacity	+	+	+	+	+	-	-	-
• Other elements	-	-	+	+	-	-	-	-
The instrument is quickly and easily applicable	no	yes	no	yes	yes	yes	no	yes
The score obtained with the instrument is directly linked to a treatment plan	no	no	no	yes	yes	yes	yes	yes
Inter-observer variability (kappa value)	0.6-1.0	-	0.5-0.8	0.7-0.9	-	-	0.7	0.8-1.0
Validity								
• Sensitivity[c]	-	64-100%	11 of 13 studies >70%	75-80%	87%	-	62%	
• Specificity[c]	-	89-100%	6 of 13 studies >70%	83%	82%	-	93%	

[a] With this instrument, other anthropometric data are taken into account (as well as or instead of the BMI).
[b] With this instrument, reduced appetite is taken into account (as well as or instead of reduced food intake).
[c] No golden standard is available to establish undernutrition. In the study about the sensitivity and specificity of the instrument, reference methods are used whose validity is just as unclear. The meaning of the values presented is therefore unclear.

A2.7.2 Screening or assessment

The names of these five instruments contain the term ‘screening’ or ‘assessment’. Which of the two is chosen proves not to correspond with the usual distinction between screening and assessment.

- It is usual that an instrument for screening is quick and easy to apply, while an assessment is more complex and demands more time and effort. In the case of undernutrition, not only both ‘screening instruments’ (NRS-2002 and MUST), but also the SNAQs, are quick and straightforward to carry out.

- It is usual that an assessment is based on other determinations or measurements than the screening that precedes it. In the case of the instruments to establish undernutrition, there is an overlap between the elements that play a role in the evaluation. For instance, all the instruments investigate whether unintentional weight loss has occurred.
- It is usual that a screening leads to the decision of whether an assessment is needed, while an assessment leads to a decision about any treatment. In the case of undernutrition, the SNAQ, NRS-2002 and MUST are directly linked to a treatment plan, while this is not the case for the SGA or MNA. Due to the lack of a golden standard, an assessment in the field of undernutrition is not possible.

A2.7.3 Reproducibility

For various instruments, the inter-observer variability is reported (this term is explained in Section A2.1.2). For most instruments (SGA, SNAQ, NRS-2002 and MUST), the reported kappa values are at the level of substantial (0.6-0.8) or near-perfect (0.8-1.0) agreement. For the MNA, substantial agreement between observers is reported in a nursing home, but the inter-observer variability in a hospital is assessed as moderate. The inter-observer variability of the MNA-SF, $SNAQ^{RC}$ and $SNAQ^{65+}$ was not investigated.

A2.7.4 Validity

The most important reservation with regard to investigations of the validity of screening instruments in the field of undernutrition (the term validity is explained in Section A2.1.2) is that no golden standard for establishing undernutrition exists. In order to determine the validity of the instruments, they are compared to reference methods, but the validity of the said reference methods is also unclear. The reference methods therefore provide no certainty about the presence or absence of undernutrition. As long as there is no golden standard, the sensitivity and specificity of the methods cannot be established with certainty, and the meaning of the available research data on the matter is unclear.

It is observed with regard to the SGA and NRS-2002 that people who are considered ‘undernourished’ or ‘at risk of undernutrition’ have a poorer prognosis that people for whom this is not the case. The relevant studies provide information about the predictive value of the instruments, but not about the causality, nor on the usefulness of treatment.

A2.8 Conclusion

The most important problem with regard to the screening instruments is that no certainty can be achieved about their validity because of the absence of a golden standard. Ideally, an instrument would lead to the identification of those patients who would benefit from nutritional intervention. Not one of the available instruments is targeted at this.

Chapter **A3**

Effectiveness of treatment with extra protein and energy

One of the Minister's advice questions concerned the gain that is possible through treatment of protein-energy undernutrition: does the health of the undernourished elderly improve when they receive extra protein and energy? In this chapter, the Committee evaluates the research published in this area.

A3.1 The Committee's approach

To answer the effectiveness question, an interventional study is necessary. This type of research is also essential to establish whether the connection between undernutrition and health is causal, which is relevant to the definition and the assessment of undernutrition. It is apparent from observational research that the undernourished elderly function less well and have a poorer clinical prognosis (see Section A1.3), but observational research cannot provide a definitive answer on causality. Because undernutrition often accompanies illness, it is possible that the illness is the cause of both the poor nutritional status and the unfavourable clinical outcome, and that the association between undernutrition and clinical outcome is not caused by undernutrition, but by illness. The question of whether the connection between undernutrition and a poorer prognosis is causal can only be answered based on interventional research: if undernutrition causes a poor prognosis, then correction of undernutrition ought to lead to a better prognosis.

The Committee evaluates how powerful the indications are that increasing protein and energy intake is beneficial for the undernourished elderly. The clinical relevance of treatment of undernutrition must be revealed by the effects on functional capacity or on prognosis. This concerns outcome measures such as mortality, complications, quality of life and functional status (including muscle strength and mobility). Reporting of effects on at least one clinically relevant end-point was therefore a condition in the selection of trials; effects on body weight and the intake of protein and energy have no clinical relevance in themselves.

Where supplementation is mentioned in this chapter, interventions with ordinary food, liquid nutrition or supplements are meant. Besides this, it is also conceivable that the nutritional situation can also be influenced indirectly, that is via interventions that do not concern the food provided. The research available into interventions other than supplementation in fact mostly concerns the effects on food intake and body weight and is seldom targeted at clinically relevant outcome measures.

For instance, two overview articles have been published about the effects of nutritional consultations with dieticians.[69,70] The data available prove to be very limited. Nutritional advice seems to have less effect on body weight than nutritional supplements and there were no indications for effects on clinically relevant end-points (mortality and morbidity).[69] Diet consultations had no statistically significant effect on the quality of life of cancer patients, although it did appear that the average effect was in a beneficial direction, and there was significant heterogeneity.[70]

Another example of an intervention that could lead in an indirect way to improvement in the nutritional status is improvement of the ambience at mealtimes. This would concern the attractiveness of the dining room, the presentation of the meal, how much time is available for eating, the presence of company (which may have both positive and negative effects) and the amount of disturbing factors during eating such as noise, bright light and less suitable tableware or furniture. A trial in Dutch nursing homes provided indications that improvement in ambience can lead to an increase in food intake and in the score in the Mini Nutritional Assessment (for a description of this instrument, see Section A2.3).[71]

In certain cases, organisational improvements such as increasing the help during mealtimes could also lead to a greater intake of protein and energy.[72]

Because the information on the effects of these indirect interventions on clinically relevant outcomes is too limited, they are not taken into consideration in the rest of this chapter, and the Committee restricts itself to the question whether treatment with extra protein and energy is beneficial.

A3.1.1 Delineation of the issue

In this chapter, the Committee describes the state of science with respect to the effectiveness of treatment with extra protein and energy. In this, it restricts itself to trials:

- on elderly people who consume normal food beside the intervention
- in which the intervention is consumed orally
- in which the intervention concerns the intake of both protein and energy
- in which the supplement does not contain specific amino acids.

Elderly people who require (additional) enteral or parenteral nutrition remain out of consideration. Examples of this are people with a serious illness, who are severely underweight, or have seriously reduced appetite or chewing or swallowing problems.

There are indications that (seriously) ill people may benefit if their energy intake is lower than their energy need for a limited period, but the interventional research available on this does not match up with the Committee's selection criteria: the trials were not done specifically in the elderly, they mainly concerned enteral and parenteral nutrition, and some of the patients were seriously ill.[73,74]

A3.1.2 The Committee's approach

A meta-analysis on the effect of providing extra protein and energy to elderly people was published by Milne and colleagues in 2009: *Protein and energy supplementation in elderly people at risk from malnutrition*.[21] The Committee describes this publication in Section A3.2.

Because the quality of many trials in this meta-analysis is very poor, the Committee also describes the picture that emerges from randomised controlled trials (RCTs) of relatively better quality. This is done in Section A3.3. The Committee assumes that relevant publications until December 2007 were identified via the meta-analysis. For potentially relevant publications from after December 2007, the Committee carried out a search procedure in the PubMed

database. Based on the abstracts, 26 publications were requested. The Committee then combined the most relevant randomised controlled trials (RCTs) in the meta-analysis of Milne et al. with the most relevant RCTs of more recent date and described the resulting picture.

A3.2 The meta-analysis of Milne et al from 2009

A3.2.1 Study design

The research questions of Milne et al.[21] were the following:

To assess the effects and acceptability of oral dietary supplements in both hospitalised elderly people and elderly people in the community, irrespective of setting:

- to test the null hypothesis that there was no difference in outcomes between participants who were given oral nutritional supplements compared to those participants who were given no intervention, a placebo, or an alternative supplement with a different amount of calories and protein.
- to carry out subgroup analysis in order to assess whether participants who were undernourished, were ill, were aged 75 years or over, were given supplements of 400 kcal or more or who had longer duration (35 days or more) of supplementation showed most benefit.

Milne and colleagues selected research in which the intervention was aimed at increasing the intake of both protein and energy; they did not include trials in which supplementation was done with protein only. Trials with tube feeding or parenteral nutrition were also excluded; the meta-analysis restricts itself to the effects of oral supplementation. Other selection criteria were an intervention duration of at least one week and an average age of 65 years. Further, trials in *intensive care* patients, and patients in the recovery stage of treatment for cancer were excluded, as were trials in which the effect of supplementation with immuno-modulating supplements or specific amino acids was investigated.

A3.2.2 Characteristics and quality of the trials included

Characteristics of the trials that Milne et al. included into their meta-analysis are summarised in Table A17. It is clear from the table that these trials leave much to be desired: 70 per cent of the trials were not RCTs; almost 70 per cent of the trials were very small in size; in more than half of the trials there was no *'intention to treat'* analysis; in almost half of the trials there was no 'blinding' regarding who received a supplement and who was in the control group; in

Table A17 Overview of the quality of the trials that were included in the meta-analysis of Milne et al.[21] with an explanation of why the indicator concerned is of importance to the quality of the trials.

Quality indicator and how this is distributed among the trials that Milne et al. included in their meta-analysis		*Explanation why the indicator concerned is of importance to quality of trials*
Allocation of intervention or control treatment		In randomisation, the allocation of participants to the different study groups is completely based on chance. In this way, potential confounders are evenly distributed over the experimental group(s) and the control group. If randomisation is not done, the probability of confounding factors in the supplemented group is different from that in the control group and the findings of the study are less reliable.
• Randomised (these are the RCTs)	19 trials	
• Non-randomised or not stated	43 trials	
'Intention to treat' analysis:		If no *'intention to treat'* analysis is conducted, the risk arises that the advantages of any randomisation procedure may be undone. In this case, the results may still become distorted.
• Yes	24 trials	
• No	38 trials	
'Blinding' regarding the information on the assigned treatment:		Blinding means that the study group to which participants are allocated is concealed: the participant or the people administering or assessing the treatment do not know which participant has had which treatment. Blinding is important, because knowledge about the treatment can affect (certain) outcomes. In 29 of the 62 trials, there was no blinding of any kind regarding the information about the treatment allocated (supplementation or control), so that the probability increases that an unwarranted beneficial effect of supplementation is found.
• Realised for researchers who established the clinical outcome	12 trials	
• Realised for participants in the study	16 trials	
• Realised for people who provided the supplement	14 trials	
• No blinding	29 trials	
Size of trials:		Chance differences between the intervention and control groups can occur due to what is called random variation. This risk is greatest in the smallest trials. Moreover, a smaller trial has a lower statistical discriminatory power: say the intervention has a beneficial effect in reality, then the probability that this effect is found by a trial becomes smaller, the smaller the size of the trial is. The number of participants necessary to achieve sufficient discriminatory power is dependent on the outcome measure. For outcomes like mortality and complications, trials with 100 participants are very small; effects on muscle strength can indeed be demonstrated with smaller trials. The FOOD trial dominates the results of the meta-analysis.
• Over 4,000 hospital patients or 40 per cent of all the people in the meta-analysis of Milne et al. were in one trial (the FOOD trial in patients with a cerebrovascular accident – a cerebral haemorrhage, stroke or TIA – of whom 8% were undernourished).	1 trial	
• Trials with 100-700 participants	19 trials	
• Trials with less than 100 participants	42 trials	
Nutritional status:		It would seem plausible that extra protein and energy are beneficial to people with undernutrition or a risk of undernutrition, but would have little or no effect on people with an adequate nutritional status. The definitions of undernutrition varied among the trials and were not or were insufficiently specified in some publications. Within the largest trial too (the FOOD trial), the method of classifying the nutritional status of the participants varied. In three trials, the outcomes for well-nourished and undernourished people were presented separately.[22,23,75]
• Undernutrition or risk of undernutrition	60% of all participants	
• Adequate nutritional status	40% of all participants	

Quality indicator and how this is distributed among the trials that Milne et al. included in their meta-analysis			*Explanation why the indicator concerned is of importance to quality of trials*
Intervention:			The energy supplementation varied from 175 to 1350 kcal/d and the protein supplementation from 10 to 50 g/d. In 35 trials, it was specifically stated that in the intervention group, as well as protein and energy, (one or more) micronutrients were supplemented; in 27 trials it was not reported or it was unclear.
• 400 kcal/d or more		32 trials	
• Less than 400 kcal/d		20 trials	
• Not specified		10 trials	
Duration of the intervention period:			With a short intervention period, the risk exists that there is insufficient time to observe any effects of the intervention.
• 35 days or more		37 trials	
• Less than 35 days		17 trials	
• From admission to discharge from hospital		5 trials	
• Unclear:		2 trials	
Distribution among settings:	% of all partici-pants	% of all trials	The care setting may influence the trial outcome: it is conceivable that people in one care setting have a greater or lesser benefit than in another setting; for example, hospital patients are sicker on average than people in either of the other settings.
• Hospital	71%	42%	
• Nursing and/or care home	14%	24%	
• Living at home	15%	34%	
Calculation of the change in body weight: If the body weight at the start of the trial was not reported, Milne et al. assumed an average body weight of 60 kg and then calculated the percentage weight change based on this and the final weight. This does not provide more than a supposition about the possible weight change. Unfortunately, Milne and colleagues failed to state in which studies they used this method.			

almost half of the trials the level of energy supplementation was relatively modest; in almost half of the trials, the intervention period was very short; in 40 per cent of the participants, the nutritional status was evaluated as adequate* and therefore in essence there was little motivation for the intervention studied; and the calculation of the weight change was highly speculative in an unknown proportion of the trials. The qualitative shortcomings are so extensive that the interpretation of the results of the meta-analysis has to be taken with a sizeable pinch of salt. The trials took place in different settings: most of them in hospitals, but also in nursing and care homes and in elderly people living at home.

A3.2.3 The findings of Milne et al.

Milne et al. carried out meta-analyses for various outcome measures.[21] The most important results are summarised in Table A18 and present the following picture.

- Milne et al. found a statistically significant effect of supplementation on body weight. The average effect was +2.2%, which for a person of 60 kilograms equates to around 1.3 kg.

* The definitions of undernutrition varied among the trials and were not or were insufficiently specified in some publications. Within the largest trial too (the FOOD trial), the method of determining the nutritional status of the participants varied.

- These researchers primarily looked at the effects of supplementation, regardless of the nutritional status of the participant. In this analysis, they found no significant effect on the mortality risk. Next, the analyses were repeated for certain subgroups, including the subgroup of undernourished elderly people. In this subgroup, Milne et al. found that supplementation caused the mortality to decrease by an estimated 20 per cent.
- Milne et al. estimate that protein-energy supplementation reduces the risk of complications by around 15 per cent.
- The meta-analysis with respect to the length of stay yielded no indications of an effect, but because there was statistically significant heterogeneity (p = 0.02) no clear conclusions are possible.
- Milne et al. found no indications that muscle strength improves through supplementation. This picture not only arises from the meta-analysis of the seven trials on the effects on hand-grip strength (see Table A18). Besides these seven trials, the effect on muscle strength was also determined in six other trials, but those six could not be included in the meta-analysis. No statistically significant increasing effect on muscle strength was found in any of the thirteen trials.

The findings with regard to various other outcome measures did not lend themselves to a meta-analysis. Milne et al. provide a description of their findings for those outcome measures.

Table A18 Results of the meta-analyses carried out by Milne et al.

Outcome measure	No. of trials	Result of meta-analysis for this outcome measure			Test of heterogeneity
		Pooled average effect or risk ratio	95% confidence interval	Test result	
Weight change	43	Average +2.2%	1.8 to 2.5%	p<0.0001	p=0.16
Change in mid-arm circumference	15	Average +1.2%	0.5 to 2.0%	p=0,002	p=0.15
Mortality risk	28	Risk ratio = 0.92	0.81 to 1.04	p=0.20	p=0.68
Mortality risk in the undernourished elderly	17	Risk ratio = 0.79	0.64 to 0.97	p=0.030	p=0.79
Risk of complications	23	Risk ratio = 0.86	0.75 to 0.99	p=0.030	p=0.63
Length of stay	14	Average = –0.75	-2.84 to 1.34	p=0.48	p=0.020
Hand grip strength	7	Average = +0.06	-0.60 to 0.72	p=0.87	p=0.23

Outcome measures with respect to functional capacity and functional status

Milne et al. indicate that there is little research into the effect that supplementation has on functional capacity and that the measures of functional status in the research available are of a very varied nature: mobility, hand-grip strength, daily activities, cognition and lung function. The results with respect to the hand-grip strength are described in the passage about the meta-analysis results. A description of the other outcome measures with respect to functional capacity and functional status is given below.

- Milne et al. found few indications for an effect of supplementation on outcome measures that concern mobility, such as fall frequency, activity score, mobility, walking, walking up stairs or speed of standing up and walking away.
- Milne et al. found fifteen trials in which the effect of giving extra protein and energy on the *health-related quality of life* (HQL) measured with either general questionnaires or disease-specific questionnaires was investigated.[21] No effect was found in the majority of these trials. In three trials, it was found that supplementation leads to a significant improvement; the effects concerned mobility[76] and physical and/or social well-being.[77, 78] In one trial, the outcome was only just statistically insignificant.[79] With regard to another trial in which a statistically significant difference was observed,[80] Milne et al. raise questions about the statistical analysis.
- Milne et al. found eleven trials in which the effect on *Activities of Daily Living* (ADL) was studied. Of the five trials that were conducted or initiated in a hospital setting, two reported an effect on ADL[24,81] and two others[22,82] an effect in a subgroup (in the subgroup of severely undernourished patients[22] and in the subgroup of patients who accepted the supplement well respectively). None of the four trials in chronic care[83-86] and none of the three trials on elderly people living at home[25, 87, 88] demonstrated an effect on ADL.[21]
- The effect of protein and energy supplementation on lung function in COPD patients was determined in four trials according to Milne et al.[21] Two of these yielded no indications of an effect.[89, 90] In one trial, a beneficial effect on the lung function of COPD patients was found after four weeks of supplementation with extra protein and energy, but not after eight weeks of supplementation.[91] In another trial in which a beneficial effect of supplementation was observed, the intervention only lasted for two weeks.[79]

- Milne et al. found five trials in which it was investigated whether the giving of extra protein and energy had an effect on the cognitive development of elderly people and concluded that none of these trials yielded indications of a beneficial effect.[21]

Side-effects

Milne et al. describe that in the publications of eighteen trials, side-effects are mentioned. In twelve trials, patients ascribe side-effects like nausea, diarrhoea and gastro-intestinal symptoms to the nutritional intervention. Every one of these is a symptom that arises frequently in people who are ill. In most trials, only the side-effects in the supplementation group were described, without comparison with the control group, so the data are non-controlled. It is not possible on the basis of these findings to reach conclusions about side-effects.

A3.3 RCTs of relatively better quality in the undernourished elderly

A3.3.1 Selection of qualitatively better trials in the undernourished elderly

In the previous Section, it proved that the quality of many of the trials included by Milne et al. was poor, leading to uncertainty about the outcomes presented. Milne et al. admit these deficiencies and state the need for qualitatively better trials of greater size and longer duration.

The Committee considers it important to investigate what picture emerges from the trials of relatively good quality. In this, it took a pragmatic approach: in order to make the selection, the departure point was the quality scores that Milne et al. assigned to the trials. Randomised assignment of treatments (supplementation or control) to individual participants is, according to the Committee, necessary for dependable research results. For this reason, it first identified the RCTs. Then the Committee investigated which of these RCTs in Milne et al. obtained at least half of the maximum available total score for the other quality indicators.

Milne et al. evaluated the research methods on the following ten quality indicators: randomised allocation of intervention and control treatment, *intention-to-treat* analysis, comparability of intervention and control groups and of the treatment plans apart from the treatment studied, clear description of interventions and of inclusion and exclusion criteria, ‘blinding’ of participants, of people providing the treatment and of people assessing clinical outcome, and clinically adequate study duration. For each indicator, Milne et al. awarded 0, 1

or 2 points. The Committee considered a score of 2 for the randomisation quality indicator to be a first requirement in the selection. The Committee then determined the sum of the scores that were awarded by Milne et al. for the other nine quality indicators. This sum could in theory be at most 9 x 2 = 18, but this was not the case for any of the RCTs. The Committee identified the RCTs for which the sum was at least 18 / 2 = 9. These trials were then labelled as the RCTs of relatively good quality.

Milne et al. included 62 trials in their meta-analyses. Only twelve of them survived the quality test described.

Because undernutrition was central to the Minister's advice questions, the Committee considers RCTs in people with an adequate nutritional status irrelevant to this advisory report: the question is whether undernourished elderly people benefit from treatment of protein-energy undernutrition. The Committee therefore identified those RCTs in which only participants with a moderate or poor nutritional status were included.* Of the twelve RCTs of relatively good quality, four were carried out on elderly people who were identified as undernourished in advance: Daniels 200**3/Miller 2006[26], Hankins 1996[25], Tidermark 2004[24] and Vlaming 2001[27]. In two other trials, part of the results were reported separately for the subgroup of elderly people who had obtained the qualification 'undernourished': the FOOD-trial 2005[23] and Potter 2001[22]. Besides the four trials on undernourished elderly people, both these subgroup analyses are included in this Section.

Via the described selection procedure based on methodological quality characteristics and the limitation to trials in undernourished elderly people, the 62 trials in the meta-analysis of Milne et al. were reduced to six.[22-27]

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* The absence of a golden standard to establish undernutrition is of course a problem. The Committee assessed whether the qualification of undernutrition was an inclusion criterion, but further took the method that was used to establish undernutrition as a given. Undernutrition was thus established in diverse ways in the RCTs selected. Information about the methods used may be found in Table 3.3

** In 2006, a publication appeared from Miller about the trial referred to as Daniels 2003 in the publication of Milne et al.; the Miller reference is cited here.

Relevant trials published in 2008 or thereafter

For potentially relevant publications from after December 2007, a literature search was carried out in PubMed.* Based on the abstracts, 26 publications were requested. Then it was checked whether the trials complied with the criteria the Committee had specified in advance and also whether they concerned participants considered to be undernourished at the start of the study. Twenty trials were rejected in this selection procedure. The reasons were as follows:

- Three trials were rejected because the assignment to intervention or control group was not randomised, or was randomised at the level of departments rather than participants.[92-94]
- Seven trials were rejected because (some of) the participants had an adequate nutritional status[a] at the start of the trial.[84, 95-100]
- Ten other trials were rejected, because the intervention studied did not fulfil the criteria the Committee had established in advance:
  - In three trials, a combination of two or more interventions was compared with a control treatment, so that no conclusions were possible about the specific effects of the nutritional intervention.[101-103]
  - Three trials were rejected because the supplement contained isolated amino acids.[104-106]
  - In two trials, it proved that the intervention consisted not of supplementation but of nutritional education and consultations.[107, 108]
  - One trial turned out to be targeted at the effect of individual guidance rather than the effect of supplementation.[109]

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* PubMed search for recent trials about the effects of supplementation with protein and energy:
Protein-Energy Malnutrition[MeSH Terms] OR dietary proteins[MeSH Terms] OR energy intake[MeSH Terms] OR undernutr*[Title/Abstract] OR under-nutri*[Title/Abstract] OR undernourish*[Title/Abstract] OR under-nourish*[Title/Abstract]
AND
enteral nutrition[MeSH Terms] OR dietary supplements[MeSH Terms] OR diet[MeSH Terms] OR nutrition[MeSH Terms] OR food,formulated[MeSH Terms] OR food,fortified[MeSH Terms] OR nutritional disorders[MeSH Terms] OR (nutritional status[MeSH Terms]
NOT
critical care[MeSH Terms] OR obesity[MeSH Terms]
AND
randomized controlled trial[Publication Type] OR controlled clinical trial[Publication Type] OR randomized controlled trials[MeSH Terms] OR random allocation[MeSH Terms] OR double-blind method[MeSH Terms] OR single-blind method[MeSH Terms] OR cross-over studies[MeSH Terms]
NOT
Animals[Mesh:noexp]
AND
Humans[Mesh].

- On one trial – in the case of severe dysphagia – the supplementation occurred via enteral feeding.[110]

The six remaining RCTs were carried out on participants who were considered to be undernourished at the start: Chapman 2009[28], McMurdo 2009[29], Persson 2007[30], Rabadi 2008[31], Neelemaat 2011[32] and Starke 2011[33]. These are described below.

A3.3.2 The methodological quality of these twelve RCTs

Via the procedure described above, the Committee identified twelve RCTs in undernourished elderly people that are of relatively good quality. Table A19 presents an overview of the study characteristics. From this it is apparent that even in these twelve 'better' trials, there are serious reservations about the methodological quality. The most important are: the non-use of placebos, failure to blind regarding the information on the allocated treatment, a limited length of intervention and a limited number of participants. The five larger RCTs (more than 200 participants) all had a limited length of intervention (4 months or less); in three trials the length of intervention was even less than one month. Undernutrition was established in diverse ways. Seven of the twelve studies concerned participants with various diagnoses.

A3.3.3 The picture that arises from these twelve RCTs

The results of the effect of supplementation on mortality and on the occurrence of complications are listed in Table A20. Mortality was an outcome measure in only some of the RCTs; these data are shown in bold in the table. Of the RCTs in which mortality was not an outcome measure, the data on mortality are shown in brackets and in italics in the table. The picture on mortality is scarcely convincing. In only one RCT was a statistically significant protective effect of supplementation against mortality found.[22] In the four other RCTs in which mortality was an outcome measure, the difference between intervention and control group was far from significant.

Table A19 Characteristics of the twelve RCTs of relatively good quality in undernourished elderly people.

Characteristic	No. of trials in which this characteristic is present	References
Intention-to-treat analysis	10	22-30, 32
Information on the assigned of intervention and control was blinded to:		
• Participants (the control group received a placebo)	3	27, 29, 31
• People providing the treatment to the participants	2	27, 31
Intervention and control group were well-matched as regards:		
• Participant characteristics	8	23-28, 31-33
• Care programmes	3	22, 24, 25
Clear description of intervention, control treatment, application protocol	8	22, 25, 27-29, 31-33
(Intended) effect of intervention was 400 kcal or more	9	22, 23, 25-29, 32, 33
Average length of intervention:		
less than 1 month	4	22, 27, 31, 33
1 to 6 months	6	23, 25, 26, 29, 30, 32
6 months or longer	2	24, 28
Average length of follow-up:		
• less than 1 month	3	22, 27, 31
• 1 to 6 months	5	25, 26, 29, 30, 32
• 6 months or longer	4	23, 24, 28, 33
More than 200 participants in intervention plus control group	5	22, 23, 27, 29, 32
Setting:		
• (Mainly) independently living	4	26, 28-30
• Hospital	4	22, 27, 32, 33
• Care institution	3	23, 25, 31
• Unclear	1	24
Diagnosis:		
• Fracture	3	24-26
• Stroke	2	23, 31
• Various	7	22, 27-30, 32, 33
Woman-man distribution:		
• Roughly as many men as women (40-65% women)	6	23, 28-32
• Mainly (75-85%; 2 RCTs) or only (1 RCT) women	3	24-26
• No information	3	22, 27, 33
Manner in which undernutrition is established:		
• Only via mid-arm circumference 0-25th percentile	2	25, 26
• Only on basis of BMI (0-25th percentile or BMI<24)	2	22, 24
• Only on basis of weight loss	1	31
• Via a combination of (part of) above criteria (and appetite)	3	27, 29, 32
• MNA-SF (1 RCT); MNA plus BMI<22 or >7.5% weight loss (1 RCT)	2	28, 30
• NRS-2002	1	33
• Not standardised	1	23

In only four of these twelve RCTs was the effect on the risk of complications determined: three RCTs[24-26] in elderly people with an acute leg fracture and one RCT[33] in elderly people who were admitted to hospital for various reasons. In total, the four RCTs were based on a bare 300 elderly people. Given the diversity of outcomes that come within the term 'complications', this is very few. The four *risk ratios* were lower than 1, but only in one RCT was there a statistically significant effect.[33] The Committee considers the indications that supplementation of undernourished elderly people may reduce the risk of complications to be very slight.

In six of these twelve RCTs, the effect on length of stay was studied.[22, 24, 25, 27, 31, 33] In none of these studies did supplementation result in a statistically significantly shorter length of stay than in the control group.

In four of the twelve RCTs it was determined whether supplementation affected hand-grip strength: in two of these, a statistically significant increase in grip strength was observed[28, 29], while in the third and fourth RCTs no significant effects were found.[30, 32]

Table A20 Results of the effect of supplementation on risks of mortality and complications.[a]

Publication	Mortality[b]			Complications		
	intervention	control	risk ratio	intervention	control	risk ratio
Potter 2001[22]	**13/124**	**27/127**	**0.49 [0.27; 0.91]**			
FOOD 2005[23]	**43/156**	**48/158**	**0.91 [0.64; 1.28]**			
Tidermark 2004[24]	*(1/20)*	*(1/20)*	*(1.00 [0.07; 14.90])*	7/18	12/18	0.58 [0.30; 1.13]
Hankins 1996[25]	**2/17**	**4/14**	**0.41 [0.09; 1.93]**	5/17	6/12	0.59 [0.23; 1.49]
Daniels 2003[26]	*(2/49)*	*(2/51)*	*(1.04 [0.15; 7.10])*	4/45	7/48	0.61 [0.19; 1.94]
Vlaming 2001[27]	*(12/275)*	*(14/274)*	*(0.85 [0.40; 1.81])*			
Chapman 2009[28]	**1/13**	**0/13**	**No difference**			
McMurdo 2009[29]	*(6/102)*	*(6/111)*	*(No difference)*			
Persson 2007[30]	*(6/51)*	*(12/57)*	*(p=0.19)*			
Rabadi 2008[31]						
Neelemaat 2011[32]	*(14/105)*	*(11/105)*	*(Not tested)*			
Starke 2011[33]	**2/66**	**5/66**	***p*=0.44**	4/66	13/66	*p*=0.035
	61/376 (16%)	**84/378 (22%)**		20/146 (14%)	38/144 (26%)	

[a] In the table, the figure before the forward slash indicates how many elderly people died or developed complications during the study. The figure after the slash indicates how many elderly people in total participated in the study.

[b] Mortality was an outcome measure in only some of the RCTs; these data are shown in bold in the table. The data on mortality from the RCTs in which mortality was not an outcome measure are shown in brackets and in italics in the table.

A3.4 Summary and consideration

In order to answer the Minister's question on what possible benefit there is from treatment of undernutrition, qualitatively good interventional research is necessary into the effects on clinically relevant outcome measures. A large proportion of the interventional studies included in the meta-analysis by Milne et al. however suffer from serious methodological deficiencies. Milne's findings that supplementation with extra protein and energy possibly reduces the risk of complications, that supplementation of undernourished elderly people possibly lowers the mortality risk, and that there are few indications for effects on functional parameters and on length of stay, are insufficiently justified. Side-effects were not studied in a systematic way. Additionally, only some of these trials were conducted in people with a moderate or poor nutritional status, while it is plausible that exactly this subgroup would benefit from supplementation.

The Committee therefore also looked at the picture that arises from the higher quality trials in undernourished elderly people in the meta-analysis from Milne et al., and relevant publications of more recent date. This resulted in a selection of twelve RCTs that are qualitatively better, but which still leave much to be desired regarding methodological quality. The results concerning mortality do not give a consistent picture. There are insufficient indications that giving extra protein and energy to undernourished elderly people leads to a reduction in the risk of complications. There are no indications for an effect of supplementation on the length of stay. As regards the other clinically relevant outcome measures, the number of RCTs and their size are too small to allow conclusions to be reached.

A3.5 Conclusion

The state of science about the effect of treatment of undernutrition in elderly people is very limited. Therefore the Committee can reach no conclusion about the health gain that may be achievable by giving extra protein and energy to undernourished elderly people. Indications that supplementation might reduce the probability of complications are inadequate. There are no indications for an effect on length of stay. Little is known about other clinically relevant effects such as mortality. The most important conclusion is that research of good quality and sufficient extent is needed. This applies to all settings (hospital, chronic care and elderly people living at home).

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