Undernutrition in community-dwelling older individuals

Recognition & treatment

Janneke Schilp

The studies presented in this thesis were conducted at the Department of Health Sciences and the EMGO+ Institute for Health and Care Research of the VU University in Amsterdam. The studies were part of the project 'Early recognition and treatment of undernutrition in primary care and home care' of the Dutch Malnutrition Steering Group. This project is funded by the Ministry of Health, Welfare, and Sports of the Netherlands. The study presented in Chapter 3 was supported by a grant from the Netherlands Organisation for Health Research and Development (ZonMw).

Financial support by the Dutch Malnutrition Steering Group and the VU University Amsterdam for the publication of this thesis is gratefully acknowledged.

Additional financial support for the printing of this thesis has been kindly provided by: Nutricia Advanced Medical Nutrition, Mediq Tefa and Nestlé Health Science.

Nederlandse titel:	Ondervoeding bij thuiswonende ouderen: herkenning & behandeling
Cover & layout:	Janneke Schilp
Printed by:	GVO drukkers & vormgevers B.V. | Ponsen & Looijen
ISBN:	978-90-6464-616-4

VRIJE UNIVERSITEIT

Undernutrition in community-dwelling older individuals

Recognition & treatment

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor aan
de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. L.M. Bouter,
in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de Faculteit der Aard- en Levenswetenschappen
op vrijdag 1 maart 2013 om 13.45 uur
in de aula van de universiteit,
De Boelelaan 1105

door

Janneke Schilp

geboren te Wageningen

promotor:	prof.dr.ir. M. Visser
copromotoren:	dr. H.M. Kruizenga
	dr. H.A.H. Wijnhoven

Contents

Contents

CHAPTER 1

General Introduction

Introduction

Life expectancy has extremely increased over the last century in most developed countries, resulting in an aging population. In the Netherlands, the number of individuals aged 65 years and older is expected to increase from 2.6 million in 2011 to approximately 4.5 million in 2050, which will be 25% of the total Dutch population. Undernutrition is a major health problem in the aging population, as the prevalence is increasing with age (1-6). In literature, the term undernutrition is often used interchangeably with malnutrition to describe the same concept. *Undernutrition* focuses on protein and energy deficiency and can be defined as "a disorder of nutritional status from reduced nutrient intake or impaired metabolism" (7). *Malnutrition* can be related to both undernutrition and overnutrition and is defined as "a state of nutrition in which a deficiency, excess or imbalance of energy, protein and other nutrients causes measurable adverse effects on tissue/body form (shape, size and composition) and function, and clinical outcome" (8). In this general term deficiencies on both macronutrient (fat, protein and carbohydrate) and micronutrients (vitamins and minerals) are included. This thesis focuses on protein and energy undernutrition and therefore, the term undernutrition will be used.

Assessment of undernutrition

There is no golden standard available to measure undernutrition. This makes the development and evaluation of measurement instruments difficult. Moreover, there is no consensus on the approach to measure undernutrition. The terms screening and assessment are both used to describe the measurement of undernutrition. Nutritional screening has been defined by the American Society for Parenteral and Enteral Nutrition (ASPEN) as "a process to identify an individual who is undernourished or who is at risk for undernutrition to determine if a detailed nutrition assessment is indicated"(9). Nutritional assessment has been defined by ASPEN as "a comprehensive approach to defining nutrition status that uses medical, nutrition, and medication histories; physical examination; anthropometric measurements; and laboratory data" (9). Due to the lack of a golden standard, a clear distinction between screening and assessment is complicated and the terms are often used interchangeably. Although it is recommended to perform an in depth nutritional assessment in those who are identified to be at nutritional risk by nutritional screening (10), in clinical practice treatment is often initiated after a positive screening.

Over the past decades, several instruments have been developed to assess (the risk of) undernutrition in older individuals (11). Most of these instruments were specifically developed for hospital patients or nursing home patients and many are poorly validated

(12). These instruments contain various measures and questions such as biochemical measures, dietary intake and use of dietary supplements, appetite, eating problems, functional ability, medical condition, social factors and anthropometric measures. To what extent these measures assess 'true' undernutrition or are markers of (an increased risk of) undernutrition is still unclear.

Low body mass index (BMI) is the most frequently used anthropometric measure included in nutritional assessment, as is unintentional weight loss. Although no clear consensus exists, the most recommended cut-off point for clinically relevant unintentional weight loss is 5% or more over 6 to 12 months (13, 14). The unintentional character of weight loss is important, since unintentional weight loss was shown to be associated with a statistically significant increase in mortality, whereas intentional weight loss had no effect on mortality (15). BMI is calculated by body weight (kg) divided by body height (m) squared. The World Health Organization defined normal body weight as BMI 18.5 to 25 kg/m^2, and underweight as BMI <18.5 kg/m^2 (16). However, in older individuals, a higher cut-off point is suggested to determine underweight. Recent studies have shown a cut-off point of 20 kg/m^2 to be the most reliable threshold to determine underweight in older individuals, based on the association with other anthropometric parameters and mortality (8, 17-19).

Assessing undernutrition in community-dwelling older individuals should easily and quickly be performed in a primary care office or in the home situation. BMI seems to not be the most feasible anthropometric measure in this setting and population (20). The measurement of body weight and height can be complicated due to the unavailability of calibrated equipment or the inability to stand. Furthermore, the measurement of body weight can be biased because of prostheses or the influence of edema. The measurement of body height in older individuals is often impeded by spinal deformities. In addition to these measurement problems, calculation of BMI is also difficult to perform without a device. Because of these drawbacks, alternative anthropometric measures for use in community-dwelling older individuals are required. Recently, a low mid-upper arm circumference (MUAC) was suggested as the preferred anthropometric measure for thinness, due to the stronger association with mortality compared to low BMI in community-dwelling older men and women (21).

Consequences of undernutrition

The presence of undernutrition is associated with several adverse consequences for both individuals and society. In general, undernutrition in older individuals is associated with an impaired immune function (22), a reduced functional status (23, 24), physical impairment

(25, 26) and a reduced quality of life (27, 28). These adverse clinical outcomes of undernutrition may lead to higher general practice consultation rates, higher medication prescription rates, higher hospitalization rates and increased mortality (29-32). Therefore, undernutrition is likely to contribute to higher health care costs (33). However, as these associations are based on observational studies, the causality of the associations cannot be established and confounding by (severity of) disease cannot totally be excluded, even after statistical adjustment.

Prevalence of undernutrition in the community

The prevalence of undernutrition depends on the setting and the characteristics of the study population. The prevalence rate is also influenced by the different criteria used for assessing undernutrition. In the Netherlands, the prevalence of undernutrition in the community is estimated in the annual Dutch National Prevalence Measurement of Care Problems (LPZ) and in the Longitudinal Aging Study Amsterdam (LASA) (12). The criteria for undernutrition used in these studies are shown in **Table 1**.

Table 1. Criteria for undernutrition used in LPZ and LASA studies.

Study	Criteria undernutrition
LPZ	• BMI ≤20 kg/m^2; or
	• unintentional weight loss >6 kg in previous 6 months or >3 kg in previous month; or
	• no nutritional intake for 3 days or reduced intake >10 days with BMI 20-23 kg/m^2
LASA	• BMI <20 kg/m^2; or
	• unintentional weight loss ≥5% in the last 6 months

LPZ, Dutch National Prevalence Measurement of Care Problems; LASA, Longitudinal Aging Study Amsterdam

The differences in prevalence rates calculated with these criteria in the two studies (**Table 2**) provides an example of the effect of using different criteria for undernutrition. The prevalence rates in individuals with or without home care are lower compared to the prevalence rate in nursing homes. However, because the large majority of the older population is living independently in the community, 95% in 2011 (34), the highest absolute number of undernourished individuals can be found in this setting. This is visualized in **Figure 1**, showing the approximated numbers of undernourished individuals in the community with and without home care and individuals living in nursing homes.

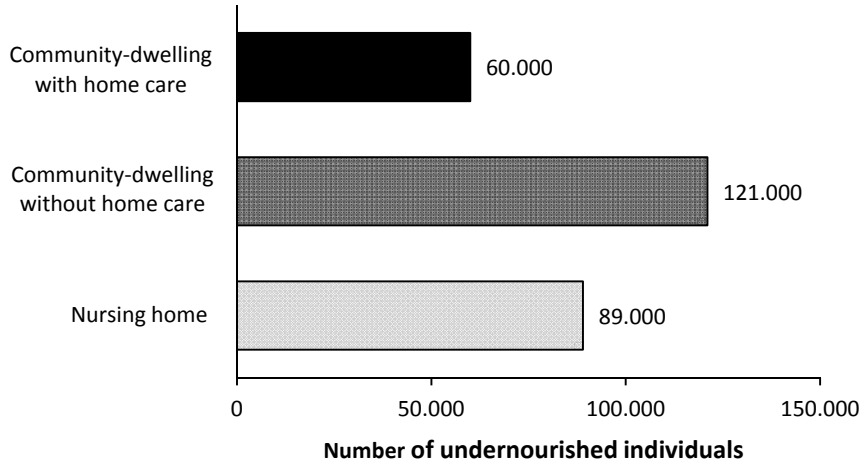
Table 2. Prevalence of undernutrition in the community and nursing homes based on the LPZ- and LASA-criteria for undernutrition.

	Prevalence	
Setting	**Criteria LPZ**	**Criteria LASA**
Community-dwelling with home care[a]	16%	12%
Community-dwelling without home care[b]	-	7%
Nursing home[a]	21%	18%

[a] The most recent available LPZ-data (2008-2010) was used to calculate the prevalence; [b] The most recent available LASA-data (2005-2006) was used to calculate the prevalence

These numbers are based on the prevalence rates calculated using the LASA-criteria for undernutrition and the most recent CBS data (2007) regarding the number of Dutch older individuals using home care and living in nursing homes (12, 35). Approximately 180.000 undernourished older individuals are living in the community. This number is even higher compared to another common problem in older individuals, osteoporosis, of which the number was approximated to be over 110.000 in 2007 (36). This high number of undernourished individuals living in the community emphasized the importance of recognition and treatment of undernutrition in this setting.

Figure 1. Approximation of absolute numbers of undernourished individuals in the community with or without home care and in nursing homes.[a]



[a] Based on the most recent CBS data about numbers using home care and numbers living in nursing homes (2007) and the prevalence rates of undernutrition based on LASA-criteria (Table 2)

Recognition of undernutrition in primary care

In 2010, the Dutch College of General Practitioners introduced the 'National Primary Care Cooperation Agreement Undernutrition' (in Dutch: Landelijke Eerstelijns Samenwerkings Afspraak; LESA) (37). This agreement encloses the collaboration of general practitioners (GPs), (district) nurses and dietitians in the recognition and treatment of undernutrition.

The central role of the GP is important in the (early) recognition of undernutrition in community-dwelling older individuals. The GP faces an increasing population at risk for undernutrition, as older individuals have a high mean consultation rate. Individuals aged 65 to 75 years old consult their GP on average 7 times a year and individuals aged 75 years and older even 9 times a year (38). Furthermore, the consultation rate is highest among those with multimorbidity (39).

The GP provides continuous general medical care and has an overview of the presence of multiple diseases, chronic conditions or use of multiple medications. The LESA recommends awareness for undernutrition in certain chronic diseases associated with undernutrition: COPD, CVA, decubitus, dementia, depression, heart failure, inflammatory bowel disease, malignancy and rheumatoid arthritis (37). Other conditions also need attention as they may be related with undernutrition, such as physical limitations, chewing or swallowing difficulties, recent hospital discharge and psychosocial difficulties.

In the home care setting, (district) nurses should also play a role in recognizing these risk conditions. Undernutrition or the risk of undernutrition should be determined using a validated screening instrument. The LESA recommends referral to the general practitioner and/or the dietitian in case of undernutrition, depending on the local situation and agreements. When a risk of undernutrition exist, recommendations in accordance with available protocols are provided and the dietitian is consulted if needed (37).

Treatment of undernutrition

Randomized controlled trials (RCTs) investigating the treatment of undernutrition are mostly focusing on the effects of oral nutrition supplements (ONS). A Cochrane meta-analysis in 2009 of these RCTs showed that supplementation of ONS results in body weight gain and a reduced mortality in undernourished older individuals (38). This suggests a causal association between undernutrition and mortality and the potential beneficial effect of a nutritional intervention in undernourished older individuals. However, the methodological quality of the studies included in this review was limited (12). More large, randomized controlled trials of high quality are needed to investigate opportunities for treatment of undernutrition in specifically defined patient groups. In addition,

investigating the effects of treatment will provide more insight in the causality of the relation between undernutrition and adverse health consequences.

Treatment of undernutrition in primary care

The effect of treating undernourished older individuals is rarely studied in a primary care setting. The few studies conducted in primary care focused on the effect of ONS (38). A statistically significant effect of ONS was shown on energy intake, body weight and number of falls, but not on functional measures in this setting (39-41). Even less attention has been given to the effect of increasing intake through individual support by a dietitian in older, community-dwelling individuals. Practice-based guidelines recommend improving nutritional intake via ordinary foods and beverages as a first step and only providing ONS if needed (42, 43). Increasing nutritional intake via ordinary foods and beverages has the advantage that it offers greater variety, is tailored to individual needs and preferences and may be associated with lower costs (44). Despite these advantages, the effect of dietetic treatment in the community was only studied in adult COPD outpatients, showing beneficial effects on nutritional intake, body weight and quality of life, but not on muscle strength (45).

Following the recommendations of the 'National Primary Care Cooperation Agreement Undernutrition', a dietetic treatment should be started to stabilize or rather improve nutritional status after recognition of undernutrition by a nurse or general practitioner. Dietitians will assess the nutritional needs and status, incorporating the level of physical activity. Subsequently, a nutrition intervention is developed together with the patient and potential informal caregivers. Depending on the severity of the individual situation, a choice will be made between an energy and protein-enriched diet, vitamin and mineral supplements, additional ONS or complete ONS/tube feeding. Until now, studies in primary care evaluating the effectiveness of dietetic treatment of older, undernourished individuals are lacking.

Outline of this thesis

The objective of this thesis is to investigate possibilities for the recognition and treatment of undernutrition in community-dwelling older individuals.

The overall aims of the work presented in this thesis are:

- To identify early determinants of undernutrition in an older community-dwelling population (**Chapter 2**).
- To develop and validate a fast and easy-to-apply set of criteria to determine (risk of) undernutrition in community-dwelling older individuals (**Chapter 3**).
- To determine the prevalence of undernutrition in older individuals in primary care and home care (**Chapter 4**).
- To evaluate the effectiveness (**Chapter 5**) and cost-effectiveness (**Chapter 6**) of a dietetic treatment in undernourished community-dwelling older individuals.
- To identify predictors of body weight loss in undernourished community-dwelling older individuals (**Chapter 7**).

Finally, the methods and results presented in this thesis and possible implications for future research will be discussed in **Chapter 8**.

References

1. Ferreira LS, do Amaral TF, de Fatima Nunes Marucci M, Costa Nascimento LF, Lebrao ML, de Oliveira Duarte YA. Undernutrition as a major risk factor for death among older Brazilian adults in the community-dwelling setting: SABE survey. Nutrition 2011;27:1017-22.
2. Halfens RJG, Meijers JMM, Du Moulin MFMT, Van Nie NC, Neyens JCL, Schols JMGA. Rapportage resultaten: Landelijke Prevalentiemeting Zorgproblemen (National Prevalence Measurement of Care Problems). Maastricht, the Netherlands: Maastricht University, 2010.
3. Johansson Y, Bachrach-Lindstrom M, Carstensen J, Ek AC. Malnutrition in a home-living older population: prevalence, incidence and risk factors. A prospective study. J Clin Nurs 2009;18:1354-64.
4. Margetts BM, Thompson RL, Elia M, Jackson AA. Prevalence of risk of undernutrition is associated with poor health status in older people in the UK. Eur J Clin Nutr 2003;57:69-74.
5. Newman AB, Yanez D, Harris T, Duxbury A, Enright PL, Fried LP. Weight change in old age and its association with mortality. J Am Geriatr Soc 2001;49:1309-18.
6. Perissinotto E, Pisent C, Sergi G, Grigoletto F. Anthropometric measurements in the elderly: age and gender differences. Br J Nutr 2002;87:177-86.
7. A.S.P.E.N. Standards for Nutrition Support: Hospitalized Patients. Nutr Clin Pract 1995;10:208-19.
8. Stratton RJ, Green CJ, Elia M. Disease-related malnutrition: an evidence-based approach to treatment. Wallingford, United Kingdom: CABI Publishing, 2003.
9. Teitelbaum D, Guenter P, Howell WH, Kochevar ME, Roth J, Seidner DL. Definition of terms, style, and conventions used in A.S.P.E.N. guidelines and standards. Nutr Clin Pract 2005;20:281-5.
10. Mueller C, Compher C, Ellen DM. A.S.P.E.N. clinical guidelines: Nutrition screening, assessment, and intervention in adults. JPEN J Parenter Enteral Nutr 2011;35:16-24.
11. Green SM, Watson R. Nutritional screening and assessment tools for older adults: literature review. J Adv Nurs 2006;54:477-90.
12. Health Council of the Netherlands. Malnutrition in the elderly. The Hague, 2011.
13. Wallace JI, Schwartz RS. Involuntary weight loss in elderly outpatients: recognition, etiologies, and treatment. Clin Geriatr Med 1997;13:717-35.
14. McMinn J, Steel C, Bowman A. Investigation and management of unintentional weight loss in older adults. BMJ 2011;342:d1732.
15. Harrington M, Gibson S, Cottrell RC. A review and meta-analysis of the effect of weight loss on all-cause mortality risk. Nutr Res Rev 2009;22:93-108.
16. World Health Organization. Obesity: Preventing and Managing the Global Epidemic. WHO Technical Report Series. Geneva: WHO, 1998.

17. Campillo B, Paillaud E, Uzan I, et al. Value of body mass index in the detection of severe malnutrition: influence of the pathology and changes in anthropometric parameters. Clin.Nutr. 2004;23:551-9.

18. Elia M. MAG screening tool and guidelines set to combat malnutrition. Guidelines in Practice 2001;4:41-50.

19. Sergi G, Perissinotto E, Pisent C, et al. An adequate threshold for body mass index to detect underweight condition in elderly persons: the Italian Longitudinal Study on Aging (ILSA). J Gerontol A Biol Sci Med Sci 2005;60:866-71.

20. Cook Z, Kirk S, Lawrenson S, Sandford S. Use of BMI in the assessment of undernutrition in older subjects: reflecting on practice. Proc.Nutr.Soc. 2005;64:313-7.

21. Wijnhoven HA, van Bokhorst-de van der Schueren MA, Heymans MW, et al. Low mid-upper arm circumference, calf circumference, and body mass index and mortality in older persons. J Gerontol A Biol Sci Med Sci 2010;65:1107-14.

22. Hudgens J, Langkamp-Henken B, Stechmiller JK, Herrlinger-Garcia KA, Nieves C, Jr. Immune function is impaired with a mini nutritional assessment score indicative of malnutrition in nursing home elders with pressure ulcers. JPEN J Parenter Enteral Nutr 2004;28:416-22.

23. Cereda E, Valzolgher L, Pedrolli C. Mini nutritional assessment is a good predictor of functional status in institutionalised elderly at risk of malnutrition. Clin Nutr 2008;27:700-5.

24. Salvi F, Giorgi R, Grilli A, et al. Mini Nutritional Assessment (short form) and functional decline in older patients admitted to an acute medical ward. Aging Clin Exp Res 2008;20:322-8.

25. Ferdous T, Cederholm T, Razzaque A, Wahlin A, Nahar Kabir Z. Nutritional status and self-reported and performance-based evaluation of physical function of elderly persons in rural Bangladesh. Scand J Public Health 2009;37:518-24.

26. Suominen M, Muurinen S, Routasalo P, et al. Malnutrition and associated factors among aged residents in all nursing homes in Helsinki. Eur J Clin Nutr 2005;59:578-83.

27. Keller HH, Ostbye T, Goy R. Nutritional risk predicts quality of life in elderly community-living Canadians. J Gerontol A Biol Sci Med Sci 2004;59:68-74.

28. Amarantos E, Martinez A, Dwyer J. Nutrition and quality of life in older adults. J Gerontol A Biol Sci Med Sci 2001;56 Spec No 2:54-64.

29. Corrada MM, Kawas CH, Mozaffar F, Paganini-Hill A. Association of body mass index and weight change with all-cause mortality in the elderly. Am J Epidemiol 2006;163:938-49.

30. Locher JL, Roth DL, Ritchie CS, et al. Body mass index, weight loss, and mortality in community-dwelling older adults. J Gerontol A Biol Sci Med Sci 2007;62:1389-92.

31. Martyn CN, Winter PD, Coles SJ, Edington J. Effect of nutritional status on use of health care resources by patients with chronic disease living in the community. Clin Nutr 1998;17:119-23.

32. Yang Y, Brown CJ, Burgio KL, et al. Undernutrition at baseline and health services utilization and mortality over a 1-year period in older adults receiving Medicare home health services. J Am Med Dir Assoc 2011;12:287-94.

33. Baumeister SE, Fischer B, Doring A, et al. The Geriatric Nutritional Risk Index predicts increased healthcare costs and hospitalization in a cohort of community-dwelling older adults: results from the MONICA/KORA Augsburg cohort study, 1994-2005. Nutrition 2011;27:534-42.

34. CBS Statline Netherlands. Elderly people live independently to increasingly older ages. http://www.cbs.nl. Accessed at 12 July 2011.

35. CBS Statline Netherlands. Health and care in figures. Den Haag, The Netherlands, 2009.

36. National Institute of Public Health and the Environment (RIVM). Prevalence and incidence to age and sex. http://www.nationaalkompas.nl. Accessed at 25 April 2012.

37. Van Avendonk MJ, Mensink PA, Drenthen AJ, van Binsbergen JJ. Primary care and public health a natural alliance? The introduction of the guidelines for obesity and undernutrition of the Dutch College of General Practitioners. Fam Pract 2012;29 Suppl 1:i31-i35.

38. Milne AC, Potter J, Vivanti A, Avenell A. Protein and energy supplementation in elderly people at risk from malnutrition. Cochrane Database Syst Rev 2009:CD003288.

39. Gray-Donald K, Payette H, Boutier V. Randomized clinical trial of nutritional supplementation shows little effect on functional status among free-living frail elderly. J Nutr 1995;125:2965-71.

40. Hampson G, Martin FC, Moffat K, et al. Effects of dietary improvement on bone metabolism in elderly underweight women with osteoporosis: a randomised controlled trial. Osteoporos Int 2003;14:750-6.

41. Payette H, Boutier V, Coulombe C, Gray-Donald K. Benefits of nutritional supplementation in free-living, frail, undernourished elderly people: a prospective randomized community trial. J Am Diet Assoc 2002;102:1088-95.

42. Manual of Dietetic Practice. 4rd Edition ed. London: Blackwell Publishing Ltd, 2007.

43. Dutch Malnutrition Steering Group. Guideline screening and treatment of undernutrition. Amsterdam, 2011.

44. Baldwin C, Parsons TJ. Dietary advice and nutritional supplements in the management of illness-related malnutrition: systematic review. Clin Nutr 2004;23:1267-79.

45. Weekes CE, Emery PW, Elia M. Dietary counselling and food fortification in stable COPD: a randomised trial. Thorax 2009;64:326-31.

CHAPTER 2

Early determinants for the development of undernutrition in an older general population - *Longitudinal Aging Study Amsterdam*

Janneke Schilp
Hanneke A.H. Wijnhoven
Dorly J.H. Deeg
Marjolein Visser

British Journal of Nutrition; 2011, 106 (5): 708-717

Abstract

Background. Undernutrition may be an important modifiable risk factor for poor clinical outcomes in older individuals. To achieve earlier detection or prevention of undernutrition, more information is needed about risk factors for the development of undernutrition in community-dwelling older individuals. The objective was to identify early determinants of incident undernutrition in a prospective population-based study.

Methods. Baseline data (1992 - 1993) on socioeconomic, psychological, medical, functional, lifestyle and social factors of 1120 participants aged 65 - 85 years of the Longitudinal Aging Study Amsterdam were used. Undernutrition, defined as a BMI <20 kg/m^2 or self-reported involuntary weight loss ≥5% in the last six months, was assessed every 3 years during a 9-year follow-up period. Cox proportional-hazards regression analysis was used to investigate the association between early determinants at baseline and incident undernutrition.

Results. In 9 years, 156 participants (13.9%) developed undernutrition. In univariate analyses, female sex, depressive symptoms, anxiety symptoms, multiple chronic diseases, high medication use (women), poor appetite, no alcohol use versus light alcohol use, loneliness, not having a partner, limitations in performing normal activities due to a health problem, low physical performance (participants aged <75 y) and reporting difficulties walking stairs (participants aged <75 y) were statistically significantly associated with incident undernutrition. In a multivariate model, poor appetite and reporting difficulties walking stairs (participants aged <75 y) remained early determinants.

Conclusion. The results of the present study can be used to identify subgroups of older individuals with increased risk of undernutrition and to identify modifiable determinants for the purpose of prevention of undernutrition.

Introduction

Undernutrition can be defined as a disorder of nutritional status resulting from reduced nutrient intake or impaired metabolism (1). There is increasing awareness that undernutrition may be an important modifiable (2) risk factor for poor clinical outcomes in older persons in developed countries (3-10). Associations are found with a reduced functional status (11, 12), physical impairment (13), reduced quality of life (3, 10), hospitalization and mortality (4, 6, 7).

In community-based populations prevalence rates range, depending on the study population and the used definition of undernutrition, from 2% diagnosed by a low albumin level (<35 mg/dL) (14), to 24% diagnosed by the Nutritional Screening Initiative (15). Previous research mainly focussed on examining the effects of treating undernutrition (2). Surprisingly, little to no attention is paid to prevention of undernutrition in community-dwelling older individuals. However, before prevention programs can be developed, information is needed on determinants for undernutrition so that high-risk groups and modifiable determinants can be identified.

Previous studies have identified several determinants for undernutrition in older individuals, such as older age (16, 17), depression (17-19), poor cognitive functioning (18), impaired physical functioning (5, 9, 18), difficulties with biting and chewing (9, 18), dementia (9), co-morbidity (5, 16, 20, 21), poor appetite (18, 21), vision problems (21) and stress (21). However, many of these studies were performed in institutionalized older individuals (9, 18, 19). Most importantly, most of these studies had a cross-sectional design (5, 9, 16, 18-21), whereby causality of an association cannot be established. Only one study among community-dwelling older individuals had a prospective design (17). However, the size of the study population was relatively small (*N* 579) and a limited number of determinants was examined in this study. For example, medication use, number of chronic diseases, appetite, alcohol use, education level and physical performance were not examined as determinants. Therefore, more longitudinal studies are needed in the community, regarding an extensive multidisciplinary set of determinants. The aim of this prospective study was to identify early determinants of incident undernutrition in a large population-based sample of men and women aged 65 - 85 years.

Subjects and methods

Subjects

Data were collected in the context of the Longitudinal Aging Study Amsterdam (LASA), an ongoing cohort study focusing on physical, emotional, cognitive and social functioning in an older population. A random sample of older individuals aged 55 - 85 years, stratified by age, sex, level of urbanization and expected 5-year mortality, was drawn from the population registers of eleven municipalities in areas in the west (Amsterdam and vicinity), northeast (Zwolle and vicinity) and south (Oss and vicinity) of the Netherlands. In total, 3107 participants were enrolled in the main baseline examination, conducted between September 1992 and September 1993. Follow-up examinations were performed every 3 years. At each examination, a general interview in the individual's home was followed after 4 - 6 weeks by a medical interview during which medical tests were performed. Participants also completed a self-administered questionnaire. Further information about the sampling and data-collection procedures have been described elsewhere in detail (22).

After exclusion of participants aged <65 years, the present study included 2141 participants aged ≥65 years who participated in the main baseline examination. Participants with missing data on BMI and/or self-reported weight change at baseline (*N* 454) and participants with missing data on BMI and/or self-reported weight change at any follow-up examination because they died (*N* 143) or dropped out of the study (*N* 100) were excluded. Participants who were undernourished at baseline (*N* 124) were excluded to be able to investigate incident undernutrition (see the section on Undernutrition below for the applied definition of undernutrition). The final study sample therefore consisted of 1120 participants: 543 men and 577 women.

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Medical Ethics Committee of the VU University Medical Center (Amsterdam, The Netherlands). Written informed consent was obtained from all participants.

Undernutrition

Body height and weight were measured during the medical interview in a standing position wearing light indoor clothing without shoes. A wall-mounted stadiometer was used to measure height to the nearest mm. If no accurate measurement of height could be obtained (*N* 71; 6.3%) due to the recorded particularities 'not able to stand', 'shoes', 'kyphosis', 'scoliosis', or 'unknown reasons, height was imputed by either: 1) a valid follow-up measurement of height (*N* 55); or 2) a sex-specific prediction rule based on age

and knee height (*N* 15) (23); or 3) self-reported height (*N* 1). Knee height of the left leg was measured with a Mediform sliding caliper (Medical Express, Beaverton, OR, USA) with the knee and ankle joints fixed at 90° angles. Height at baseline was used in the calculation of BMI at follow-up examinations, because height may decrease over time due to spinal deformities. Body weight was measured to the nearest 0.1 kg using a standard balance beam scale. In deviating situations adjustments were made for clothing (-1 kg), corset (-1 kg) and shoes (-1 kg) (24). In all medical interviews a self-reported weight has been obtained, which was used when no measured weight was available (seven, six and five participants, respectively at baseline, 3-, 6- and 9-year follow up). BMI was calculated as body weight (kg) divided by height (m) squared. Weight change in the last 6 months was assessed by asking the following questions: 'Did your weight change in the last 6 months?'. Furthermore, the amount of weight change (kg) and the reason for weight change were asked. Involuntary weight loss was defined as weight loss due to disease, loss of appetite, (psycho)social factors or 'unknown reasons'. Undernutrition was defined as either a BMI <20 kg/m^2 or self-reported involuntary weight loss ≥5% in the last 6 months (25). This definition was applied to determine both undernutrition at baseline (these participants were excluded) as well as incident undernutrition.

Determinants of undernutrition

All information of determinants were obtained at baseline during the general interview (*N* 1120), except for medication use which was assessed during the medical interview (*N* 1113) and self reported pain and problems with biting and chewing which were assessed in the self-administered questionnaire (*N* 936).

Socioeconomic factors

Education level was categorized into high (university, college and higher vocational education), medium (general secondary, intermediate vocational, general intermediate and lower vocational education) and low education (elementary education or elementary education not completed). Monthly household income was categorized into tertiles: high (≥1035 euro), medium (625 - 1035 euro), low (<625 euro) and missing. If the participant had a partner living in the household, income was multiplied by 0.7 (26).

Psychological factors

Cognitive functioning was measured with the Mini-Mental State Examination (MMSE), with scores ranging from 0 to 30 (27), whereby scores ≤23 were defined as a poor

cognitive status (28). Depression was measured with the Dutch translation of the Center for Epidemiologic Studies Depression scale, with scores ranging from 0 to 60 (29). Scores ≥16 were defined as depression (30). Anxiety was measured with the anxiety subscale of the Hospital Anxiety and Depression Scale, with scores ranging from 0 to 21 (31). The cut-off point ≥7 was used to determine anxiety disorders (32).

Medical factors

The presence of chronic diseases was determined by explicitly asking the participants whether they had any of the following diseases: cardiac diseases (including myocardial infarction), peripheral artherosclerosis, stroke, diabetes mellitus, obstructive lung disease (asthma, chronic bronchitis or pulmonary emphysema), arthritis (rheumatoid arthritis or osteoarthritis) or cancer. The accuracy of self-report data for these diseases as compared with general practitioners' information was shown to be adequate (33). To define co-morbidity three categories were created: no chronic disease; one chronic disease; and two or more chronic diseases. Medication use was determined by having the interviewer check the containers of drugs that the respondent was taking, with or without prescription, and three categories were created: no medication use; use of one or two medications, and use of three or more medications. Appetite during the last week was assessed with the following question from the Dutch translation of the Center for Epidemiologic Studies Depression Scale (29): 'I did not feel like eating; my appetite was poor', with answering categories: 1) 'rarely or none of the time'; 2) 'some or little of the time'; 3) 'occasionally or moderate amount of the time'; and 4) 'most or all of the time'. For appetite two categories were created: no problems with appetite (answer 1) and poor appetite last week (answer 2-4). Subjective pain was determined asking five questions from a subscale of the Nottingham Health Profile (34). Sum scores were calculated and divided into no pain (score 5), pain (score 6 - 10), and missing. Problems with biting and chewing were assessed by asking 'Are you able to bite or chew hard food?'. Participants answering 'almost never', or 'some of the time', were categorized as having no problem, and those answering 'often' or 'most of the time' as having problems. A third category for missing values was made.

Functional factors

Visual impairment, with glasses or contact lenses if needed, was ascertained by two items: 1) read the fine print in a newspaper and 2) recognize a face at 4 m distance. Hearing impairment, with hearing aid if needed, was ascertained by two items: 1) follow a

conversation with one individual and 2) follow a conversation in a group of four individuals. For visual and hearing impairment two categories were created: 'none' and 'one or two items with some difficulty'. Limitation of normal activities due to a health problem was assessed by asking 'Are health problems limiting your normal daily activity?'. Participants answering 'yes, severely' and 'yes, mild' were categorized as having limitations and those answering 'no' as not having limitations. Physical performance was measured with three standardized performance tests: chair stands, tandem stand and walk test, each with scores ranging from 0 to 4. Scores on the three tests were summed, resulting in a total score ranging from 0 (poor performance) to 12 (35). Difficulties walking stairs was assessed by the question 'Can you climb up and down a staircase of 15 steps without stopping?' with answering categories 1) 'yes'; 2) 'yes, with difficulty'; 3) 'not able without help'; and 4) 'cannot'. For difficulty walking stairs two categories were created: no difficulties (answer 1) and difficulties (answer 2 - 4) (36).

Lifestyle factors

Smoking status was categorized into: current smoker; former smoker; never smoker; and missing. Former smokers who stopped smoking more than 15 years ago were classified as never smoker (37). Alcohol use was based on the number of days per month drinking alcohol and the number of alcohol consumptions each time. Four categories were created: no alcohol; light; moderate; and (very) excessive alcohol use (38). Physical activity in the previous two weeks was assessed using the validated Longitudinal Aging Study Amsterdam (LASA) Physical Activity Questionnaire (LAPAQ) (39), whereby information on the frequency and duration of walking, bicycling, household activities, and sport activities was obtained. Total physical activity was expressed in min per d.

Social factors

Loneliness was measured with a Dutch validated loneliness scale (40). The scale consisted of eleven items, with three possible answers: 0) 'no'; 1) 'more or less'; and 2) 'yes'. We used a cut-off score of ≥3, as applied by others (41), to identify participants suffering from loneliness. Individuals without a partner inside or outside the household were defined as not having a partner. Type of housing was observed at the main interview, whereby a distinction was made between independent living, including those who receive home care, and not independent living, including institutionalized participants.

Statistical analyses

At 3, 6, and 9 years' follow-up, the incidence of undernutrition was determined according to the definition described earlier. Baseline characteristics of the group developing undernutrition and the group not developing undernutrition were compared using the Chi square test for dichotomous and categorical variables and the independent-samples *t* tests for continuous variables. Time to event was defined as the number of days between the baseline examination and the first follow-up examination where undernutrition was diagnosed. Follow-up time of censored participants was calculated using the date of the 9-year follow-up examination, the date of the last follow-up examination or the date of death, whichever came first.

Cox proportional-hazards regression analysis was used to investigate the association between potential determinants of undernutrition at baseline and the incidence of undernutrition during a 9-year follow-up period. To investigate the proportional hazard assumption, log(-log(survival)) curves of categorical determinants were visually inspected and for continuous variables a time interaction test was performed, with statistical significance based on a *P* value < 0.01. Effect modification by age and sex was examined by adding interaction terms to the univariate regression model. In case of a statistically significant interaction ($P < 0.05$), associations were presented stratified by age (<75 years and ≥75 years) and/or sex. The linearity of the association between each continuous covariate and undernutrition was checked by adding a quadratic term to the model.

All determinants that were found to be statistically significantly associated with the development of undernutrition in the univariate analyses were included in a multivariate model. Multicollinearity diagnostics (with linear regression analysis) were used to identify possible linear dependencies among determinants. In case of a variance inflation factor value above 10 (42), one of the involved determinants was removed from the multivariate analysis. In the case of a statistical significant interaction ($P < 0.05$) between a covariate and age and/or sex in the univariate model, interaction terms were added for these covariates in the multivariate model as well. Results were presented as hazard ratios with 95% CI. Two-sided *P* values of 0.05 were considered statistically significant. Analyses were performed using SPSS software (version 15.0; SPSS, Inc, Chicago, IL, USA).

Results

The baseline characteristics of the study sample are presented in **Table 1**. During the 9-year follow-up period (mean follow-up 7.1 (SD 2.2) years) 156 out of 1120 participants (13.9%) developed undernutrition. Of these, 114 participants (73.1%) met the criterion '≥5% self-reported involuntary weight loss in the last 6 months during any of the follow-up examinations', thirty participants (19.2%) met the criterion 'BMI <20 kg/m^2 during any of the follow-up examinations' and twelve participants (7.7%) met both criteria. Of the participants developing undernutrition, fifty-three died before the end of the 9-year follow-up. At the 3- and 6-year follow-ups the cumulative incidences of undernutrition were 6.5 and 11.4% respectively. A total of 281 participants (25.1%) died during the follow-up without a prior classification of undernutrition.

The univariate and multivariate associations between potential determinants and incident undernutrition are shown in **Table 2**. For all analyses, the proportional hazard assumption was valid.

The following sociodemographic and lifestyle factors were found to be associated (P < 0.05) with the risk of developing undernutrition in the univariate analyses: female sex; no alcohol use versus light alcohol use; loneliness and not having a partner. The following psychological, medical and functional factors were identified (P < 0.05): depressive symptoms; anxiety symptoms; presence of two or more chronic diseases versus no chronic diseases; poor appetite; experiencing limitations in performing normal activities due to a health problem; use of three or more medications (women only) versus no medication; low physical performance test score (age <75 year only) and reporting difficulties walking stairs (age <75 year only) versus reporting no difficulties. Using one or two medications versus no medication use was associated with a reduced risk of developing undernutrition in men.

Table 1. Baseline characteristics of the study sample.

	All (*N* 1120)		Undernutrition (*N* 156)[a]		No undernutrition (*N* 964)[b]		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	***P***
Demographic factors							
Female (%)	51.5		60.3		50.1		0.02
Age (y)	74.1	5.7	74.2	6.0	74.1	5.7	0.77
Socioeconomic factors							
Education							
Low (%)	43.2		47.4		42.5		0.46
Medium (%)	45.5		41.0		46.3		
High (%)	11.3		11.5		11.2		
Income in euro							
Low (%)	27.4		28.2		27.3		0.98
Medium (%)	37.3		37.8		37.2		
High (%)	23.7		22.4		23.9		
Missing (%)	11.6		11.5		11.6		
Psychological factors							
Poor cognitive status (MMSE≤23) (%)	7.9		6.5		8.1		0.48
Depressive symptoms (CES-D≥16) (%)	11.7		19.2		10.4		<0.01
Anxiety symptoms (HADS≥7) (%)	9.0		13.8		8.3		0.03
Medical factors							
Number of chronic diseases							
No chronic disease (%)	22.6		15.5		23.7		<0.01
One chronic disease (%)	37.8		32.9		38.6		
Two or more chronic diseases (%)	39.6		51.6		37.7		
Medication use							
No medication (%)	31.8		27.9		32.4		<0.01
One or two medications (%)	36.3		26.0		38.0		
Three or more medications (%)	31.9		46.1		29.6		
Poor appetite (%)	10.9		17.9		9.8		<0.01
Pain							
No pain (%)	52.2		48.1		52.9		0.48
Pain (%)	22.5		25.6		22.0		
Missing (%)	25.3		26.3		25.1		

Table 1. Continued

	All (*N* 1120)		Undernutrition (*N* 156)[a]		No undernutrition (*N* 964)[b]		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	***P***
Problems with biting and chewing							
Never or some of the time (%)	27.1		30.1		26.7		0.63
Often or most of the time (%)	53.2		51.9		53.4		
Missing (%)	19.6		17.9		19.9		
Functional factors							
Vision problems (%)	17.7		17.1		17.8		0.84
Hearing problems (%)	15.2		17.1		14.8		0.47
Limitation of normal activities due to a health problem (%)	28.8		39.7		27.0		<0.01
Physical performance test (0-12)	7.0	2.6	6.7	2.5	7.0	2.6	0.10
Difficulties walking stairs (%)	26.2		35.5		24.7		<0.01
Lifestyle factors							
BMI (kg/m^2)	27.2	3.9	26.4	4.5	27.3	3.8	<0.01
Smoking							
Never (%)	64.3		66.7		64.0		0.58
Former (%)	14.9		12.2		15.4		
Current (%)	20.7		21.2		20.7		
Alcohol use							
No alcohol use (%)	22.4		28.4		21.4		0.13
Light (%)	53.7		45.8		55.0		
Moderate (%)	20.5		21.3		20.4		
(Very) excessive (%)	3.4		4.5		3.2		
Physical activity (min/d)	161.5	192.6	146.3	117.0	164.0	202.1	0.12
Social factors							
Loneliness (score ≥3) (%)	30.1		36.6		29.1		0.06
Having a partner (%)	64.0		53.8		65.6		0.01
Living independent (%)	97.9		99.4		97.6		0.16

MMSE, Mini-Mental State Examination; CES-D, Center for Epidemiologic Studies Depression scale; HADS, Hospital Anxiety and Depression Scale

[a] Participants developing undernutrition during the 9-year follow up; [b] Participants not developing undernutrition during the 9-year follow up

Table 2. Associations of socio-economic, lifestyle, social, psychological, medical and functional factors at baseline and 9-year incident undernutrition

	N[a]	Univariate model HR (95% CI)	Multivariate model HR (95% CI)
Female	1120	1.40 (1.01-1.92)	0.73 (0.38-1.39)
Age			
<75 y	625	1	1
≥75 y	495	1.30 (0.95-1.79)	0.88 (0.29-2.63)
Education			
Low	484	1	
Medium	510	0.78 (0.56-1.09)	
High	126	0.94 (0.56-1.58)	
Income in euro			
Low	307	1	
Medium	418	0.98 (0.66-1.44)	
High	265	0.89 (0.57-1.39)	
Missing	130	0.93 (0.54-1.62)	
Poor cognitive status	1116	0.94 (0.49-1.78)	
Depressive symptoms (yes vs. no)	1112	1.96 (1.32-2.93)	0.89 (0.52-1.52)
Anxiety symptoms (yes vs. no)	1094	1.75 (1.11-2.78)	1.26 (0.72-2.21)
Number of chronic diseases			
No chronic disease	252	1	1
One chronic disease	422	1.23 (0.76-2.00)	1.10 (0.64-1.88)
Two or more chronic diseases	442	2.08 (1.31-3.28)	1.32 (0.75-2.33)
Medication use			
No medication	354	1	1
One or two medications, male	195	0.47 (0.23-0.95)[b]	1.10 (0.60-2.02)[b]
One or two medications, female	209	0.36 (0.76-2.41)[b]	0.39 (0.18-0.83)[b]
Three or more medications, male	154	1.51 (0.86-2.66)	1.80 (0.99-3.27)
Three or more medications, female	201	2.57 (1.50-4.38)	1.03 (0.54-1.96)
Poor appetite	1119	1.99 (1.32-3.00)	1.63 (1.02-2.61)
Pain			
No pain	585	1	
Pain, male	100	1.29 (0.70-2.37)	
Pain, female	152	1.37 (0.82-2.27)	
Missing, male	109	0.62 (0.29-1.33)[b]	
Missing, female	174	1.62 (1.01-2.61)[b]	

Table 2. Continued

	N[a]	Univariate model HR (95% CI)	Multivariate model HR (95% CI)
Problems with biting and chewing			
Never or some of the time	304	1	
Often or most of the time	596	1.81 (0.57-1.16)	
Missing	220	0.83 (0.52-1.32)	
Vision problems (yes vs. no)	1096	1.00 (0.65-1.52)	
Hearing problems (yes vs. no)	1095	1.42 (0.93-2.16)	
Limitation of normal activities due to a health problem	1118	1.76 (1.28-2.43)	1.20 (0.81-1.77)
Physical performance test score, age <75 y	601	0.89 (0.81-0.96)[c]	0.98 (0.89-1.08)
Physical performance test score, age ≥75 y	475	1.01 (0.92-1.11)[c]	1.06 (0.95-1.18)
Difficulties walking stairs			
No difficulties walking stairs	824	1	1
Difficulties walking stairs, age <75 y	115	2.50 (1.59-3.91)[c]	1.91 (1.14-3.22)[c]
Difficulties walking stairs, age ≥75 y	177	1.08 (0.67-1.75)[c]	0.88 (0.51-1.50)[c]
Smoking			
Never	720	1	
Former	167	0.82 (0.50-1.33)	
Current	232	1.08 (0.73-1.61)	
Alcohol use			
No alcohol use	249	1	1
Light	598	0.67 (0.46-0.98)	0.82 (0.55-1.96)
Moderate	228	0.82 (0.52-1.30)	1.11 (0.67-1.83)
(Very) excessive	38	1.16 (0.52-2.58)	1.42 (0.58-3.46)
Physical activity	1120	0.99 (0.997-1.000)	
Loneliness (yes vs. no)	1105	1.47 (1.06-2.04)	1.11 (0.75-1.64)
Having a partner (no vs. yes)	1118	1.70 (1.24-2.33)	1.37 (0.92-2.02)
Living independent (no vs. yes)	1120	3.13 (0.44-22.33)	

[a] Number of participants for the categories of the determinants in which the univariate analyses were performed; [b] Statistically significant interaction with sex ($P < 0.05$); [c] Statistically significant interaction with age ($P < 0.05$)

Because no multicollinearity was found, all statistically significant determinants of the univariate analyses were included in a multivariate model. Interaction terms were tested for medication use X sex, physical performance test score X age, and reporting difficulties walking stairs X age. The interaction terms of sex X using one or two medications (and not

using three or more medications) and age X reporting difficulties walking stairs were statistically significant in the multivariate model ($P < 0.05$). Poor appetite and reporting difficulties walking stairs were the only determinants that statistically significantly increased the risk of developing undernutrition in the multivariate model. Thereby, reporting difficulties walking stairs increased the risk only in participants <75 years. Using one or two medications statistically significantly decreased the risk compared with using no medication in women. In men no statistical significance was found for medication use.

An additional analysis was performed to investigate whether poor appetite could be seen as an intermediate risk factor for undernutrition. For example, depression, chronic disease or medication use might lead to undernutrition (partly) through a poor appetite. We therefore repeated the multivariate model, excluding the variable poor appetite. The results are presented in **Table 3** and show that even after exclusion of poor appetite these factors are not associated with incident undernutrition in the multivariate model.

Table 3. Associations of depressive symptoms, chronic disease and medication use at baseline and 9-year incident undernutrition (multivariate analysis)[a]

	HR	**95% CI**
Depressive symptoms (yes vs. no)	0.99	0.58-1.66
Number of chronic diseases		
No chronic disease	1	Reference
One chronic disease	1.11	0.65-1.91
Two or more chronic diseases	1.30	0.74-2.29
Medication use		
No medication	1	Reference
One or two medications, male	0.39*	0.18-0.83
One or two medications, female	1.08*	0.59-1.98
Three or more medications, male	1.05	0.55-1.99
Three or more medications, female	1.75	0.96-3.20

[a] Adjusted for all statistically significant determinants of the univariate model, except appetite (sex, depressive symptoms, anxiety symptoms, number of chronic diseases, medication use, loneliness, not having a partner, limitations in performing normal activities due to a health problem, low physical performance test score and reporting difficulties walking stairs)

*Statistically significant interaction with sex ($P < 0.05$)

Figure 1 shows the cumulative incidence of undernutrition according to those with a normal appetite and those with a poor appetite. **Figure 2** shows the cumulative incidence of undernutrition for those who reported no difficulties walking stairs and those who did report difficulties walking stairs, stratified for age.

Figure 1. Cumulative hazard of incident undernutrition according to appetite at baseline, adjusted for the variables included in the multivariate model (see Table 2).

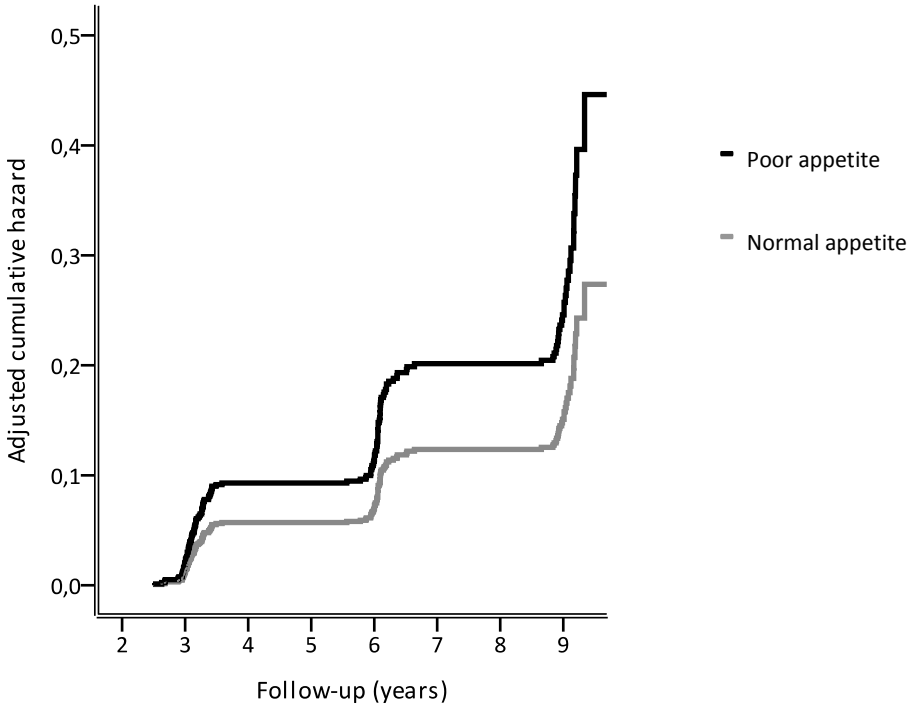
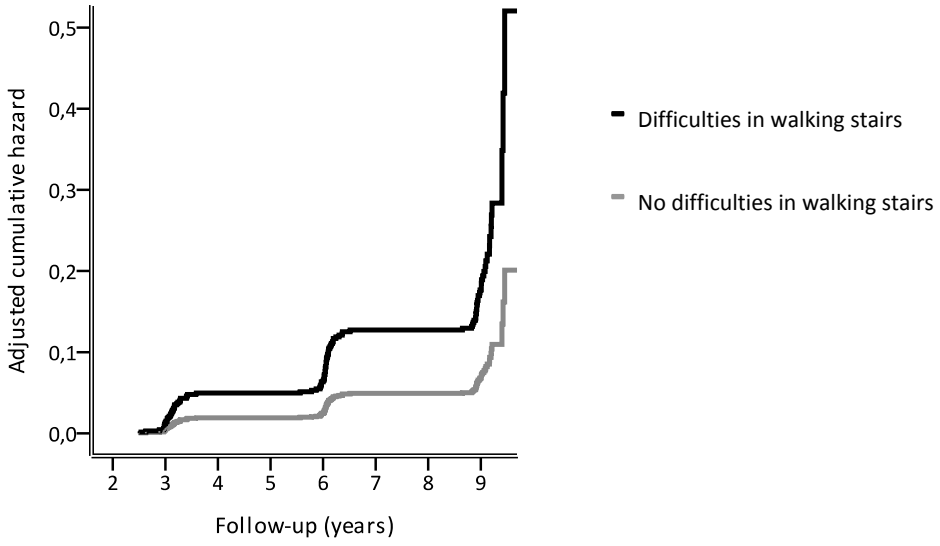
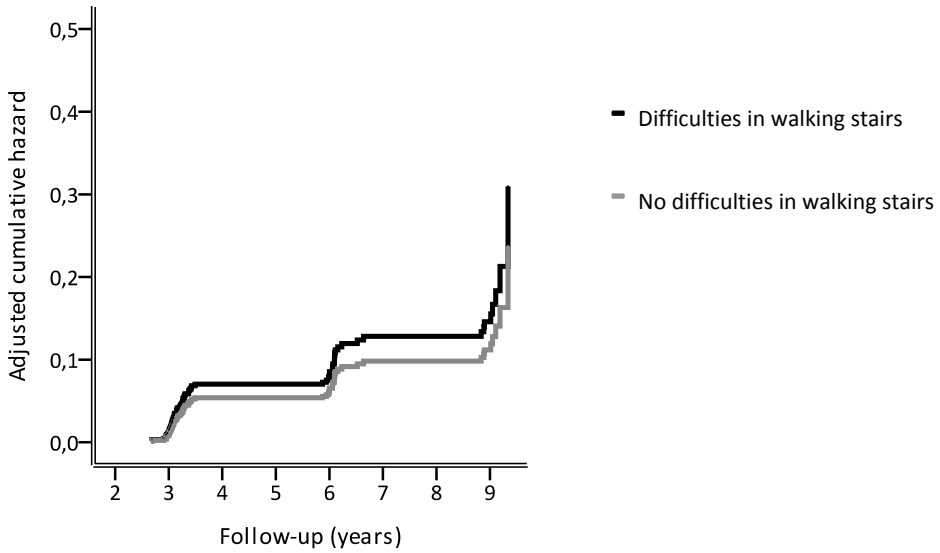


Figure 2. Cumulative hazard of incident undernutrition according to reporting of difficulties walking stairs at baseline in those under 75 years (a) and in those aged 75 years or older (b), adjusted for the variables included in the multivariate model (see Table 2).

(a)



(b)



Discussion

To our knowledge, this is the first prospective study to investigate early determinants of incident undernutrition from a large multidisciplinary set of variables in community-dwelling older individuals. The 9-year incidence of undernutrition in this population-based sample of men and women aged 65 to 85 years was 13.9%. Our multi-disciplinary approach showed that several determinants were statistically significantly associated with an increased risk of developing undernutrition in univariate analyses, including: female sex, depressive symptoms, anxiety symptoms, having two or more chronic diseases, using three or more medication (women only), poor appetite, experiencing limitations in performing normal activities due to a health problem, low physical performance test score (participants aged <75 years only), reporting difficulties walking stairs (participants aged <75 years only), loneliness and not having a partner. Light alcohol use, compared with no alcohol use, statistically significantly decreased the risk of developing undernutrition. In the multivariate analysis, poor appetite and reporting difficulties walking stairs (participants aged <75 years) were the only remaining statistically significant determinants that increased the risk of incident undernutrition. Furthermore, light medication use decreased the risk of undernutrition in women.

The associations between most of these determinants and undernutrition have been suggested based on previous cross-sectional studies, but have not been confirmed in a prospective study among community-living older individuals. A cross-sectional relation between poor functional status and prevalent undernutrition (as assessed by the Mini Nutritional Assessment) in older individuals was previously reported for hospital patients (18), nursing home patients (9) and community-dwelling individuals (5). In the present study, function-related factors were statistically significantly associated with incident undernutrition in univariate analyses in the group aged 65 - 75 years. The oldest group (≥75 years) reported more functional limitations walking stairs compared with the youngest group (65 - 75 years), 36 compared with 18%. The oldest group also had a lower physical performance test score (mean 6.1 (SD 2.5)) compared with the youngest group (mean 7.7 (SD 2.5)). Although poor functional status is more prevalent at higher ages, only when they occur at an earlier age they seem to be associated with the development of undernutrition. In the present study, the strongest early functional determinant of incident undernutrition was reporting difficulties walking stairs, independent of health status.

An earlier prospective study of Johansson et al. (17) reported associations between older age and depressive symptoms (assessed with the Geriatric Depression Scale) and incident risk of undernutrition (as assessed by the Mini Nutritional Assessment), which were

comparable with the present results in the univariate analyses. In the multivariate analyses, these associations became statistically insignificant in the present study but remained statistically significant in the study of Johansson et al (17). This may be explained by the fact that we adjusted for a wider range of covariates. Furthermore, in the study of Johansson et al. (17) lower self-perceived health predicted incident risk of undernutrition, but this could not be replicated in the present study. This can be explained by the fact that our used definition of undernutrition does not include questions directly related to poorer health status like the Mini Nutritional Assessment does.

Following the strong association between poor appetite and incident undernutrition in our study, it is remarkable that only a few earlier studies have investigated this association. The cross-sectional association between appetite and prevalent undernutrition was found in hospital patients (18) and in home-care patients where poor appetite was independently associated with lower energy and protein intakes (21). Some determinants that were found to be associated with prevalent undernutrition in earlier cross-sectional studies, such as cognitive problems (18), difficulties with biting and chewing (9, 18) and vision problems (21), were not confirmed in our prospective study. These results may suggest that these determinants are associated with present undernutrition but do not predict the development of undernutrition over time. An alternative explanation could be that the prevalence and/or severity of these problems is lower in community-dwelling individuals and that these problems will only have an impact on nutritional status in institutionalized patients (18, 21). The present study also identified other determinants of undernutrition that have not yet been studied (43). For example, participants with anxiety had an increased risk of developing undernutrition.

In the present study, a decreased risk of incident undernutrition was found for light alcohol use compared with no alcohol use. Previous studies have shown that light alcohol use reduces morbidity and mortality (44, 45). The beneficial effect of light alcohol consumption on morbidity and mortality could be partly explained by the high energy content of alcoholic drinks, which may influence the risk of developing undernutrition.

Using one or two medications compared to no medication use seems to be protective for the development of undernutrition in the present study. A clarification for this apparently controversial outcome could be that single medication-users probably more often use preventive medication, which may have a beneficial effect on health. Furthermore, participants using one or two medications could be more ‘healthy minded’ compared with non-users.

An important strength of the present study is the unique substantial multidisciplinary set of factors that could be included to examine their association with the development of

undernutrition, ranging from social factors to psychological and medical factors. Another strength of the present study is the use of a definition of undernutrition that was confirmed in recent literature to be an appropriate definition in community-dwelling older individuals (46-48). In this definition self-reported weight change is used to investigate weight loss. A study among 4716 men aged 57 - 78 years showed that self-reported weight change corresponded well with changes in measured weight (49). Furthermore, in contrast to many other studies, a distinction was made between involuntary and voluntary weight loss in the present study to determine undernutrition. This is important, because individuals with involuntary weight loss have different characteristics and health outcomes compared with individuals with voluntary weight loss (49).

There are some limitations of this study. First, following the design of our cohort study, we only had measurements of undernutrition at 3-year intervals. Undernutrition can develop rapidly, for example, in the case of acute disease (50). It is possible that some participants developed undernutrition in between two examinations and were censored because they died. Participants could also be recovered from undernutrition before a follow-up measurement took place. This limitation probably resulted in an underestimation of the cumulative incidence of undernutrition in the present study. Furthermore, some potential determinants could not be investigated because they were not assessed in the study, such as difficulties with shopping or cooking, taste and smell problems or low nutritional intake, which are mentioned in earlier reviews to be associated with undernutrition (43, 46, 50, 51). Future prospective studies are needed to confirm and extend our findings.

The present prospective study provides insight into the factors that could contribute to the development of undernutrition. We conclude that several socio-economic, psychological, medical, functional, lifestyle and social factors were associated with the future development of undernutrition in community-dwelling older individuals. In multivariate analyses, only a poor appetite and reporting difficulties walking stairs (aged <75 years) remained in the model as determinants of undernutrition. Both determinants can easily be assessed by simple questions and are therefore useful in screening and early recognition of community-dwelling older individuals at risk of undernutrition. Other determinants found in the univariate models may be underlying factors of a poor appetite and difficulties walking stairs and may therefore help to target preventive interventions.

References

1. A.S.P.E.N. Standards for Nutrition Support: Hospitalized Patients. Nutr Clin Pract 1995;10:208-219.
2. Milne AC, Potter J, Vivanti A, Avenell A. Protein and energy supplementation in elderly people at risk from malnutrition. Cochrane Database Syst Rev 2009:CD003288.
3. Amarantos E, Martinez A, Dwyer J. Nutrition and quality of life in older adults. J Gerontol A Biol Sci Med Sci 2001;56 Spec No 2:54-64.
4. Corrada MM, Kawas CH, Mozaffar F, Paganini-Hill A. Association of body mass index and weight change with all-cause mortality in the elderly. Am J Epidemiol 2006;163:938-49.
5. Han Y, Li S, Zheng Y. Predictors of nutritional status among community-dwelling older adults in Wuhan, China. Public Health Nutr 2008:1-8.
6. Knudtson MD, Klein BE, Klein R, Shankar A. Associations with weight loss and subsequent mortality risk. Ann Epidemiol 2005;15:483-91.
7. Locher JL, Roth DL, Ritchie CS, et al. Body mass index, weight loss, and mortality in community-dwelling older adults. J Gerontol A Biol Sci Med Sci 2007;62:1389-92.
8. Newman AB, Yanez D, Harris T, Duxbury A, Enright PL, Fried LP. Weight change in old age and its association with mortality. J Am Geriatr Soc 2001;49:1309-18.
9. Suominen M, Muurinen S, Routasalo P, et al. Malnutrition and associated factors among aged residents in all nursing homes in Helsinki. Eur J Clin Nutr 2005;59:78-583.
10. Thomas DR. The critical link between health-related quality of life and age-related changes in physical activity and nutrition. J Gerontol A Biol Sci Med Sci 2001;56:599-602.
11. Cereda E, Valzolgher L, Pedrolli C. Mini nutritional assessment is a good predictor of functional status in institutionalised elderly at risk of malnutrition. Clin Nutr 2008;27:700-5.
12. Salvi F, Giorgi R, Grilli A, et al. Mini Nutritional Assessment (short form) and functional decline in older patients admitted to an acute medical ward. Aging Clin Exp Res 2008;20:322-8.
13. Ferdous T, Cederholm T, Razzaque A, Wahlin A, Nahar Kabir Z. Nutritional status and self-reported and performance-based evaluation of physical function of elderly persons in rural Bangladesh. Scand J Public Health 2009;37:518-24.
14. Dirren H, Decarli B, Lesourd B, Schlienger JL, Deslypere JP, Kiepurski A. Nutritional status: haematology and albumin. Euronut SENECA investigators. Eur J Clin Nutr 1991;45 Suppl 3:43-52.
15. Marshall JA, Lopez TK, Shetterly SM, et al. Indicators of nutritional risk in a rural elderly Hispanic and non-Hispanic white population: San Luis Valley Health and Aging Study. J Am Diet Assoc 1999;99:315-22.
16. Margetts BM, Thompson RL, Elia M, Jackson AA. Prevalence of risk of undernutrition is associated with poor health status in older people in the UK. Eur J Clin Nutr 2003;57:69-74.

17. Johansson Y, Bachrach-Lindstrom M, Carstensen J, Ek AC. Malnutrition in a home-living older population: prevalence, incidence and risk factors. A prospective study. J Clin Nurs 2009;18:1354-64.

18. Feldblum I, German L, Castel H, et al. Characteristics of undernourished older medical patients and the identification of predictors for undernutrition status. Nutr J 2007;6:37.

19. Thomas DR, Zdrowski CD, Wilson MM, et al. Malnutrition in subacute care. Am J Clin Nutr 2002;75:308-13.

20. Martin CT, Kayser-Jones J, Stotts NA, Porter C, Froelicher ES. Risk for low weight in community-dwelling, older adults. Clin Nurse Spec 2007;21:203-11.

21. Payette H, Gray-Donald K, Cyr R, Boutier V. Predictors of dietary intake in a functionally dependent elderly population in the community. Am J Public Health 1995;85:677-83.

22. Deeg DJH, van Tilburg T, Smit JH, de Leeuw ED. Attrition in the Longitudinal Aging Study Amsterdam. The effect of differential inclusion in side studies. J Clin Epidemiol 2002;55:319-28.

23. Chumlea WC, Roche AF, Steinbaugh ML. Estimating stature from knee height for persons 60 to 90 years of age. J Am Geriatr Soc 1985;33:116-20.

24. Frank E, Dunlop AL. What does a patient's outfit weight? Fam Med 2000;32:595-6.

25. Elia M. MAG screening tool and guidelines set to combat malnutrition. Guidelines in Practice 2001;4:41-50.

26. Koster A, Bosma H, Broese van Groenou MI, et al. Explanations of socioeconomic differences in changes in physical function in older adults: results from the Longitudinal Aging Study Amsterdam. BMC Public Health 2006;6:244.

27. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.

28. Wind AW, Schellevis FG, van Staveren G, Scholten RP, Jonker C, van Eijk JT. Limitations of the Mini-Mental State Examination in diagnosing dementia in general practice. Int J Geriatr Psychiatry 1997;12:101-8.

29. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Applied Psychological Measurement 1977;1:385-401.

30. Berkman LF, Berkman CS, Kasl S, et al. Depressive symptoms in relation to physical health and functioning in the elderly. Am J Epidemiol 1986;124:372-88.

31. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361-70.

32. Bunevicius A, Peceliuniene J, Mickuviene N, Valius L, Bunevicius R. Screening for depression and anxiety disorders in primary care patients. Depress Anxiety 2007;24:455-60.

33. Kriegsman DM, Penninx BW, van Eijk JT, Boeke AJ, Deeg DJ. Self-reports and general practitioner information on the presence of chronic diseases in community dwelling elderly.

A study on the accuracy of patients' self-reports and on determinants of inaccuracy. J Clin Epidemiol 1996;49:1407-17.

34. Hunt SM, McEwen J, McKenna SP. Measuring health status: a new tool for clinicians and epidemiologists. J R Coll Gen Pract 1985;35:185-8.

35. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49:M85-94.

36. Verghese J, Wang C, Xue X, Holtzer R. Self-reported difficulty in climbing up or down stairs in nondisabled elderly. Arch Phys Med Rehabil 2008;89:100-4.

37. Ostbye T, Taylor DH, Jung SH. A longitudinal study of effects of tobacco smoking and other modifiable risk factors on ill health in middle-aged and old Americans: results from Health and Retirement Study and Asset and Health Dynamics among the Oldest Old survey. Prev Med 2002;34:334-45.

38. Ministerie van Welzijn, Volksgezondheid en Cultuur. Alcohol Prevalentie Onderzoek Rotterdam/ Limburg, landelijk eindrapport. Leidschendam, 1983.

39. Stel VS, Smit JH, Pluijm SM, Visser M, Deeg DJ, Lips P. Comparison of the LASA Physical Activity Questionnaire with a 7-day diary and pedometer. J Clin Epidemiol 2004;57:252-8.

40. de Jong-Gierveld J, Kamphuis F. The development of a Rasch-type loneliness scale. Applied Psychological Measurement 1985;9:89-299.

41. Comijs HC, Dik MG, Aartsen MJ, Deeg DJH, Jonker C. The impact of change in cognitive functioning and cognitive decline on disability, well-being, and the use of healthcare services in older persons. Results of Longitudinal Aging Study Amsterdam. Dement Geriatr Cogn Disord 2005;19:316-23.

42. Chatterjee S, Hadi AS, Price B. Regression Analysis by Example. 3rd ed. New York: John Wiley and Sons, 2000.

43. Hickson M. Malnutrition and ageing. Postgrad Med J 2006;82:2-8.

44. Chen LY, Hardy CL. Alcohol consumption and health status in older adults: a longitudinal analysis. J Aging Health 2009;21:824-47.

45. Sadakane A, Gotoh T, Ishikawa S, Nakamura Y, Kayaba K. Amount and frequency of alcohol consumption and all-cause mortality in a Japanese population: the JMS Cohort Study. J Epidemiol 2009;19:107-15.

46. Chen CC, Schilling LS, Lyder CH. A concept analysis of malnutrition in the elderly. J Adv Nurs 2001;36:131-42.

47. Sergi G, Perissinotto E, Pisent C, et al. An adequate threshold for body mass index to detect underweight condition in elderly persons: the Italian Longitudinal Study on Aging (ILSA). J Gerontol A Biol Sci Med Sci 2005;60:866-71.

48. Stratton RJ, Green CJ, Elia M. Disease-related malnutrition: an evidence-based approach to treatment. Wallingford, United Kingdom: CABI Publishing, 2003.

49. Wannamethee SG, Shaper AG, Whincup PH, Walker M. Characteristics of older men who lose weight intentionally or unintentionally. Am J Epidemiol 2000;151:667-75.

50. McCormack P. Undernutrition in the elderly population living at home in the community: a review of the literature. J Adv Nurs 1997;26:856-63.

51. Kubrak C, Jensen L. Malnutrition in acute care patients: a narrative review. Int J Nurs Stud 2007;44:1036-54.

CHAPTER 3

Development and validation of criteria for determining undernutrition in community-dwelling older men and women: the Short Nutritional Assessment Questionnaire 65+

Hanneke A.H. Wijnhoven
Janneke Schilp
Marian A.E. van Bokhorst-de van der Schueren
Henrica C.W. de Vet
Hinke M. Kruizenga
Dorly J.H. Deeg
Luigi Ferrucci
Marjolein Visser

Clinical Nutrition; 2012, 31 (3): 351-358

Abstract

Background. There is no valid, fast and easy-to-apply set of criteria to determine (risk of) undernutrition in community-dwelling older persons. The aim of this study was to develop and validate such criteria.

Methods. Selection of potential anthropometric and undernutrition-related items was based on consensus literature. The criteria were developed using 15-year mortality in community-dwelling older persons ≥65 years (Longitudinal Aging Study Amsterdam, *N* 1687) and validated in an independent sample (InCHIANTI, *N* 1142).

Results. Groups distinguished were: 1) undernutrition (mid-upper arm circumference <25 cm or involuntary weight loss ≥4 kg/6 months); 2) risk of undernutrition (poor appetite and difficulties climbing staircase); and 3) no undernutrition (others). Respective hazard ratio's for 15-year mortality were: 1) 2.22 (95% CI 1.83; 2.69); and 2) 1.57 (1.22; 2.01) (3= reference). The area under the curve (AUC) was 0.55. Comparable results were found stratified by sex, excluding cancer/obstructive lung disease/(past) smoking, using 6-year mortality, and applying results to the InCHIANTI study (hazard ratio's 2.12 and 2.46, AUC 0.59).

Conclusion. The developed set of criteria ($SNAQ^{65+}$) for determining (risk of) undernutrition in community-dwelling older persons shows good face validity and moderate predictive validity based on the consistent association with mortality in a second independent study sample.

Introduction

There is an increasing awareness and evidence that undernutrition is an important modifiable risk factor for poor clinical outcome in older persons in Western society. Based on observational studies, undernutrition is found to be associated with increased morbidity (1), mortality (2) and a reduced quality of life (3), even after adjustment for (severity of) illness. A recent Cochrane review of (quasi) randomized controlled trials (4), showed that the provision of extra energy and protein to undernourished older persons results in weight gain and a reduced mortality, providing evidence for the causality of the association between undernutrition and mortality and for a beneficial effect of a nutritional intervention among undernourished older persons. This emphasizes the importance of screening for and subsequently treating undernutrition in older persons.

Over the last two decades, more than 20 tools have been developed that determine (the risk of) undernutrition in older persons (5). However, many of them are poorly validated and most have been developed for institutionalized persons (including nursing homes and hospitals) only. However, also in community-dwelling older persons, the prevalence of undernutrition is estimated to be relatively high - varying around 15 - 24% depending on the specific study population and the applied criteria to determine undernutrition (6), thus stressing the need for screening for undernutrition in this population as well.

For determining undernutrition among community-dwelling older persons, a set of criteria needs to be valid and fast and easy-to-apply, without the need of calculation or – especially for the home situation – use of heavy or expensive equipment. At present, reliability and validity has been thoroughly established only for three tools that can be used in community-dwelling older persons (5). These include the (short form) 'Mini Nutritional Assessment' (MNA-SF) (7), the 'Seniors in the community: Risk evaluation for eating and nutrition' (SCREEN) (8), and the 'Nutrition Screening Initiative DETERMINE checklist' (9). However, the latter two tools are quite extensive, consisting of 178 and 109 questions respectively, and require specific skills from professionals which make them less applicable for use at home. Initially, the MNA-SF incorporated the assessment of body mass index (BMI), which is an impractical measure in the home situation (10), but recently, BMI was substituted by calf circumference (11). However, the MNA-SF incorporates questions on mobility, psychological stress or acute disease, and neuropsychological problems that may increase the risk for undernutrition, but do not assess undernutrition itself. Although the MNA-SF distinguishes 'risk of undernutrition' from 'undernutrition', this is based on the calculation of a total score that incorporates all these items, which likely results in a highly sensitive but non-specific tool (12-15).

Recently, the National Institute for Clinical Excellence (16) recommended the use of another simple tool, the Malnutrition Universal Screening Tool (MUST) (17) for determining undernutrition in the hospital or community. The MUST incorporates questions on unintentional weight loss, BMI or mid-upper arm circumference (MUAC), and acute illness combined with reduced nutritional intake. However, the MUST was developed for adults and uses cutoffs (for BMI and MUAC) that are applicable to adults and probably inadequate to older persons. Moreover, there are no published peer-reviewed validation studies conducted in community-dwelling older persons.

To summarize, there is at present no valid, and fast and easy-to-apply set of criteria to determine (risk of) undernutrition in community-dwelling older persons. Therefore, the aim of the present study was to develop and validate such criteria.

Subjects and methods

The present study uses existing data from two ongoing longitudinal epidemiological studies in older persons in the Netherlands and Italy.

Development study sample

The Longitudinal Aging Study Amsterdam (LASA) is an ongoing study on predictors and consequences of changes in physical, emotional, cognitive and social functioning in older people in the Netherlands. A random sample stratified by age and sex according to expected mortality after 5 years, was drawn from the population registries of 11 municipalities in three geographical areas of the Netherlands. A total of 3107 men and women aged 55 - 85 year were enrolled at the baseline examination in 1992-1993. The total sample is representative of the Dutch general older population. Examinations consist of a general face-to-face interview and a medical interview in the respondent's home. The details of the LASA study have been described elsewhere (18). For the present study, respondents aged ≥65 years at baseline (*N* 2141) who were community-dwelling (*N* 2001) were included. The study was approved by the Ethics Review Board of the VU University Medical Center, and informed consent was obtained from all respondents.

Validation study sample

InCHIANTI (Invecchiare in Chianti, aging in the Chianti area) is an epidemiological study with a main focus on factors contributing to loss of mobility in older persons in Italy. A random sample was drawn from the population registries of two municipalities (Greve in

Chianti and Bagno a Ripoli) in the Chianti geographic area. A total of 1155 men and women aged ≥65 years were enrolled at the baseline examination in 1998. Examinations consist of a face-to-face interview at the respondent's home and a clinical test session, a medical examination and a functional evaluation on separate days at the study clinic. The details of the InCHIANTI study have been described elsewhere (19). For the present study, only community-dwelling respondents (*N* 1142) were included. The study was approved by the Italian National Institute of Research and Care on Aging review board and informed consent was obtained from all respondents.

Selection of items

We selected fast and easy-to-assess anthropometric and other undernutrition-related-items that potentially could be included in the set of criteria based on (recent) consistency in the literature on items that assess: 1) undernutrition: BMI and self-reported involuntary weight loss (5, 16, 20); or 2) risk of undernutrition: a reduced nutritional intake (5, 16) or a poor appetite (5).

Since BMI may not always be a feasible measure in older persons (10) especially in a home situation, MUAC is proposed as an alternative anthropometric measure (17). This was supported by a recent study in community-dwelling older persons that showed that a low MUAC was more strongly associated with mortality than a low BMI (21). Therefore, MUAC was selected as a potential item instead of BMI.

Since a reduced nutritional intake should be involuntary and not based on following an energy restricted diet because of overweight, this item may be subject to bias and requires additional questioning and specific skills from home-care workers which makes it less applicable for use at home. In LASA nutritional intake was not assessed. Based on the InCHIANTI study, of 321 older persons who reported that they ate less over the last year, indeed, 54% indicated the reason was following a diet. A reduced appetite was reported in 35% and other reasons like difficulty chewing (10%) and swallowing (1%) were less often reported (data not shown, available on request). Therefore, a poor appetite was selected as a potential item and not a reduced nutritional intake.

In a unique longitudinal study, we previously found that poor appetite and functional limitations, as assessed by difficulties walking stairs, were the main independent determinants of incident undernutrition in community-dwelling older persons (22). Therefore, these two items were selected as potential items that increase the risk of (future) undernutrition. However, as functional limitations are likely related to an increased mortality risk, but not necessarily through the pathway of undernutrition, this

item was added to the model in a final step and only in combination with a poor appetite (see statistical analyses). To summarize, the potential items to be included in the set of criteria were: a low MUAC, self-reported involuntary weight loss, a poor appetite, and functional limitations.

Measures LASA

Vital status and date of death was traced until June 1, 2007 through the registers of municipalities in which the respondents were living. Survival time was calculated in days from the baseline measurement in 1992 - 1993 to June 1, 2007. For 6 respondents, survival time was censored at April 1, 2003 due to incomplete follow-up after this date.

Anthropometric data were collected during the medical interview by trained research nurses using a standardized protocol. Height was measured to the nearest 0.1 cm using a stadiometer and weight was measured to the nearest 0.1 kg using a calibrated bathroom scale (Seca, model 100, Lameris, Utrecht, the Netherlands). Knee height of the left leg was measured using a Mediform sliding caliper (Medical Express, Beaverton, OR, USA) with the knee and ankle joints fixed at 90° angles. In 112/1604 respondents with no valid height measurement, height was imputed by either a follow-up measurement, a prediction rule based on knee height, or self-reported height (21). BMI was calculated as body weight (kg) divided by height (m) squared. MUAC was measured at the left arm in duplicate to the nearest 0.001 m at a point midway between the lateral projection of the acromion process of the scapula and the inferior margin of the olecranon process of the ulna. The midway point was determined with the arm bent at the elbow at a 90° angle, while the actual measure was performed with the arm hanging loose. The mean of two MUAC measurements was used for the analyses. MUAC was dichotomized into <25 cm and $\geq$25 cm based on the 5th percentile of the LASA study sample (for both men and women separately). The cut-off of 5% was chosen on the principle of defining limits of normal in continuously normally distributed variables by determining the lower 95% confidence limit in a random population-based sample and has been applied before for MUAC (6).

Self-reported weight change in the last 6 months was assessed during the face-to-face medical interview by trained research nurses. Information was obtained on the direction of weight change (gained or lost), the amount (in kg) and the reason of weight change. Based on the latter question, a distinction was made between voluntary and involuntary weight change in the past 6 months. Voluntary weight change was due to diet or physical activity, while involuntary weight change was the result of disease, poor appetite, social factors, or a by the participant reported 'unknown' reason. For involuntary weight loss a cut-off of 4 kg (<4 kg versus $\geq$4 kg) was used. This was based on a change of $\geq$5% in 6

months, which is considered clinically relevant (6, 23, 24), and corresponded to 4 kg when applied to the average men and women of LASA. A cut-off in kg instead of percentages was used to facilitate an easy assessment.

Appetite during the last week was assessed with the following question from the Dutch translation of the Center for Epidemiologic Studies Depression Scale (CES-D) (25): 'I did not feel like eating; my appetite was poor,' with response categories: 1) 'rarely or none of the time'; 2) 'some or little of the time'; 3) 'occasionally or moderate amount of the time'; and 4) 'most or all of the time'. Two categories were created: no problems with appetite (answer 1) and poor appetite last week (answer 2-4). Difficulty walking up and down a staircase was used to determine functional limitations and was assessed by the question 'Can you walk up and down a staircase of 15 steps without stopping?' Response categories were: 1) 'yes'; 2) 'yes, with difficulty'; 3) 'not able without help'; and 4) 'cannot'. Two categories were created: no difficulties (answer 1) and difficulties (answer 2-4).

To examine the influence of pre-existing illness and smoking on the association between risk groups and mortality (see paragraph on statistical analyses), the analyses were repeated excluding those with a smoking history or two important thinness associated chronic diseases: obstructive lung disease (OLD) and cancer (26). The presence (yes or no) of OLD (asthma, chronic bronchitis or pulmonary emphysema) and cancer (malignant neoplasms) was determined by explicitly asking the participants whether they had these diseases. Smoking status and history was assessed and categorized into current, former, and never smokers. Former smokers who stopped smoking more than 15 years ago were classified as never smokers since mortality in former smokers approaches the level of never smokers after a smoking cessation time of 10 - 20 years (27, 28).

Measures InCHIANTI

Vital status and date of death were traced until October 1, 2006 through the Mortality General Registry maintained by the Tuscany Region and the death certificates that are deposited after the death at the Registry office of the Municipality of residence. Survival time was calculated in days from the baseline measurement in 1998 to October 1, 2006. Follow-up was 100% complete.

Anthropometric data were collected at the study clinic. Height was measured without shoes to the nearest 0.1 cm (HEALTH METER Inc, Bridgeview Illinois, USA). Weight was measured to the nearest 0.1 kg, with the participant wearing light clothes and without shoes, using a high precision mechanical scale (Seca, model 700, Medical Center, Artsana, Italy). BMI was calculated as body weight (kg) divided by height (m) squared. MUAC was

measured once on the non dominant arm at the midpoint between the acromion and the olecranon with a flexible tape meter while the participant was standing and with the arm hanging loose. MUAC was similarly dichotomized into <25 cm and ≥25 cm based on the 5th percentile of the LASA study sample.

Self-reported weight loss and the amount (kg) of weight loss in the last 12 months were assessed during the face-to-face interview. No information was available on the reason of weight loss. A cut-off of 6 kg was used instead of 4 kg in LASA to account for the difference in time interval. Appetite during the last week was assessed using the Italian translation of same question from the CES-D (25) as described above. Difficulty climbing up and down a staircase was assessed by the question 'Can you walk up and down a staircase of 10 steps without stopping?' Response categories were: 1) 'no difficulty'; 2) 'can without help but does not'; 3) 'with difficulty but without help'; and 4) 'unable to do it'. Two categories were created: no difficulties (answer 1 - 2) and difficulties (answer 3 - 4).

The presence (yes or no) of OLD and cancer was ascertained according to pre-established criteria that combine information on medical history, current pharmacological treatment, signs and symptoms, medical documents and hospital discharge records. Smoking status was assessed and categorized into current (within 3 years of the interview), former and never smokers. For former smokers, there was no information available on the cessation time.

Statistical analyses

Tree-structured survival analysis (TSSA) (29-31) was used for the development of a risk model for predicting 15-year mortality risk in the LASA study sample. Advantages of this method over traditional model building strategies such as stepwise Cox regression are that it mimics the actual clinical thinking process and provides a clear description of complex interactions of the included items. In addition, compared to a multivariate model, a tree structure might be more efficient when applied to clinical practice since there is no need for applying a prediction formula and – depending on the finally developed tree – one or two items might already be sufficient to determine (risk of) undernutrition.

Potential predictors that were first examined were: self-reported involuntary weight loss ≥4 kg/6 months; MUAC <25 cm; and poor appetite last week. The analysis started with the entire cohort, called the root node. From this root node, for all candidate dichotomous items (involuntary weight loss, low MUAC, and poor appetite) the subsequent log rank statistic comparing the Kaplan-Meier survival curves were calculated. The predictor with the highest statistical significant value of the log rank statistic was used for the first

partition after the root node. The emerging two subgroups were again partitioned using the same procedure and a tree structure was created. The partitioning stopped when the log rank statistic was not statistically significant for any of the predictors. The groups that emerged without further splitting were called the end nodes. The right side of the node of each binary split contained the highest proportion of deaths at 15 years. Cases with missing values (a maximum of 15% was allowed) on the splitting variable were sent to the left daughter node. When the final tree was completed based on the described procedure above, 'difficulties walking up and down a staircase' was added to the tree after the end node 'poor appetite last week'. Based on the log rank statistic (statistically significant or not), further splitting by this item was decided upon.

Kaplan-Meier curves for predicting 15-year mortality rates in LASA were created based on the (five) end nodes of the finally developed classification tree. This classification tree was then validated using data from the InCHIANTI study, creating Kaplan-Meier curves for predicting 6-year mortality rates. For comparability, similar analyses were performed in LASA using 6-year mortality. Differences in survival curves between (five) subgroups were tested by a pairwise Wilcoxon (Gehan) test.

Finally, based on visual inspection of the Kaplan-Meier curves and the proportion of deaths in each end node, different risk groups were created. Cox regression models were applied to study the mortality risk within these risk groups. To be able to compare the results between LASA and InCHIANTI, area under the curve (AUC), sensitivity and specificity were calculated, using the dichotomous outcome mortality (yes or no) at 15 year (LASA) and 6 year (InCHIANTI and LASA) respectively. These indices (AUC, sensitivity and specificity) are expected to be poor because people are dying for various reasons other than undernutrition. To examine if the results were consistent for men and women, the analyses were also performed stratified by sex. The analyses were also repeated excluding those with a smoking history (current or former <15 years) or OLD and cancer (see paragraph on measures LASA).

Results

Of the 2001 eligible LASA respondents, 314 (15.7%) were excluded because they had missing data on *both* MUAC and weight loss; leaving 1687 respondents to be included in the final analyses. Compared to included respondents, excluded respondents were somewhat older (75.9 year versus 74.5 year), more often had difficulties walking up and down a staircase (37% versus 30%), but had no higher prevalence of a poor appetite. None of the InCHIANTI respondents was excluded because the percentages of missing values for MUAC (135/1142 = 11.8%) and weight loss (17/1142 = 1.5%) were less than 15%.

During the follow-up period of 15 years, 609/836 (73%) of men and 488/851 (57%) of women in the LASA study died (**Table 1**), with mortality rates of 84 and 55 per 1000 person-y respectively. Based on 6-y follow-up, mortality rates per 1000 person-y were 70 (men) and 39 (women) in LASA and 57 (men) and 38 (women) in InCHIANTI. In both men and women of LASA, those who died within 15 years had a lower MUAC and more often reported involuntary weight loss, poor appetite, or difficulty walking up and down a staircase ($P < 0.05$), but had similar BMI (Table 1) compared to those who survived.

Comparable results were found for 6-year mortality in both LASA and InCHIANTI (**Table 2**). Participants who died within 6 years in InCHIANTI were slightly older (mean difference of 1 year). Furthermore, participants of InCHIANTI were more often female and had a higher BMI but a lower MUAC than participants of LASA. Furthermore, the prevalence of a low MUAC (<25 cm) was more than twice as high in InCHIANTI and the prevalence of a poor appetite was higher (19% versus 13%). The prevalence of (involuntary and voluntary) weight loss and difficulties walking up and down a staircase was comparable in the 2 studies (Table 2).

The classification tree for predicting 15-year mortality risk in LASA is presented in **Figure 1** and the log rank statistics used for building this tree are shown in **Table 3**. Overall, 65% of the LASA sample died within 15 years. The first partition in the tree was based on the item 'MUAC <25 cm' (largest log rank chi-square as shown in Table 3). Of the respondents with a MUAC <25 cm, 89% died within 15 years, while of those with a MUAC ≥25 cm, 64% died. Those with a MUAC ≥25 cm were further partitioned into respondents who reported involuntary weight loss ≥4 kg/ 6 months (81% died) or respondents who did not (63% died), and so on.

Table 1. Baseline characteristics of the Longitudinal Aging Study Amsterdam (questionnaire development) by 15-year all-cause mortality and sex.

	Men				Women			
	Overall	**Survived**	**Died**	***P*[a]**	**Overall**	**Survived**	**Died**	***P*[a]**
	***N* 836**	***N* 227**	***N* 609**		***N* 851**	***N* 363**	***N* 488**	
Age in years, mean (SD)	74.7 (5.7)	70.6 (4.7)	76.2 (5.2)	0.000	74.2 (5.9)	70.7 (4.6)	76.8 (5.4)	0.000
BMI in kg/m^2, mean (SD)	25.8 (3.3)	25.9 (2.8)	25.7 (3.4)	0.470	27.7 (4.6)	27.8 (4.6)	27.6 (4.7)	0.534
MUAC in cm, mean (SD)	30.4 (3.1)	31.1 (2.6)	30.2 (3.2)	.000	31.5 (3.9)	31.9 (3.6)	31.2 (4.0)	0.011
MUAC <25 cm (%)	4.4	1.3	5.8	0.011	3.4	1.1	5.4	0.002
Involuntary weight loss ≥4 kg in 6 months (%)	4.3	0.9	5.6	0.005	6.0	3.6	7.9	0.015
Poor appetite last week (%)	9.2	5.3	10.7	0.023	16.8	12.4	20.2	0.004
Difficulty climbing up and down a staircase (%)	23.0	9.7	28.0	0.000	37.3	24.7	47.4	0.000
Smoking status (% current or past <15 yrs)	54.2	45.8	57.4	0.004	22.3	19.6	24.6	0.095
Presence of OLD (%)	13.9	9.7	15.5	0.042	10.7	8.5	12.3	0.101
Presence of cancer (%)	8.2	4.0	9.7	0.010	11.5	8.6	13.8	0.025

[a] The difference between alive and deceased persons is tested by a Yates corrected chi-square test for frequency measures and the Student's t-test for normally distributed data.

Table 2. Baseline characteristics of the LASA sample (development sample) and InCHIANTI sample (validation sample) by 6-year all-cause mortality.

	LASA				InCHIANTI			
	Overall	**Survived**	**Died**	***P*[a]**	**Overall**	**Survived**	**Died**	***P*[a]**
	***N* 1687**	***N* 1215**	***N* 472**		***N* 1142**	***N* 862**	***N* 280**	
Age in years, mean (SD)	74.5 (5.8)	73.3 (5.6)	77.3 (5.3)	.000	75.4 (7.6)	73.3 (6.3)	81.8 (7.6)	0.000
Sex (% male)	49.6	44.6	62.3	.000	43.6	40.7	52.5	0.001
BMI in kg/m^2, mean (SD)	26.7 (4.1)	27.0 (4.0)	26.1 (4.3)	.000	27.5 (4.1)	27.5 (4.1)	27.1 (4.0)	0.176
MUAC in cm, mean (SD)	31.0 (3.5)	31.3 (3.4)	30.1 (3.7)	.000	28.6 (3.3)	29.1 (3.2)	26.9 (3.2)	0.000
MUAC <25 cm (%)	4.0	2.6	7.8	.000	10.5	6.8	24.3	0.000
Voluntary and involuntary weight loss[b]	7.4	5.4	12.7	.000	5.3	4.4	8.3	0.014
Poor appetite last week (%)	13.1	11.6	16.8	.006	18.7	17.4	24.0	0.024
Difficulty climbing up and down a staircase (%)[c]	30.4	25.6	42.6	.000	26.9	18.4	52.9	0.000
Smoking status (% current or past <15 yrs)[d]	38.1	34.9	47.0	.000	40.9	40.1	43.2	0.363
Presence of OLD (%)	12.3	10.8	16.1	.003	9.7	8.1	14.6	0.001
Presence of cancer (%)	9.9	8.3	13.8	.001	6.2	6.7	4.6	0.209

[a] The difference between alive and deceased persons is tested by a Yates corrected chi-square test for frequency measures and the Student's t-test for normally distributed data; [b] LASA: ≥4 kg in past 6 months; InCHIANTI: ≥6 kg in past 12 months; [c] LASA: 15 steps without stopping; InCHIANTI: 10 steps; [d] InCHIANTI: % current or past smoking

Figure 1. Classification tree for predicting 15-year mortality risk in community-dwelling older persons by undernutrition-related-items, developed in LASA. The end nodes are indicated by squares including roman numerals to indicate the emerging groups (I-V) and the intermediate nodes by circles. Both contain the group size (top number), the number of deaths (middle number), and the proportion of deaths at the end of the 15-year follow-up (bottom number). The split variable is shown on the resulting branches.

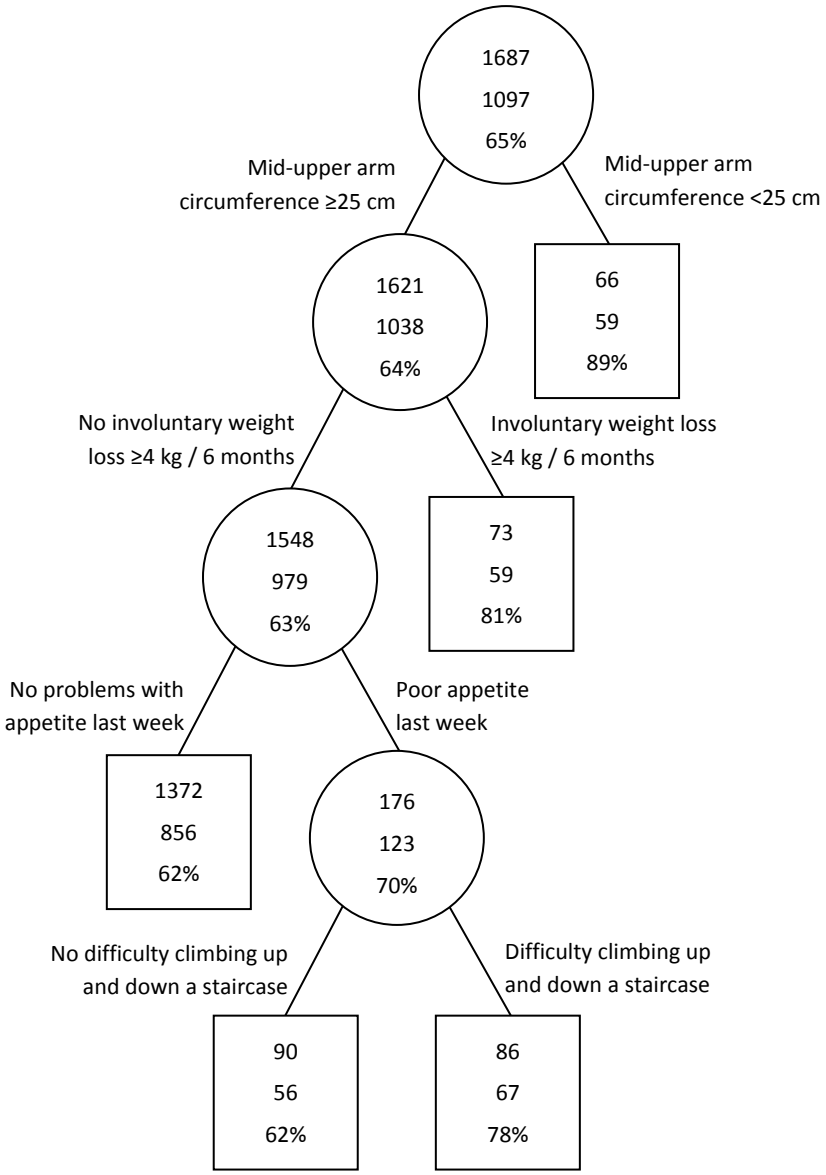


Table 3. Steps taken during tree-structured survival analysis to develop a risk model for predicting 15-year mortality risk in the LASA study sample (see also Figure 1).

Items included (Sample)	Log rank chi-square (*P*)	Proportion dead at 15 y	Conclusion
Entire cohort:		65%	
Mid-upper arm circumference (MUAC) <25 cm[a]	39.7 (0.000)	89%	1th partition
Involuntary weight loss ≥4 kg /6 months[b]	32.0 (0.000)	83%	
Poor appetite last week[c]	14.0 (0.000)	74%	
MUAC ≥25 cm:		64%	
Involuntary weight loss ≥4 kg /6 months[b]	27.6 (0.000)	81%	2th partition
Poor appetite last week[c]	10.2 (0.001)	72%	
MUAC ≥25 cm & no involuntary weight loss:		62%	
Poor appetite last week[c]	4.9 (0.027)	70%	3th partition
MUAC ≥25 cm & no involuntary weight loss & poor appetite:		70%	
Difficulty climbing up and down a staircase[d]	6.7 (0.010)	78%	4th partition
MUAC <25 cm:		89%	
Involuntary weight loss ≥4 kg /6 months[b]	0.1 (0.714)	93%	No further partition
Poor appetite last week[c]	0.5 (0.462)	94%	No further partition
MUAC ≥25 cm & involuntary weight loss:		81%	
Poor appetite last week[c]	2.2 (0.135)	88%	No further partition

[a] Versus mid-upper arm circumference ≥25 cm; [b] Versus no involuntary weight loss ≥4 kg /6 months; [c] Versus no poor appetite last week; [d] Versus no difficulty climbing up and down a staircase

The final classification tree consisted of five end nodes. Kaplan-Meier curves for predicting 15-year mortality based on these five groups are depicted in **Figure 2**. All emerging subgroups I, II and III (not IV) had statistically significantly poorer survival when compared to group V. After visual inspection of these curves, three different groups can be created. Groups I and II from Figure 1 have the highest mortality risk and include the items MUAC <25 cm and involuntary weight loss ≥4 kg/6 months which determine the actual state of undernutrition so that this group was labeled as 'undernutrition'. Group III had an intermediate mortality risk and was labeled as 'at risk of undernutrition' since poor appetite and difficulties climbing stairs are risk factors of undernutrition rather than that they measure the actual state of undernutrition. Groups IV and V were labeled as 'no undernutrition'. Similar curves were found for 6-year mortality on the LASA and InCHIANTI sample (**Figure 3**), except that in InCHIANTI, the mortality risk of weight loss (group II) seemed somewhat lower and the mortality risk of a poor appetite and difficulties climbing stairs (group III) somewhat higher (relative to 'no undernutrition'; groups I and II), when compared to LASA.

Figure 2. Kaplan-Meier curves for predicting 15-year mortality in community-dwelling older persons in the LASA-study by 5 groups based on the 5 end nodes of the developed classification tree depicted in Figure 1. Groups I, II, and III had a statistically significantly poorer survival ($P < 0.01$) compared to group V.

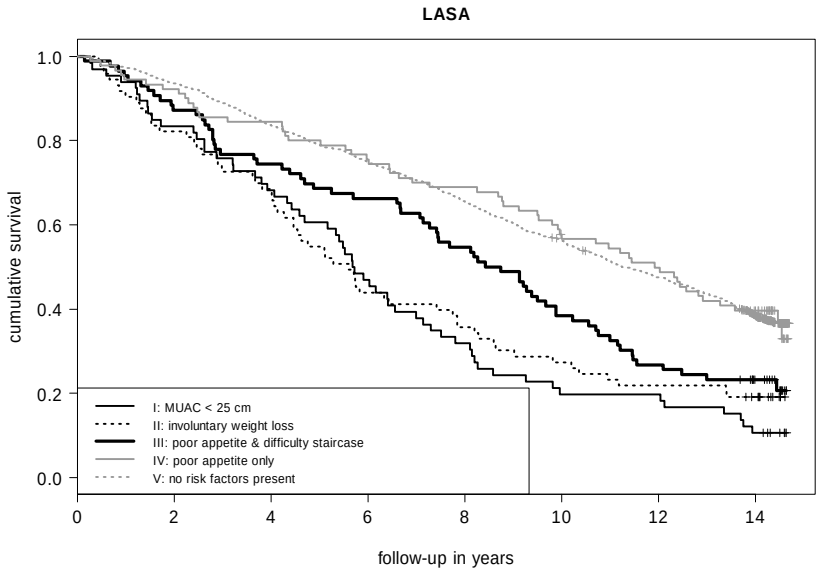
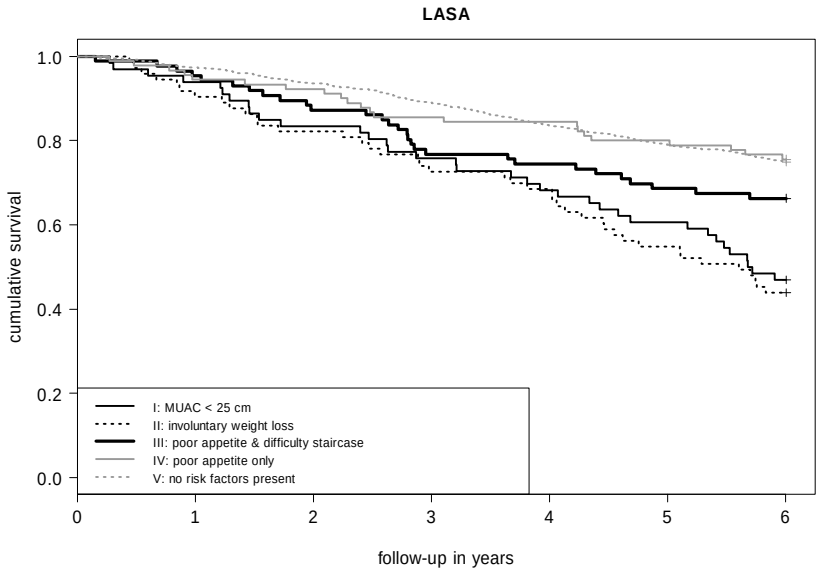
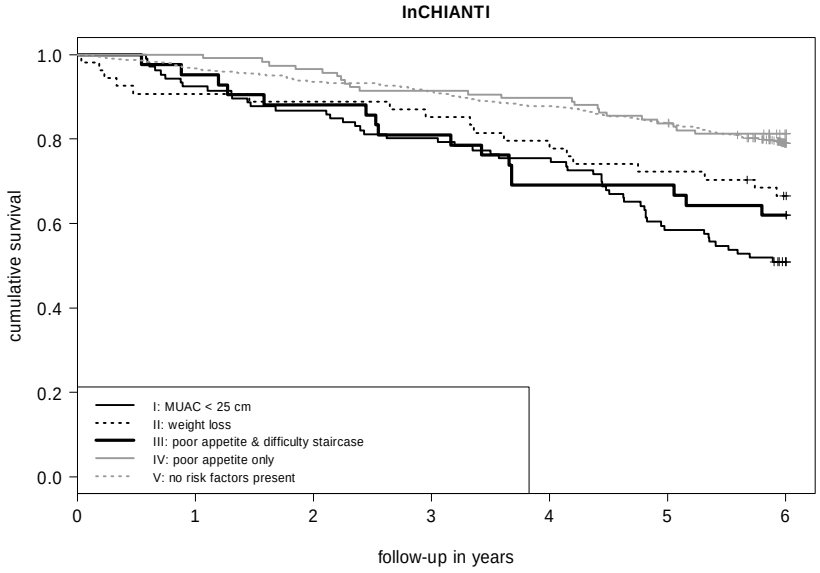


Figure 3. Kaplan-Meier curves for predicting 6-year mortality in community-dwelling older persons in the LASA and InCHIANTI study by 5 groups based on the 5 end nodes of the developed classification tree depicted in Figure 1. Groups I, II, and III had a statistically significantly poorer survival ($P < 0.05$) compared to group V.





As shown in **Table 4**, the hazard of 15-year mortality was raised in the group at risk of undernutrition (hazard ratio (HR) = 1.57 (95% CI 1.22 - 2.01)) and was highest in the group with undernutrition (HR = 2.22 (95% CI.1.83 - 2.69)) when compared to the group without undernutrition. The area under the curve (AUC) for predicting mortality was 0.55 (0.52 - 0.58) when comparing those with or at risk of undernutrition with no undernutrition. Similar results were found for men (respective HR's: 1.73 (1.13 - 2.65); and 2.44 (1.86 - 3.20), AUC = 0.55 (0.51 - 0.56)) and women (respective HR's: 1.81 (1.33 - 2.47); and 2.24 (1.70 - 2.96), AUC = 0.56 (0.52 - 0.60)). When excluding those with OLD, cancer or (past) smoking, the mortality hazards remained elevated in LASA (respective HR's: 1.83 (1.23 - 2.27); and 1.83 (1.35 - 2.49), AUC = 0.54 (0.50 - 0.58)). Similar HR's were found for 6-year mortality in the LASA sample (respective HR's: 1.47 (1.01 - 2.15); and 2.64 (2.03 - 3.39), AUC = 0.56 (0.53 - 0.59)) and somewhat higher HR's in the InCHIANTI sample (respective HR's: 2.12 (1.27 - 3.62); and 2.46 (1.87 - 3.23), AUC = 0.59 (0.55 - 0.63)) (Table 4).

Table 4. Prediction of 15-year (LASA) and 6-year (LASA and InCHIANTI) mortality risk by three groups[a] based on the end nodes of the classification tree depicted in Figure 1.

Groups (I-II; III; IV-V)[a]	HR (95% CI)	Cut-off risk groups	AUC (95% CI)	Sens	Spec
IV-V (no undernutrition): ref	1.00				
III (risk of undernutrition)	1.57 (1.22-2.01)	I-II-III *versus* IV-V	0.55 (0.52-0.58)	0.17	0.93
I-II (undernutrition)	2.22 (1.83-2.69)	I-II *versus* III-IV-V	0.54 (0.51-0.56)	0.11	0.96
LASA, 6 year mortality:					
III (risk of undernutrition)	1.47 (1.01-2.15)	I-II-III *versus* IV-V	0.56 (0.53-0.59)	0.22	0.90
I-II (undernutrition)	2.64 (2.07-3.39)	I-II *versus* III-IV-V	0.56 (0.52-0.59)	0.16	0.95
InCHIANTI, 6 year mortality					
III (risk of undernutrition)	2.12 (1.27-3.62)	I-II-III *versus* IV-V	0.59 (0.55-0.63)	0.31	0.87
I-II (undernutrition)	2.46 (1.87-3.23)	I-II *versus* III-IV-V	0.57 (0.53-0.61)	0.25	0.90

AUC, Area Under the Curve; Sens, sensitivity; Spec, specificity

[a] I-II: MUAC <25 cm or involuntary weight loss; III: poor appetite & difficulty climbing staircase; IV-V: poor appetite only or no risk factors present

Discussion

This study describes the development and validation of a fast and easy-to-apply set of criteria, named the Short Nutritional Assessment Questionnaire 65+ (SNAQ^{65+}), for determining (the risk of) undernutrition in community-dwelling older persons. Because a gold standard to determine undernutrition is lacking, the development of the SNAQ^{65+} was performed based on the association with 15-year mortality using undernutrition-related items that are considered important according to recent consensus literature. Based on the SNAQ^{65+} the following groups can be distinguished: 1) undernutrition (MUAC <25 cm or involuntary weight loss $\geq$4 kg in 6 months); 2) risk of undernutrition (poor appetite last week and difficulties climbing a staircase); and 3) no undernutrition (others).

The predictive validity of the SNAQ^{65+} was consistent for men and women and for those without cancer/obstructive lung disease or a past smoking status. For the development of the SNAQ^{65+} we used long-term, i.e. 15-year, mortality as an outcome measure. This strengthens the conclusions because it provides more conservative effect estimates compared to short-term mortality which may be confounded by (severe) underlying illness. This likely explains the slightly higher AUCs in the analyses with 6-year mortality. Another strength of the study is that the developed set of criteria was applied to another comparable community-dwelling study sample from Italy, the InCHIANTI study. In this validation step similar or even higher AUCs were observed when compared to LASA, despite slight differences in how items were measured and the prevalence of the items. This supports the generalizability of our findings to community-dwelling older persons.

Because there is no generally accepted, gold standard to determine undernutrition, a novel approach was used to develop and validate the SNAQ^{65+} by using all-cause mortality as an outcome measure. A disadvantage of this method is that traditional diagnostic parameters such as the area under the curve, sensitivity and specificity cannot be interpreted in the traditional sense. The predictive value of the SNAQ^{65+} for predicting mortality was overall poor (area under the curve (AUC) of 0.55 (0.52 - 0.58) when comparing those with or at risk of undernutrition with no undernutrition). This was to be expected because people are dying for various other reasons than undernutrition. Likewise, the presented values for sensitivity and specificity, and for AUC in Table 4 cannot be compared to diagnostic situations where there is a gold standard and correspondence of the index test is expected to be close to 100%. We used these diagnostic parameters in a prediction setting solely to find the best determinants for (risk of) undernutrition and not to maximize prediction of mortality. When in the future a (consensus) definition of undernutrition in older persons is available, the performance of the SNAQ^{65+} and other screening instruments need to be evaluated using these traditional diagnostic statistics.

The validity to the SNAQ^{65+} was tested by comparing its relationship with mortality using an independent sample of older persons.

For the selection of items, we used predefined cut-off scores for MUAC and involuntary weight loss based on previous consensus (6, 23, 24). Furthermore, we only included items that are directly related to (risk of) undernutrition according to consensus literature and not underlying risk factors of undernutrition like chronic diseases and social factors. This choice is justified by a previous longitudinal study, in which several socio-economic, psychological, medical, functional, lifestyle, and social factors were found to be associated with the development of undernutrition in community-dwelling older persons, but only a poor appetite and difficulties walking stairs remained in a multivariate model (22). For example, it is well possible that some patients with diabetes develop a poor appetite as a result of their disease. When determining the risk of undernutrition with the SNAQ^{65+}, only those with a poor appetite are included - when they also have difficulties climbing stairs - and not all patients with diabetes.

In practice, it may be difficult for older persons to differentiate voluntary from involuntary weight loss, especially for those with cognitive impairment. This may require specific skills from homecare workers. However, additional analyses with respect to the 15-year mortality risk in LASA, incorporating voluntary weight loss $\geq$4 kg in 6 months as a separate category showed that voluntary weight loss was not associated with an increased mortality risk (HR = 1.04 (95% CI 0.67 - 1.60)) when compared to the reference group without risk factors present (group V, Fig. 2) while involuntary weight loss was (2.05 (95% CI 1.58 - 2.67)). This analysis confirms previous reports that involuntary should be separated from voluntary weight loss (32).

To justify determining (the risk of) undernutrition in community-dwelling older persons, it needs to be an important health problem, there should be an acceptable (screening) tool, and there should be a beneficial (cost-effective) (nutritional) intervention (33). Although recent evidence summarizing 25 controlled trials suggests a beneficial effect of protein and energy supplements on weight gain and reduced mortality in undernourished older persons in general (4), the beneficial effect in community-dwelling undernourished older persons specifically (7 controlled trials) is still not clear. However, the quality of some of the included trials was suboptimal and the methods of defining undernutrition varied and were usually based on a low BMI (with cut-off varying from 21 to 27) with or without taking 'weight loss' into account. Therefore, in an ongoing study our group is investigating whether intensive treatment by the dietitian is (cost) effective compared to usual care in community-dwelling older persons ($\geq$65 years) who are considered undernourished persons according to the SNAQ^{65+}.

In conclusion, the SNAQ^{65+} can be used to determine (the risk of) undernutrition in older community-dwelling persons. It uses a fast and easy-to-apply set of criteria, without the need of calculation or heavy or expensive equipment, which is very relevant for application in the home situation. The inclusion of items was based on (recent) consistency in the literature on items that determine (the risk of) undernutrition. The SNAQ^{65+} shows good face validity and moderate predictive validity based on the consistent association with all-cause mortality in a second independent study sample. Future studies are needed to determine the association of the SNAQ^{65+} with other outcome measures such as frailty, disability, hospitalization and institutionalization and to determine the benefits of nutritional or other interventions on these outcomes in older community-dwelling persons identified with (risk of) undernutrition according to the SNAQ^{65+}.

References

1. Sullivan DH, Bopp MM, Roberson PK. Protein-energy undernutrition and life-threatening complications among the hospitalized elderly. J Gen Intern Med 2002;17:923-32.
2. Liu L, Bopp MM, Roberson PK, Sullivan DH. Undernutrition and risk of mortality in elderly patients within 1 year of hospital discharge. J Gerontol A Biol Sci Med Sci 2002;57:741-6.
3. Keller HH, Ostbye T, Goy R. Nutritional risk predicts quality of life in elderly community-living Canadians. J Gerontol A Biol Sci Med Sci 2004;59:68-74.
4. Milne AC, Potter J, Vivanti A, Avenell A. Protein and energy supplementation in elderly people at risk from malnutrition. Cochrane Database Syst Rev 2009:CD003288.
5. Green SM, Watson R. Nutritional screening and assessment tools for older adults: literature review. J Adv Nurs 2006;54:477-90.
6. Chen CC, Schilling LS, Lyder CH. A concept analysis of malnutrition in the elderly. J Adv Nurs 2001;36:131-42.
7. Guigoz Y. The Mini Nutritional Assessment (MNA) review of the literature--What does it tell us? J Nutr Health Aging 2006;10:466-85.
8. Keller HH, Goy R, Kane SL. Validity and reliability of SCREEN II (Seniors in the community: risk evaluation for eating and nutrition, Version II). Eur J Clin Nutr 2005;59:1149-57.
9. White JV, Dwyer JT, Posner BM, Ham RJ, Lipschitz DA, Wellman NS. Nutrition screening initiative: development and implementation of the public awareness checklist and screening tools. J Am Diet Assoc 1992;92:163-7.
10. Cook Z, Kirk S, Lawrenson S, Sandford S. Use of BMI in the assessment of undernutrition in older subjects: reflecting on practice. Proc.Nutr.Soc. 2005;64:313-7.
11. Kaiser MJ, Bauer JM, Ramsch C, Uter W, Guigoz Y, Cederholm T, Thomas DR, Anthony P, Charlton KE, Maggio M, et al. Validation of the Mini Nutritional Assessment short-form (MNA-SF): a practical tool for identification of nutritional status. J Nutr Health Aging 2009;13:782-8.
12. Azad N, Murphy J, Amos SS, Toppan J. Nutrition survey in an elderly population following admission to a tertiary care hospital. Cmaj 1999;161:511-5.
13. Kruizenga HM, de Vet HC, Van Marissing CM, Stassen EE, Strijk JE, Van Bokhorst-de Van der Schueren MA, Horman JC, Schols JM, Van Binsbergen JJ, Eliens A, et al. The SNAQ(RC), an easy traffic light system as a first step in the recognition of undernutrition in residential care. J Nutr Health Aging 2010;14:83-9.
14. Murphy MC, Brooks CN, New SA, Lumbers ML. The use of the Mini-Nutritional Assessment (MNA) tool in elderly orthopaedic patients. Eur J Clin Nutr 2000;54:555-62.
15. Thorsdottir I, Jonsson PV, Asgeirsdottir AE, Hjaltadottir I, Bjornsson S, Ramel A. Fast and simple screening for nutritional status in hospitalized, elderly people. J Hum Nutr Diet 2005;18:53-60.

16. National Collaborating Centre for Acute Care. Nutrition support for adults oral nutrition support, enteral tube feeding and parenteral nutrition. London, 2006.

17. BAPEN. Malnutrition universal screening tool (MUST). Redditch: British Association of Enteral and Parenteral Nutrition, 2003.

18. Deeg DJH, van Tilburg T, Smit JH, de Leeuw ED. Attrition in the Longitudinal Aging Study Amsterdam. The effect of differential inclusion in side studies. J Clin Epidemiol 2002;55:319-28.

19. Ferrucci L, Bandinelli S, Benvenuti E, Di Iorio A, Macchi C, Harris TB, Guralnik JM. Subsystems contributing to the decline in ability to walk: bridging the gap between epidemiology and geriatric practice in the InCHIANTI study. J Am Geriatr Soc 2000;48:1618-25.

20. Elia M. MAG screening tool and guidelines set to combat malnutrition. Guidelines in Practice 2001;4:41-50.

21. Wijnhoven HA, van Bokhorst-de van der Schueren MA, Heymans MW, de Vet HC, Kruizenga HM, Twisk JW, Visser M. Low mid-upper arm circumference, calf circumference, and body mass index and mortality in older persons. J Gerontol A Biol Sci Med Sci 2010;65:1107-14.

22. Schilp J, Wijnhoven HA, Deeg DJ, Visser M. Early determinants for the development of undernutrition in an older general population: Longitudinal Aging Study Amsterdam. Br J Nutr 2011;106:708-17.

23. McMinn J, Steel C, Bowman A. Investigation and management of unintentional weight loss in older adults. BMJ 2011;342:d1732.

24. Wallace JI, Schwartz RS. Involuntary weight loss in elderly outpatients: recognition, etiologies, and treatment. Clin.Geriatr.Med. 1997;13:717-35.

25. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Applied Psychological Measurement 1977;1:385-401.

26. Kruizenga HM, Wierdsma NJ, van Bokhorst MA, de van der S, Haollander HJ, Jonkers-Schuitema CF, van der Heijden E, Melis GC, van Staveren WA. Screening of nutritional status in The Netherlands. Clin Nutr 2003;22:147-52.

27. Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Rosner B, Hunter DJ, Hennekens CH, Speizer FE. Smoking cessation in relation to total mortality rates in women. A prospective cohort study. Ann Intern Med 1993;119:992-1000.

28. Paganini-Hill A, Hsu G. Smoking and mortality among residents of a California retirement community. Am J Public Health 1994;84:992-5.

29. Ciampi A, Negassa A, Lou Z. Tree-structured prediction for censored survival data and the Cox model. J Clin Epidemiol 1995;48:675-89.

30. Gordon L, Olshen RA. Tree-structured survival analysis. Cancer Treat Rep 1985;69:1065-9.

31. Stel VS, Pluijm SM, Deeg DJ, Smit JH, Bouter LM, Lips P. A classification tree for predicting recurrent falling in community-dwelling older persons. J Am Geriatr Soc 2003;51:1356-64.

32. Wannamethee SG, Shaper AG, Whincup PH, Walker M. Characteristics of older men who lose weight intentionally or unintentionally. Am J Epidemiol 2000;151:667-75.

33. Wilson JM, Jungner YG. Principles and practice of mass screening for disease. Bol Oficina Sanit Panam 1968;65:281-393.

CHAPTER 4

High prevalence of undernutrition in Dutch community-dwelling older individuals

Janneke Schilp
Hinke M. Kruizenga
Hanneke A.H. Wijnhoven
Eva Leistra
Anja M. Evers
Jaap J. van Binsbergen
Dorly J.H. Deeg
Marjolein Visser

Nutrition; 2012, 28 (11-12): 1151-1156

Abstract

Background. To examine the prevalence of undernutrition in community-dwelling older individuals (≥65 years) using data from various settings.

Methods. A cross-sectional observational study was performed to examine the prevalence of undernutrition in three samples (all ≥65 years): 1) 1267 community-dwelling individuals participating in a large prospective population based study, the Longitudinal Aging Study Amsterdam (LASA) in 1998 - 1999; 2) 814 patients receiving home care in 2009 - 2010; and 3) 1878 patients from general practices during the annual influenza vaccination in 2009 - 2010. Undernutrition was assessed by the Short Nutritional Assessment Questionnaire 65+ ($SNAQ^{65+}$).

Results. Mean age was 77.3 (SD 6.7) years in the LASA sample, 81.6 (SD 7.4) years in the home care sample and 75.3 (SD 6.5) years in the general practice sample. The prevalence of undernutrition was highest in the home care sample (35%), followed by the general practice (12%) and LASA (11%) samples. The prevalence of undernutrition increased significantly with age in the general practice and LASA samples. Gender differences were observed in the general practice and home care samples; women were more likely to be undernourished in the general practice sample and men were more likely to be undernourished in the home care sample.

Conclusion. The prevalence of undernutrition in Dutch community-dwelling older individuals was relatively high, especially in home care patients.

Introduction

Undernutrition is an important problem in all health care settings. Undernutrition can be defined as a disorder of nutritional status resulting from reduced nutrient intake or impaired metabolism (1). In Western society, the presence of undernutrition is found to be associated with delayed wound healing (2, 3), impaired immune function (4), poor muscle function (5, 6), mental health problems (7, 8), impaired quality of life (9, 10), and even increased morbidity and mortality rates (11-15). In the Netherlands in 2010, the prevalence of undernutrition was estimated to be 25% in hospitals, 21% in nursing home residents and 17% in patient receiving home care (16). Although undernutrition is present in all age groups, the prevalence of undernutrition increase with age (16-18) and appear to be highest in older individuals (15, 19-21). Studies performed in institutionalized older patients showed that treatment of undernutrition could lead to improved wound healing (22, 23), less complications (24), better quality of life (24, 25) and lower mortality (26).

In the past years, more attention is given to recognize and treat undernourished patients in Dutch institutional settings. Screening and treatment of undernutrition in hospital patients were added as performance indicators to the national benchmarks on quality of care in the Netherlands in 2007 - 2008 (27). On the contrary, recognition and treatment of undernutrition in older individuals in the home situation has received less attention. The results of the Dutch Annual National Prevalence Measurement of Care Problems (LPZ prevalence study) in 2010 showed that nutritional status was assessed in only 16% of the home care patients (16). In 71% of this subgroup, undernutrition was assessed by just looking at the patient and in only 5% a validated screening instrument was used (16). The Dutch College of General Practitioners introduced the 'National Primary Care Cooperation Agreement Undernutrition' on the collaboration of primary care workers in 2010 to enhance awareness and early intervention in case of undernutrition (28). Recognition of undernutrition in an early phase is important to timely initiate treatment and to prevent aggravation of the nutritional status. The importance of early detection is emphasized by the fact that older individuals have a reduced ability to recover from weight loss (29).

Studies determining the prevalence of undernutrition in community-dwelling older individuals are scarce. Depending on the specific older study population and the definition used to determine undernutrition, prevalence's range from 0 to 24% (16, 30, 31). More knowledge about the prevalence in specific populations at risk of undernutrition in the home situation is needed to provide recommendations for the assessment and treatment of undernutrition in community-dwelling older individuals. Recently, a new instrument was specifically developed and validated to determine undernutrition in community-dwelling older individuals: the Short Nutritional Assessment Questionnaire 65+ (SNAQ^{65+})

(32). This instrument is feasible and fast to use, without the need of any calculation or heavy equipment, and is therefore well applicable in the home situation. The aim of the present study was to identify the prevalence of undernutrition in three different samples of Dutch community-dwelling older individuals using the $SNAQ^{65+}$.

Materials and methods

Data of three samples were collected within two cohort studies: one sample from the Longitudinal Aging Study Amsterdam (LASA) and two samples from the Nutrition in Primary Care Study (NPCS). Both studies were approved by the Ethics Review Board of the VU University Medical Center and informed consent was obtained from all participants.

Study samples

LASA is an ongoing cohort study focusing on predictors and consequences of changes in autonomy and well-being in the aging population in the Netherlands. A representative sample of older individuals (55 - 85 years old), stratified by age and sex according to expected mortality after 5 years, was drawn from the population registries of eleven municipalities in areas in the west (Amsterdam and vicinity), northeast (Zwolle and vicinity) and south (Oss and vicinity) of the Netherlands. Further details about the sampling and data-collection procedures have been described elsewhere (33). A total of 3107 participants were enrolled at the baseline examination (1992 - 1993). Examinations were performed every three years and consist of a general face-to-face interview and a medical interview at the participants' home. Data for the present study was collected in 1998 and 1999, in a medical interview by trained research nurses using a standardized protocol. Participants aged ≥65 years (*N* 1289) were included. Subsequently, participants with missing data on nutritional status were excluded (*N* 22), resulting in a sample of 1267 participants.

NPCS is an ongoing intervention study investigating the (cost) effectiveness of early treatment by a dietitian of undernourished community-dwelling older individuals in Dutch primary care and home care. Undernourished participants were recruited through 12 general practices and a home care organization in Amsterdam and vicinity. Nutritional status was assessed by 24 research assistants during the annual influenza vaccination on a specific day in the general practices from October 2009 to December 2009 (8 general practices) or in November 2010 (4 general practices). After exclusion of individuals with missing data on gender (*N* 25), 1878 participants aged ≥65 years were included in the sample. In the home care organization, nurses were trained to assess nutritional status at

the individuals' home during an intake consultation when the care needs were determined or during an evaluation consultation. Terminally ill individuals or individuals suffering from dementia were excluded from the assessment. Data collected by 54 home care nurses between November 2009 and December 2010 were used. Individuals with missing data on gender (*N* 1) or nutritional status (*N* 18) were excluded, resulting in a sample of 814 participants aged ≥65 years.

The total study sample consisted of 1267 participants from the LASA-study, 1878 participants from the general practices and 814 participants receiving home care.

Nutritional status

Undernutrition was assessed by the SNAQ^{65+} (32). This instrument consists of four items: the measurement of mid-upper arm circumference (MUAC) and three questions on involuntary weight loss in the past 6 months, poor appetite and difficulties walking stairs. Participants with a MUAC <25 cm *and/or* involuntary weight loss ≥4 kg in the past six months were defined as undernourished. Not undernourished participants reporting a poor appetite in the past week in combination with reporting difficulties walking staircase were defined as being at risk of undernutrition (32). In LASA the answers on the items were defined retrospectively, because the data was already collected.

Weight loss

To determine involuntary weight loss in the past 6 months in the LASA sample, the answers on three questions were used: 1) 'did your weight change in the past six months'; 2) 'how many kilograms did your weight change'; and 3) 'what is the reason your weight change'. Involuntary weight loss was defined as weight loss due to disease, poor appetite, social factors or a by the participant reported 'unknown' reason. A cut-off point of ≥4 kg involuntary weight loss in the past six months was used to define undernutrition. This corresponds with a 5% weight change in the LASA study (32). In the NPCS samples, one question was asked to define involuntarily weight loss: 'Did you involuntary lose 4 kilogram or more in the past six months?' with answering categories yes and no.

Mid-upper arm circumference

MUAC was measured at the left arm to the nearest millimeter at a point midway between the lateral projection of the acromion process of the scapula and the inferior margin of the olecranon process of the ulna. The midway point was determined with the arm bent at

the elbow at a 90 degree angle, while the actual measure was performed with the arm hanging loose. In LASA, the MUAC was measured in duplicate, whereby the mean of two MUAC measurements was used in the analyses. MUAC was dichotomized into <25 cm and ≥25 cm based on the 5th percentile of the total LASA study sample (34).

Appetite

In the LASA sample, appetite during the past week was assessed with the following question from the Dutch translation of the Center for Epidemiologic Studies Depression Scale (CES-D) 'In the past week, I did not feel like eating; my appetite was poor' (35). Two categories were created: no problems with appetite (answer rarely or never) and poor appetite last week (answer some of the time/ occasionally/ mostly or always). In the NPCS samples appetite was assessed by the question: 'Did you have a poor appetite in the past week', with answering categories yes and no.

Walking staircase

Difficulty walking up and down a staircase was assessed by the question 'Can you walk up and down a staircase of 15 steps without resting?'. In the LASA sample, two categories were created: no difficulties (answer yes, without help) and difficulties (answer yes, with some/much difficulty/ only with help/ no, I cannot). In the NPCS samples response categories were yes and no.

Statistical analyses

The prevalence of (the risk of) undernutrition with the SNAQ^{65+} was calculated in the three different study samples and characteristics of the study samples were examined. Differences between the study samples were tested using ANOVA for continuous variables and Chi square tests for dichotomous and categorical variables. The percentage of undernourished participants with a MUAC <25 cm, with ≥4 kg involuntary weight loss in the past 6 months or both, were calculated for every sample. The prevalence of undernutrition was presented in age quintiles (based on including all three individual samples) and for men and women separately. Differences were tested with Chi square test and Linear-by-Linear Associations were calculated to obtain insight into the trend of the prevalence across age quintiles. A P-value < 0.05 was considered statistically significant. The analyses were performed using SPSS version 16.0 (SPSS inc. Chicago, USA).

Results

Table 1 shows the characteristics of the three study samples and the prevalence of (the risk of) undernutrition. In total, 3959 participants (59.2% women) were included in the study, with a mean age of 77.2 (SD 7.2) years. The home care sample differed from the other samples on all investigated characteristics. Participants in the home care sample were more often women, were older and had the lowest mean MUAC ($P < 0.001$). The characteristics of the LASA and general practice samples were most comparable. The prevalence of undernutrition was 10.7% (95% CI 9.0, 12.4) in the LASA sample, 11.8% (95% CI 10.3; 13.3) in the general practice and 34.8% (95% CI 31.5; 38.1) in the home care sample. The risk of undernutrition was 7.7% (95% CI 6.2; 9.2) in the LASA sample, 2.2% (95% CI 1.4; 3.0) in the general practice sample and 9.2% (95% CI 7.6; 10.8) in the home care sample. The mean overall prevalence of undernutrition was 16.2% (95% CI 15.0; 17.4) and the mean overall prevalence of the risk of undernutrition was 5.4% (95% CI 4.1; 6.7).

Table 1. Characteristics of the study samples and prevalence of undernutrition.

	LASA	**GP**	**HC**	***P*[a]**		
	***N* 1267**	***N* 1878**	***N* 814**	**LASA-GP**	**LASA-HC**	**GP-HC**
Women, %	54.9	57.7	69.3	0.118	<0.001	<0.001
Age in years, mean (SD)	77.3 (6.7)	75.3 (6.5)	81.6 (7.4)	<0.001	<0.001	<0.001
MUAC in cm, mean (SD)	30.3 (3.6)	29.4 (3.4)	28.9 (5.5)	<0.001	<0.001	0.001
MUAC <25 cm, %	5.8	7.1	15.7	0.168	<0.001	<0.001
≥4 kg involuntary weight loss, %	5.4	6.7	27.0	0.125	<0.001	<0.001
Poor appetite last week, %	15.9	8.9	29.4	<0.001	<0.001	<0.001
Difficulties walking stairs, %	38.3	17.0	59.2	<0.001	<0.001	<0.001
Nutritional status, %				<0.001	<0.001	<0.001
• Undernutrition	10.7	11.8	34.8			
• Risk of undernutrition	7.7	2.2	9.2			
• No undernutrition	81.7	86.0	56.0			

LASA, Longitudinal Aging Study Amsterdam; GP, general practice; HC, home care; MUAC, mid-upper arm circumference

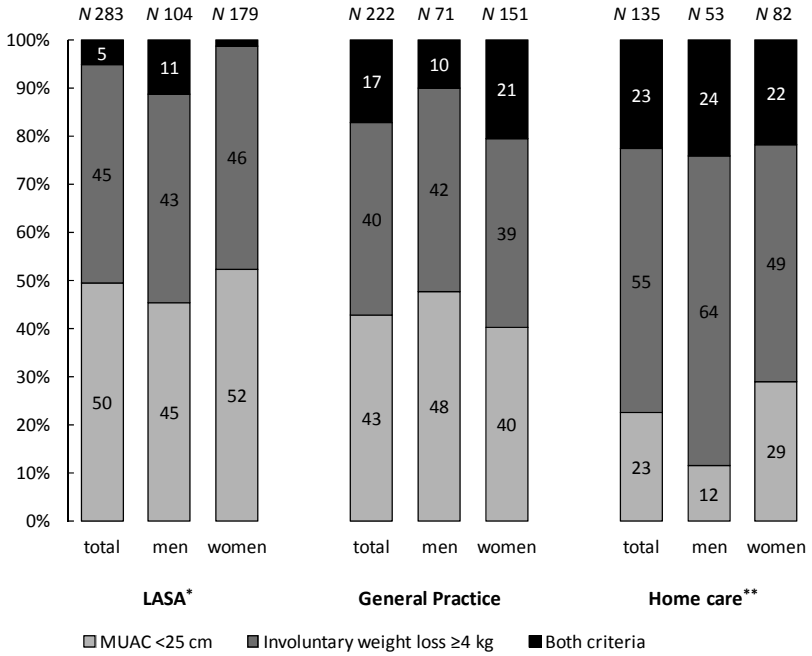
[a] Differences between the 3 samples were mutually tested with ANOVA and Chi square tests

Additional characteristics of the LASA sample were examined: 12% had a poor cognitive status (Mini-Mental State Examination score ≤23), 39% had a poor self-perceived health

and 88% reported having one or more chronic diseases. The mean handgrip strength of the LASA sample was 31.9 (SD 9.7) kg in men and 18.9 (SD 6.9) kg in women. Furthermore, 70% of the men and 34% of the women was married and 22% of the men and 54% of the women was widowed. No comparison on these characteristics could be made between the samples, as this information was not available for the other two study samples.

The underlying criteria for undernutrition according to the SNAQ^{65+} are illustrated in **Figure 1**. In the LASA and general practice samples most undernourished participants were undernourished based on a low MUAC. In LASA a statistically significant difference was found between men and women (P = 0.04). In the home care sample most undernourished participants were undernourished based on their involuntary weight loss ≥4 kg. This percentage was significantly higher in men compared to women (P = 0.003). In the home care sample almost one out of four undernourished participants was undernourished based on both criteria.

Figure 1. Underlying criteria for undernutrition according to the SNAQ^{65+} within undernourished participants.

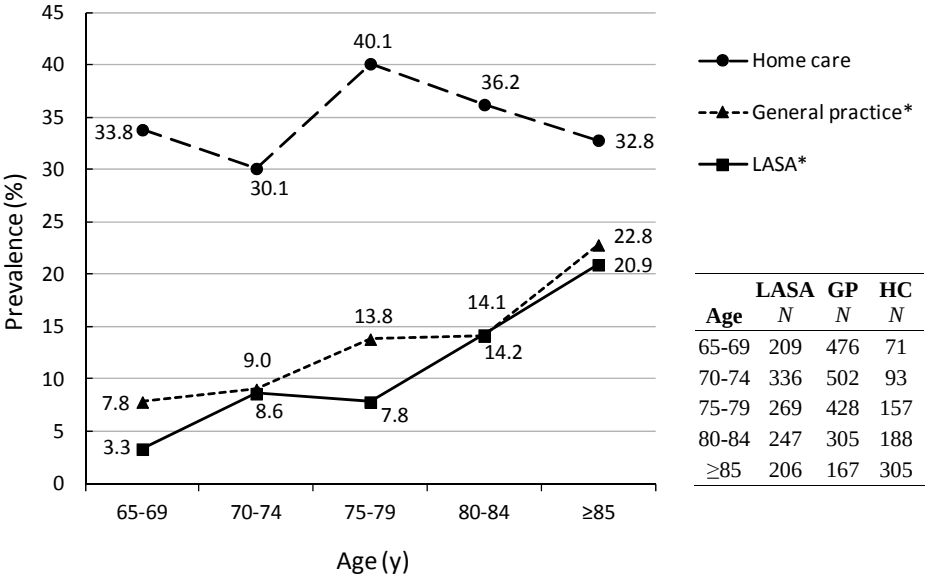


* Statistically significant difference (P < 0.05) between men and women

** Statistically significant difference (P < 0.01) between men and women

Figure 2 shows the prevalence of undernutrition for the age quintiles in the total study sample. The prevalence of undernutrition increased statistically significantly ($P < 0.001$) with age in the general practice and LASA samples. In these samples the prevalence was highest in the age group ≥85 years; 20.9% (95% CI 15.2; 26.6) in the LASA sample and 22.8% (95% CI 16.3; 29.3) in the general practice sample. In the home care sample, the prevalence of undernutrition did not differ between the age quintiles.

Figure 2. Prevalence of undernutrition within the study samples, in age quintiles.



Age	LASA *N*	GP *N*	HC *N*
65-69	209	476	71
70-74	336	502	93
75-79	269	428	157
80-84	247	305	188
≥85	206	167	305

LASA, Longitudinal Aging Study Amsterdam; GP, general practice; HC, home care

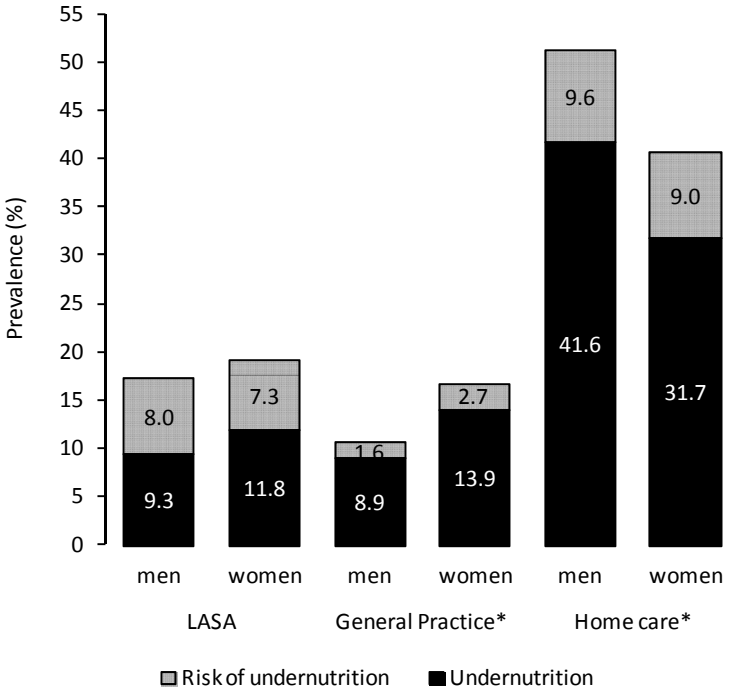
* Statistically significant difference ($P < 0.001$) in prevalence of undernutrition between the age quintiles within the three study samples

The prevalence of the *risk of* undernutrition differed significantly between the age quintiles in the LASA sample, but there was no trend across the age quintiles (Linear-by-Linear Association $P = 0.46$). The highest prevalence (13.0%, 95% CI 10.4; 15.6) was found in the age group 80 - 84 years and the lowest prevalence (4.9%, 95% CI 3.3; 6.5) in the age group ≥85 years. In the general practice and home care samples no statistically significant differences were found between the age quintiles. In the home care sample, the

prevalence range from 5.9% (95% CI 4.1; 7.7) in the age group 65 - 69 years to 11.1% (95% CI 8.7; 13.5) in the age group ≥85 years. In the general practice sample, the prevalence range from 1.0% (95% CI 0.2; 1.8) in the age group 70 - 74 years to 3.0% (95% CI 1.7; 4.3) in the age group ≥85 years.

Figure 3 shows the prevalence of (the risk of) undernutrition for men and women in the three study samples. In the general practice and home care samples statistically significant differences were found between men and women. Women were more likely to be undernourished than men in the general practice sample ($P < 0.001$). In the home care sample men were more likely to be undernourished than women ($P = 0.02$). In the LASA sample no significant gender differences were found. An additional analysis showed that potential age differences between men and women did not explain the observed gender differences in prevalence.

Figure 3. Gender specific prevalence of undernutrition in the three study samples.



* Statistically significant difference ($P < 0.05$) in prevalence of undernutrition between men and women

Discussion

In Dutch community-dwelling older individuals (≥65 years), the prevalence of undernutrition was 11% in a representative sample of 1267 community-dwelling older individuals from the LASA study, 12% in a sample of 1878 general practice patients (during the annual influenza vaccination) and 35% in a sample of 814 home care patients (during an intake or evaluation consultation). The prevalence of undernutrition increased statistically significantly with age in the LASA and general practice samples and gender differences were observed in the general practice and home care samples.

This is the first study investigating the prevalence of undernutrition in community-dwelling older individuals using the $SNAQ^{65+}$. Thereby, comparing the observed prevalence's to the results of other studies is difficult, because they largely depend on the used criteria to define (the risk of) undernutrition and the considered population and setting. Studies reporting the prevalence in older individuals in general practice are scarce, with values ranging from 0% assessed with the Mini Nutritional Assessment (36) to 11.6% using a low Body Mass Index (BMI) as the criteria (the used cutoff point for low BMI was not reported) (37). The prevalence of undernutrition observed in our general practice and LASA samples are comparable to the latter study. The prevalence of undernutrition in our home care sample is higher than the prevalence (17.1%) found in the earlier mentioned LPZ prevalence study (16). However, the home care sample of the LPZ prevalence study was younger (mean age 76.2 years) compared to our sample (mean age 81.8 years). In addition, more stringent criteria were used to assess undernutrition in the LPZ prevalence study: BMI ≤20 kg/m^2, >6 kg involuntary weight loss in the past 6 months or >3 kg in the past month, and reduced nutritional intake. The cut-off value of 25 cm for MUAC used in our study was comparable with a BMI of 20.7 kg/m^2 in LASA (approximated with a linear regression analysis). Moreover, the cutoff value for involuntary weight loss (≥4 kg) was also less strict in our study compared to the LPZ prevalence study.

The increasing prevalence of undernutrition with age shown in earlier studies (17, 18, 20, 21) was confirmed in the LASA and general practice samples, but not in the home care sample. Besides the increasing prevalence of undernutrition, other health problems and diseases such as depression, cancer, heart disease and the presence of multimorbidity are also known to increase with increasing age (38-42). The decreasing prevalence in the home care sample was comparable to the results of the LPZ prevalence study and could be due to the assumption that older individuals with higher disease severity are more likely to die or to be admitted to an institution, whereby the healthier older individuals will be more likely to stay at home (16). Because of the observed age differences in the general

practice sample it could be useful to consider only assessing undernutrition in the highest age groups in this setting.

The contradictory results between the samples with regard to gender differences in the prevalence of undernutrition are difficult to interpret. In general, women are more often frail then men (43), which was reflected in the prevalence of undernutrition in our general practice sample. The higher prevalence of undernutrition in men compared to women in our home care sample could be due to the fact that the frailest patients in home care are more likely to be men (44). Women receive generally more often home care compared to men, because women are more often living without a partner, but men are more frail (45). An earlier study pooled data from published datasets and showed that the prevalence of undernutrition was higher in community-dwelling older men compared to women (46), but it was not mentioned whether this population received home care. In the LPZ prevalence study no statistically significant gender differences were found in the home care setting (47). Based on the results of our study we will recommend to assess nutritional status in both men and women and not to differentiate the assessment for gender.

A strength of our study is that three large and diverse samples were used to determine the prevalence of undernutrition in community-dwelling older individuals. Probably some overlap exists between the three samples, because for example individuals assessed during the influenza vaccination in general practices as well as participants of LASA could also potentially receive home care. Another strength is the unique direct comparison of different settings of community-dwelling older individuals. Advantage of assessment during the influenza vaccination in general practice or during consultation in home care is that assessment can be performed regularly in large samples of older individuals allowing monitoring of nutritional status over time.

A limitation of this study is that undernutrition in the LASA sample was assessed in 1998 - 1999, while undernutrition in the other two samples was assessed in 2009 - 2010. The MUAC was only measured until the third cycle of LASA (1998 - 1999) and more recent cycles could therefore not be used to determine the prevalence of undernutrition based on the SNAQ^{65+}. An additional analysis, using BMI <20 kg/m^2 instead of MUAC <25 cm, showed comparable prevalence's of undernutrition between 1998 - 1999 (6.3%) and 2005 - 2006 (6.6%) in individuals between age 65 and 85 years. These data suggests that the prevalence's did not vary over time allowing a direct comparison of the three study samples. Another potential limitation was that the questions used in the SNAQ^{65+} were not identically asked in the LASA sample as compared to the other two samples, which may explain some of the differences in the prevalence between the samples.

In the present study home care nurses were instructed to assess the nutritional status of all individuals aged 65 years and older during an intake or evaluation consultation, but not all individuals were actually assessed since terminally ill individuals or individuals suffering from dementia were excluded from assessment, causing selection bias. Furthermore, it is possible that during the start-up phase nurses may have been selectively screened those individuals who appeared undernourished. However, the prevalence of undernutrition (38.1%, 95% CI 33.2; 43.0) of the first four months (November 2009 to February 2010) was not statistically significant different (P = 0.16) from the prevalence (31.7%, 95% CI 27.0; 36.4) of the last four months of recruitment (September to December 2010).

This study demonstrates that the prevalence of undernutrition in community-dwelling older individuals is substantial. The prevalence of undernutrition was highest in a sample of older individuals receiving home care, in both men and women and in all age groups (≥65 years). Therefore, assessment of undernutrition in home care during regular consultations is warranted. In general practice, almost one out of four patients (both men and women) aged 85 years and older was undernourished during the influenza vaccination. Concerning investment of time and money, it could be useful to consider only assessing undernutrition in the highest age groups in general practice. Early recognition of undernutrition in community-dwelling older individuals is important to timely initiate treatment and prevent aggravation of the nutritional status.

References

1. August DA, Kushner RF. The 1995 A.S.P.E.N. Standards for Nutrition Support: Hospitalized Patients. Nutr Clin Pract 1995;10:206-7.
2. Haydock DA, Hill GL. Impaired wound healing in surgical patients with varying degrees of malnutrition. J Parenter Enteral Nutr 1986;10:550-4.
3. Shahin ES, Meijers JM, Schols JM, Tannen A, Halfens RJ, Dassen T. The relationship between malnutrition parameters and pressure ulcers in hospitals and nursing homes. Nutrition 2010;26:886-9.
4. Kawakami K, Kadota J, Iida K, Shirai R, Abe K, Kohno S. Reduced immune function and malnutrition in the elderly. Tohoku J Exp Med 1999;187:157-71.
5. Bourdel-Marchasson I, Joseph PA, Dehail P, et al. Functional and metabolic early changes in calf muscle occurring during nutritional repletion in malnourished elderly patients. Am J Clin Nutr 2001;73:832-8.
6. Engelen MP, Schols AM, Baken WC, Wesseling GJ, Wouters EF. Nutritional depletion in relation to respiratory and peripheral skeletal muscle function in out-patients with COPD. Eur Respir J 1994;7:1793-7.
7. Cabrera MA, Mesas AE, Garcia AR, de Andrade SM. Malnutrition and depression among community-dwelling elderly people. J Am Med Dir Assoc 2007;8:582-4.
8. Kvamme JM, Gronli O, Florholmen J, Jacobsen BK. Risk of malnutrition is associated with mental health symptoms in community living elderly men and women: the Tromso study. BMC Psychiatry 2011;11:112.
9. Amarantos E, Martinez A, Dwyer J. Nutrition and quality of life in older adults. J Gerontol A Biol Sci Med Sci 2001;56 Spec No 2:54-64.
10. Thomas DR. The critical link between health-related quality of life and age-related changes in physical activity and nutrition. J Gerontol A Biol Sci Med Sci 2001;56:599-602.
11. Corrada MM, Kawas CH, Mozaffar F, Paganini-Hill A. Association of body mass index and weight change with all-cause mortality in the elderly. Am J Epidemiol 2006;163:938-49.
12. Liu L, Bopp MM, Roberson PK, Sullivan DH. Undernutrition and risk of mortality in elderly patients within 1 year of hospital discharge. J Gerontol A Biol Sci Med Sci 2002;57:741-6.
13. Locher JL, Roth DL, Ritchie CS, et al. Body mass index, weight loss, and mortality in community-dwelling older adults. J Gerontol A Biol Sci Med Sci 2007;62:1389-92.
14. Sullivan DH, Bopp MM, Roberson PK. Protein-energy undernutrition and life-threatening complications among the hospitalized elderly. J Gen Intern Med 2002;17:923-32.
15. Ferreira LS, do Amaral TF, de Fatima Nunes Marucci M, Costa Nascimento LF, Lebrao ML, de Oliveira Duarte YA. Undernutrition as a major risk factor for death among older Brazilian adults in the community-dwelling setting: SABE survey. Nutrition 2011;27:1017-22.

16. Halfens RJG, Meijers JMM, Du Moulin MFMT, Van Nie NC, Neyens JCL, Schols JMGA. Rapportage resultaten: Landelijke Prevalentiemeting Zorgproblemen (National Prevalence Measurement of Care Problems). Maastricht, the Netherlands: Maastricht University, 2010.

17. Pirlich M, Schutz T, Kemps M, et al. Prevalence of malnutrition in hospitalized medical patients: impact of underlying disease. Dig Dis 2003;21:245-51.

18. Newman AB, Yanez D, Harris T, Duxbury A, Enright PL, Fried LP. Weight change in old age and its association with mortality. J Am Geriatr Soc 2001;49:1309-18.

19. Margetts BM, Thompson RL, Elia M, Jackson AA. Prevalence of risk of undernutrition is associated with poor health status in older people in the UK. Eur J Clin Nutr 2003;57:69-74.

20. Johansson Y, Bachrach-Lindstrom M, Carstensen J, Ek AC. Malnutrition in a home-living older population: prevalence, incidence and risk factors. A prospective study. J Clin Nurs 2009;18:1354-64.

21. Perissinotto E, Pisent C, Sergi G, Grigoletto F. Anthropometric measurements in the elderly: age and gender differences. Br J Nutr 2002;87:177-86.

22. Ek AC, Unosson M, Larsson J, Von Schenck H, Bjurulf P. The development and healing of pressure sores related to the nutritional state. Clin Nutr 1991;10:245-50.

23. Collins CE, Kershaw J, Brockington S. Effect of nutritional supplements on wound healing in home-nursed elderly: a randomized trial. Nutrition 2005;21:147-55.

24. Starke J, Schneider H, Alteheld B, Stehle P, Meier R. Short-term individual nutritional care as part of routine clinical setting improves outcome and quality of life in malnourished medical patients. Clin Nutr 2011;30:194-201.

25. Rufenacht U, Ruhlin M, Wegmann M, Imoberdorf R, Ballmer PE. Nutritional counseling improves quality of life and nutrient intake in hospitalized undernourished patients. Nutrition 2010;26:53-60.

26. Milne AC, Potter J, Vivanti A, Avenell A. Protein and energy supplementation in elderly people at risk from malnutrition. Cochrane Database Syst Rev 2009:CD003288.

27. Dutch Health Care Inspectorate, Ministry of Health Welfare and Sports. Performance indicators hospitals, 2010. Utrecht, The Netherlands, 2009:43-49.

28. Van Avendonk MJ, Mensink PA, Drenthen AJ, van Binsbergen JJ. Primary care and public health a natural alliance? The introduction of the guidelines for obesity and undernutrition of the Dutch College of General Practitioners. Fam Pract 2012;29 Suppl 1:i31-i35.

29. Roberts SB, Fuss P, Heyman MB, et al. Control of food intake in older men. Jama 1994;272:1601-6.

30. Chen CC, Schilling LS, Lyder CH. A concept analysis of malnutrition in the elderly. J Adv Nurs 2001;36:131-42.

31. Van Wayenburg CA, Van de Laar FA, Van Weel C, Van Staveren WA, Van Binsbergen JJ. Nutritional deficiency in general practice: a systematic review. Eur J Clin Nutr 2005;59 Suppl 1:S81-7; discussion S88.

32. Wijnhoven HA, Schilp J, Van Bokhorst-de van der Schueren MA, et al. Development and validation of criteria for determining undernutrition in community-dwelling older men and women: the Short Nutritional Assessment Questionnaire 65+. Clin Nutr 2012;31:351-8.

33. Huisman M, Poppelaars J, van der Horst M, et al. Cohort Profile: The Longitudinal Aging Study Amsterdam. Int J Epidemiol 2011.

34. Wijnhoven HA, van Bokhorst-de van der Schueren MA, Heymans MW, et al. Low mid-upper arm circumference, calf circumference, and body mass index and mortality in older persons. J Gerontol A Biol Sci Med Sci 2010;65:1107-14.

35. Radloff L. The CES-D scale: a self-reported depression scale for research in the general population. Applied Psychological Measurement 1977;1:385-401.

36. Beck AM, Ovesen L, Schroll M. A six months' prospective follow-up of 65+-y-old patients from general practice classified according to nutritional risk by the Mini Nutritional Assessment. Eur J Clin Nutr 2001;55:1028-33.

37. DeVore PA. Assessment of nutritional status and obesity in elderly patients as seen in general medical practice. South Med J 1993;86:1008-10.

38. Hung WW, Ross JS, Boockvar KS, Siu AL. Recent trends in chronic disease, impairment and disability among older adults in the United States. BMC Geriatr 2011;11:47.

39. Salisbury C, Johnson L, Purdy S, Valderas JM, Montgomery AA. Epidemiology and impact of multimorbidity in primary care: a retrospective cohort study. Br J Gen Pract 2011;61:e12-21.

40. Janssen-Heijnen ML, Houterman S, Lemmens VE, Louwman MW, Maas HA, Coebergh JW. Prognostic impact of increasing age and co-morbidity in cancer patients: a population-based approach. Crit Rev Oncol Hematol 2005;55:231-40.

41. Solhaug HI, Romuld EB, Romild U, Stordal E. Increased prevalence of depression in cohorts of the elderly: an 11-year follow-up in the general population - the HUNT study. Int Psychogeriatr 2012;24:151-8.

42. Davis JW, Chung R, Juarez DT. Prevalence of comorbid conditions with aging among patients with diabetes and cardiovascular disease. Hawaii Med J 2011;70:209-13.

43. Puts MT, Lips P, Deeg DJ. Sex differences in the risk of frailty for mortality independent of disability and chronic diseases. J Am Geriatr Soc 2005;53:40-7.

44. Armstrong JJ, Stolee P, Hirdes JP, Poss JW. Examining three frailty conceptualizations in their ability to predict negative outcomes for home-care clients. Age Ageing 2010;39:755-8.

45. Geerlings SW, Pot AM, Twisk JWR, Deeg DJH. Predicting transitions in the use of informal and professional care by older adults. Ageing & Society 2005;25:111-30.

46. Kaiser MJ, Bauer JM, Ramsch C, et al. Frequency of malnutrition in older adults: a multinational perspective using the mini nutritional assessment. J Am Geriatr Soc 2010;58:1734-8.

47. Meijers JM, Schols JM, van Bokhorst-de van der Schueren MA, Dassen T, Janssen MA, Halfens RJ. Malnutrition prevalence in The Netherlands: results of the annual Dutch national prevalence measurement of care problems. Br J Nutr 2009;101:417-23.

CHAPTER 5

Effects of a dietetic treatment in older, undernourished, community-dwelling individuals in primary care: a randomized controlled trial

Janneke Schilp
Hinke M. Kruizenga
Hanneke A.H. Wijnhoven
Jaap J. van Binsbergen
Marjolein Visser

European Journal of Nutrition; in revision

Abstract

Background. Undernutrition is a prevalent problem in older, community-dwelling individuals. Aim of this study was to determine the effects of a dietetic treatment in older, undernourished, community-dwelling individuals.

Methods. A parallel randomized controlled trial was performed in 146 non-institutionalized, undernourished individuals aged ≥65 years in primary care. Participants were randomly assigned to the intervention (referral to and treatment by a trained dietitian) or control group (no referral). Body weight, physical performance, handgrip strength, energy intake, protein intake and fat free mass were assessed at baseline, after 3 months and after 6 months.

Results. All randomized participants (*N* 146) were included in the intention-to-treat Generalized Estimating Equations analysis (72 in intervention and 74 in control group). No treatment effect was found on the primary outcomes body weight (β = 0.49 kg, 95% CI -0.15; 1.12), physical performance (β = 0.15 points, 95% CI -0.33; 0.64) and handgrip strength (β = 0.49 kg, 95% CI -0.62; 1.60). Furthermore, no treatment effect was found for the secondary outcomes. Predefined subgroup analyses showed a treatment effect on body weight in physically active participants (β = 1.25 kg, 95% CI 0.70; 2.11) and not in inactive participants (β = -0.20 kg, 95% CI -1.16; 0.75).

Conclusion. After 6 months, a dietetic treatment by trained dietitians does not lead to increases in body weight and physical functioning in older, undernourished, community-dwelling individuals.

Introduction

Although undernutrition is present within all age groups, the most vulnerable persons for undernutrition in developed countries are older individuals. Older age is associated with a decreased food intake (1) and higher prevalence of undernutrition (2), resulting from the higher disease rate and the psychological and social changes that occur with aging (3-6). Undernutrition in older individuals is found to be associated with several adverse clinical outcomes such as reduced functional status (7, 8), poorer quality of life (9), higher risk of institutionalization (10) and increased mortality (11-13).

Undernutrition is most prevalent in institutionalized patients, but studies in older, community-dwelling individuals have also shown significant prevalence rates between 15 and 35% (3, 14). As in the Netherlands 95% of individuals aged 65 years and older live independently in the community (15), the absolute number of older, undernourished individuals is highest in this setting. Therefore, it is important to recognize and treat undernutrition in the primary care setting.

There are no internationally accepted protocols for the treatment of undernutrition in older individuals in primary care as only a limited number of randomized controlled trials (RCTs) have been performed. Most nutritional intervention studies were performed in specific hospital or nursing home populations. Furthermore, most RCTs focused on the effect of oral nutritional supplements (ONS) (16). Much less attention has been given to increasing energy intake via ordinary foods and beverages through individual support by a dietitian. Increasing energy intake via ordinary foods and beverages has the advantage that it offers greater variety and is tailored to individual needs (17). Beneficial effects of dietetic treatment were found on nutritional intake and body weight in adult COPD outpatients (18), nutritional intake in adult colorectal cancer patients after radiotherapy (19) and mortality in older, hospital patients (20). RCTs in older, undernourished, community-dwelling individuals in primary care are lacking. Therefore, we investigated the 6-months effects of dietetic treatment in older, undernourished, community-dwelling individuals in primary care.

Methods

Study design

The Nutrition in Primary Care Study (NPCS) was designed as a randomized controlled trial performed in the region of Amsterdam in the Netherlands between October 2009 and June 2011. The study was in accordance with the Declaration of Helsinki and was approved by the Ethics Review Board of the VU University Medical Center Amsterdam. Written informed consent was obtained from all participants. The study was registered at the Dutch Trial Register (http://www.trialregister.nl; NTR1808).

Recruitment

In the first phase of recruitment, nutritional status was assessed in a total of 3591 individuals aged 65 years and older in different primary care locations by trained nurses, researchers and research assistants. Individuals were eligible for NPCS if they were non-institutionalized and were identified as undernourished according to the Short Nutritional Assessment Questionnaire 65+ ($SNAQ^{65+}$): mid-upper arm circumference (MUAC) <25 cm and/or self report of ≥4 kg unintentional weight loss within the past 6 months (21). MUAC was measured with a measuring tape at the centre point of the left upper-arm to the nearest mm with the arm hanging loosely. Unintentional weight loss was assessed by the question: 'Have you unintentionally lost 4 kilograms or more within the past 6 months?'. Individuals were excluded from enrollment if they were under current dietetic treatment, were medically diagnosed with dementia, were not living in vicinity of Amsterdam (where the treatment is provided), were severely overweight (MUAC >32 cm), or were not speaking the Dutch language.

In the second phase, all potentially eligible participants received an information letter, accompanied by the informed consent form, and were asked by telephone if they were willing to participate. Those willing to participate were scheduled for the baseline examination, during which cognitive functioning was measured with the Mini-Mental State Examination (MMSE) (22). Participants with a MMSE score <18 (23) and participants who were unable to stand on the weighing scale were excluded.

Randomization

The randomization was performed by the primary investigator within 1 day after completion of the baseline examination. Random allocation to either the intervention group or to the control group was individually performed in blocks of 4 and 6 by using the

website Randomization.com (http://www.randomization.com). Participants recruited at an outpatient clinic department were randomized with a separate scheme, because they were expected to be more severely undernourished. Participants, researcher and research assistants were no longer blinded for the intervention assignment from this point.

Study protocol

Participants of the intervention group received dietetic treatment from a qualified trained dietitian. The control group received usual care and was not referred to a dietitian through the study. They received a standard brochure of the Netherlands Nutrition Centre with general information about healthy eating habits. To avoid bias of potential prescription of vitamin D as part of the dietetic treatment, all participants were prescribed a combined calcium (1000 mg calcium carbonate) plus vitamin D (800 IU cholecalciferol) supplement by their general practitioner if this was not already used.

Dietetic treatment

The 18 participating dietitians received a specific training about the treatment of older, undernourished individuals. This training was based on a recently developed method for diabetic patients: the Pro-active Interdisciplinary Self-MAnagement (PRISMA) program, which has been shown to have a significant effect on nutritional intake in diabetic patients (24). PRISMA triggers individuals to consider their own personal risk factors that have led to undernutrition and to choose a specific goal of behavioral change to achieve, using a motivational interviewing technique. The treatment was a combination of both face-to-face and telephone consultations and the amount of consultations was depending on the nutritional situation, needs and desires of the participant. According to the PRISMA method, a workbook including a questionnaire on the presence of predefined risk factors associated with undernutrition and a personal action plan on how to successfully achieve the set treatment goals was used. General practical information related to undernutrition was also added to the workbook. The instructed aim of the treatment was to obtain adequate protein and energy intake, preferable by regular foods and beverages. The dietitians were instructed to prescribe additional nutritional supplements and/or tube feeding if the intake of regular foods and beverages was insufficient (<100% from requirement as calculated by the Harris and Benedict formula + 30% and ≥1.20 gram protein per kg body weight (25-27)). After 6 month follow-up, the dietitians sent an evaluation form to the primary investigator about the number and total duration of the provided consultations and the treatment goals that were set for each participant.

Within two days after randomization the primary investigator contacted a trained dietitian through email and sent an information letter to the participants' general practitioner containing a request for signing and sending a referral letter to the dietitian. The dietitians were instructed to schedule the first consult within five days and to send the above mentioned workbook to the participants' home to be filled in before the first consult. The personal action plan was completed during the first consultation and discussed during each consecutive consultation. The dietetic treatment was covered by the basic health insurance of the participants.

Measures

Two follow-up examinations were performed 3 and 6 months after the baseline examination. All examinations took place at the participants' home and were executed by a trained researcher or research assistant using a standardized protocol. Socio-demographic factors, body height, presence of chronic diseases and medication use were assessed at the baseline examination. Other measures were assessed at all examinations.

Primary outcome measures

Body weight was measured without shoes to the nearest 0.5 kg using a calibrated mechanical scale (Seca 761). Adjustments were made for clothing (-1.77 kg for men; -1.13 kg for women) and in deviating situations adjustments were made for shoes (-0.40 kg for men; -0.28 kg for women) or corset (-1 kg) (respectively 3% and 1% of all assessments) (28, 29).

Physical performance was assessed using the Short Physical Performance Battery which consists of a 4-m walk test, repeated chair stands test and standing balance test (30). The total score ranged from 0 (worst performance) to 12.

Handgrip strength (kg) was measured twice on each hand using a hand-held dynamometer (JAMAR; Sammons Preston, UK). The mean value of the maxima of both hands was used. If the left or right handgrip strength measure was missing at an examination, this measure was also set to missing at the previous or follow-up examinations.

Secondary outcome measures

A food diary was filled in by the participant the day prior to each examination and was reviewed for completeness by the researcher (or assistant) during the examination. If missing, a 24-hour recall was conducted during the examination. Daily energy (kcal) and

protein (gram) intake were calculated using the NEVO Dutch Food Composition Table 2006 (31). A copy of the baseline examination food diary and the calculation of the baseline energy and protein intake was send to the treating dietitian.

Whole-body resistance (R, Ohm) was measured at the left side of the body at a frequency of 50 kHz using a Bodystat 1500 MDD (Euromedix, Belgium). Fat-free mass (kg) was predicted with the formula of Kyle (2001) (32). Participants with an invalid measurement (fat percentage <5%) were excluded from the analysis (7.5%) (33). Other reasons for missing data were: shoes could not be taken off (1.3%), dysfunction of the equipment (2.0%), pacemaker (3.0%), presence of stocking or bandages (3.8%) and not able/refuse (5.3%).

Statistical analysis

Linear Generalized Estimating Equations (GEE) analysis with an exchangeable correlation structure was used to analyze the effectiveness of the intervention. This longitudinal analysis technique is suitable to compare the course over time of the repeated outcome measures between two groups. A minimum of 62 participants per group was required to detect a statistically significant ($P < 0.05$) treatment effect of 2.23% (34) in body weight after 6 months with 80% power. The GEE analyses included all randomized participants and were performed according to the intention-to-treat principle with the last-observation-carried-forward. The outcome measures were analyzed as dependent variables using intervention group as the independent variable. All analyses were adjusted for the baseline values of the outcome variable which led to equal starting points for both groups. Results are presented as Beta coefficients with 95% confidence intervals and can be interpreted as the mean difference between the intervention and the control group. A two-tailed significance level of $\alpha = 0.05$ was used.

To study whether the effect of the intervention differed between the first three months and the next three months, the variables time and intervention X time were added to the model. Furthermore, predefined subgroup analyses were performed for the primary outcome measures according to sex, assessment criteria of the $SNAQ^{65+}$ (MUAC <25 cm, unintentional weight loss ≥4 kg or both criteria) and physical activity measured with the validated LASA Physical Activity Questionnaire (35) (stratified at the median of 728 minutes/week). In addition, post hoc analyses were performed for the primary outcome measures according to appetite (poor/ normal appetite) and energy intake (stratified at the median of 1568 kcal/day).

All statistical analyses were performed using SPSS version 16.0 (SPSS, Chicago, USA).

Results

The participant flow of the NPCS is shown in **Figure 1**. During the first recruitment phase, nutritional status was assessed with the SNAQ^{65+} in 3591 individuals. A total of 731 individuals (20%) were undernourished, of which 362 refused to participate and 211 were not eligible for enrollment. During the second recruitment phase, 158 of the 520 eligible individuals (30%) were enrolled for the baseline examination of which 12 were excluded before randomization. In total, 72 participants were allocated to the intervention and 74 to the control group. The majority of the participants was recruited in general practices (*N* 62), followed by a home care organization (*N* 45), an outpatient clinic department (*N* 22), senior citizen centers (*N* 13), advertisements (*N* 3) and pharmacies (*N* 1). The recruitment locations did not differ between the intervention and control group (*P* = 0.90). A total of 127 participants completed the 6 months examination: 62 (86%) in the intervention group and 65 (88%) in the control group. The reasons for drop-out are described in Figure 1. There were no statistically significant differences in baseline characteristics between participants who discontinued early and study completers, except for education level. A low education level was present in 56% of those who discontinued and in 18% of the study completers (*P* = 0.002).

The baseline characteristics of the intervention and control group are shown in **Table 1**. Mean age of the total study population was 80.5 year (SD 7.5) and 64.4% was women. One out of five participants suffered from 3 or more chronic diseases and two out of five participants used 5 or more medications. Thirty to forty percent reported a poor appetite and depressive symptoms. After 3 months 53% of the intervention group and 65% of the control group was using calcium plus vitamin D supplements (*P* = 0.20) and 25% of the intervention group and 10% of the control group was using ONS (*P* = 0.02). After 6 months 63% of the intervention group and 66% of the control group was using calcium plus vitamin D supplements (*P* = 0.58) and 37% of the intervention group and 12% of the control group was using ONS (*P* = 0.001). Main goals of the treatment during the first consult, as indicated by the dietitian in the evaluation form, were preventing further weight loss (35%) and gaining body weight (27%). Participants in the intervention group received on average 2.4 (SD 1.4) hours dietetic consultations and the control group 0.2 (SD 0.9) hours (*P* < 0.001).

Figure 1. Consort flow chart Nutrition in Primary Care Study.

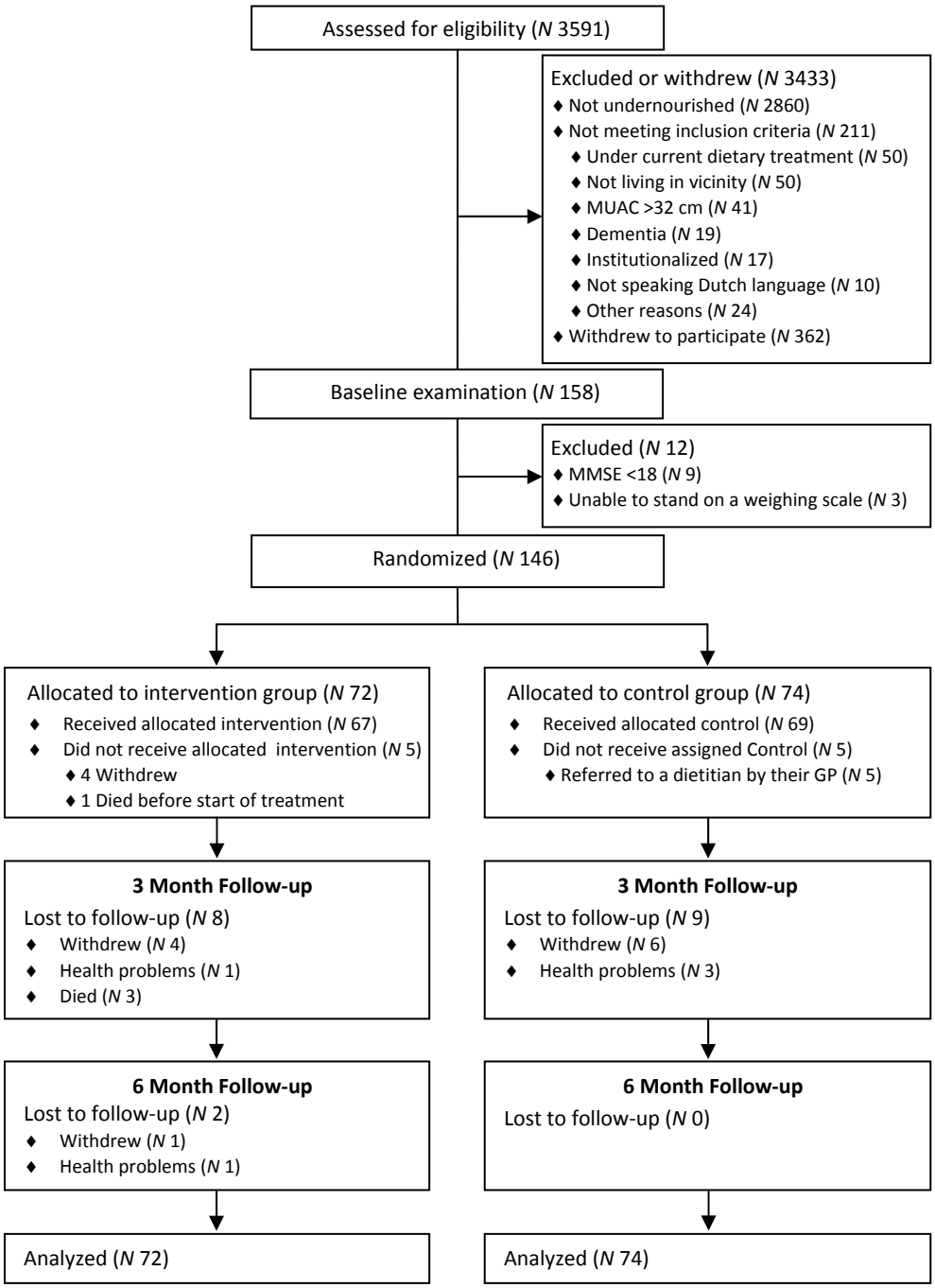


Table 1. Baseline characteristics of the participants.

Characteristics	Intervention (*N* 72)	Control (*N* 74)
Age in years, mean (SD)	80.6 ± 7.5	80.5 ± 7.5
Women, N (%)	45 (62.5)	49 (66.2)
Education, N (%)[a]		
Low	13 (18.8)	19 (26.0)
Medium	43 (62.3)	43 (58.9)
High	13 (18.8)	11 (15.1)
Income, N (%)[b]		
Low	5 (6.9)	9 (12.2)
Medium	24 (33.3)	17 (23.0)
High	33 (45.8)	38 (51.4)
Unknown/refuse	10 (13.9)	10 (13.5)
Living alone, N (%)	43 (60.6)	53 (71.6)
Help with personal care, N (%)		
No help	50 (70.4)	53 (71.6)
Informal help	2 (2.8)	2 (2.7)
Professional help	19 (26.8)	19 (25.7)
Help with household care, N (%)		
No help	21 (30.0)	21 (28.4)
Informal help	12 (17.1)	19 (25.7)
Professional help	37 (52.9)	34 (45.9)
$SNAQ^{65+}$ criteria undernutrition, N (%)		
Weight loss ≥4 kg/ 6 months	23 (31.9)	26 (35.1)
MUAC <25 cm	35 (48.6)	37 (50.0)
Both criteria	14 (19.4)	11 (14.9)
BMI in kg/m^2, mean (SD)	21.6 ± 3.1	21.7 ± 3.6
MUAC in cm, mean (SD)	24.8 ± 3.3	24.7 ± 2.6
Number of chronic diseases, N (%)		
0	14 (19.4)	19 (25.7)
1	33 (45.8)	19 (25.7)
2	11 (15.3)	20 (27.0)
≥3	14 (19.4)	16 (21.6)
Number of used medication, N (%)		
0	5 (6.9)	9 (12.2)
1 – 2	14 (19.4)	18 (24.3)
3 – 4	24 (33.3)	15 (20.3)
≥5	29 (40.3)	32 (43.2)

Table 1. Continued.

Characteristics	Intervention (*N* 72)	Control (*N* 74)
Use of calcium plus vitamin D supplement, N (%)	15 (21.1)	13 (17.8)
Use of oral nutritional supplements in past month, N (%)	11 (15.5)	8 (10.8)
Poor appetite past week, N (%)	24 (34.3)	29 (39.2)
MMSE score (range 18-30), mean (SD)	27.0 ± 2.6	26.6 ± 3.1
Depressive symptoms, N (%)[c]	25 (36.2)	26 (35.1)
Poor self-rated health, N (%)[d]	9 (12.7)	6 (8.1)

MMSE, Mini Mental State Examination; MUAC, mid-upper arm circumference; SNAQ^{65+}, Short Nutritional Assessment Questionnaire 65+

[a] Categories education level: 'low' = no education completed and lower general education; 'medium' = lower vocational education, intermediate general education, intermediate vocational education and higher general education; 'high' = higher vocational education and scientific education; [b] Categories household monthly income: 'low' ≤€900; 'medium' €901 - €1299; 'high' ≥€1300; [c] Assessed by the Center for Epidemiologic Studies Depression scale (CES-D, range 0-60). Scores ≥16 were defined as depressive symptoms; [d] Assessed by the question: 'How is your health in general?', with response categories 'sometimes good, sometimes poor' and 'poor' defined as poor self-rated health

The mean values of the primary outcome measures at the 3 examinations and the results of the GEE analyses are shown in **Table 2**. No treatment effect on any of the primary outcome measures was observed. The treatment effect during 6 months follow-up was 0.49 kg on body weight, 0.15 points on physical performance and 0.49 kg on handgrip strength. The results of the GEE analyses for the secondary outcomes are shown in **Table 3**. No treatment effect was found on the secondary outcomes.

Predefined subgroup analyses showed that the treatment effect was not modified by time, sex or the assessment criteria of the SNAQ^{65+} ($P > 0.10$), but was modified by physical activity (statistically significant interaction with body weight ($P = 0.03$), but not with physical performance and handgrip strength). The treatment effect was 1.25 kg on body weight in physically active participants versus -0.20 kg in physically inactive participants (**Table 4**). Post hoc analyses showed that for appetite a statistically significant interaction was found with body weight ($P = 0.003$) and for energy intake with physical performance ($P = 0.10$) and handgrip strength ($P = 0.02$). The treatment effect was 1.21 kg on body weight in participants with a normal appetite versus -0.79 kg in participants with a poor appetite. The treatment effect was 1.69 kg on handgrip strength in participants with a low energy intake versus -0.92 kg in participants with a high energy intake.

Table 2. Primary outcome measures at all examinations and mean difference during 6 months follow-up.

Outcome measures	Baseline	3 months	6 months	Beta (95% CI)[a]	*P*
Body weight, kg					
Intervention	58.0 (11.2)	58.2 (11.4)	58.3 (10.9)	0.49 (-0.15; 1.12)	0.13
Control	57.5 (9.9)	57.4 (9.9)	57.0 (9.7)		
Physical performance score					
Intervention	7.4 (3.2)	7.5 (3.1)	7.2 (3.3)	0.15 (-0.33; 0.64)	0.53
Control	7.2 (3.4)	7.1 (3.2)	7.1 (3.6)		
Handgrip strength, kg					
Intervention	21.1 (9.6)	21.1 (8.9)	21.6 (9.1)	0.49 (-0.62; 1.60)	0.39
Control	21.3 (8.5)	21.2 (8.9)	21.4 (8.7)		

Table 3. Secondary outcome measures at all examinations and mean difference during 6 months follow-up.

Outcome variables	Baseline	3 months	6 months	Beta (95% CI)[a]	*P*
Fat Free Mass, kg					
Intervention	40.9 (8.7)	41.9 (9.2)	41.9 (9.2)	-0.02 (-0.93; 0.79)	0.95
Control	39.9 (7.6)	40.4 (7.6)	40.4 (7.6)		
Energy intake, kcal					
Intervention	1655.3 (691.9)	1697.6 (594.0)	1770.9 (714.9)	97.18 (-48.91; 243.27)	0.19
Control	1726.5 (536.0)	1635.9 (436.5)	1694.6 (472.3)		
Protein intake, gram					
Intervention	66.1 (31.6)	69.3 (27.3)	69.2 (30.2)	2.42 (-4.38; 9.21)	0.49
Control	71.7 (29.2)	67.5 (21.1)	69.4 (23.0)		

[a] The β coefficient (and *P* value) represents the overall treatment effect on the outcome measures over time (adjusted for baseline) and was derived from a generalized estimating equation (GEE) model (coefficient on study group)

Table 4. Predefined and post-hoc subgroup analyses for physical activity, appetite and energy intake at baseline**.**

	Body weight		Physical performance score		Handgrip strength	
Subgroups	**Beta (95% CI)**	***P***	**Beta (95% CI)**	***P***	**Beta (95% CI)**	***P***
Physical activity						
<728 min/ week	-0.20 (-1.16; 0.75)	0.67	0.27 (-0.50; 1.03)	0.49	-0.32 (-2.01; 1.38)	0.72
≥728 min/ week	1.25 (0.70; 2.11)	<0.001	0.29 (-0.29; 0.88)	0.32	1.30 (-0.14; 2.74)	0.08
Appetite last week						
Poor appetite	-0.79 (-1.86; 0.27)	0.14	0.22 (-0.80; 1.25)	0.67	1.43 (-0.60; 3.45)	0.17
Normal appetite	1.21 (0.45; 1.96)	0.002	0.20 (-0.34; 0.74)	0.47	0.09 (-1.26; 1.43)	0.90
Energy intake						
<1568 kcal/ day	0.59 (-0.38; 1.55)	0.23	0.60 (-0.10; 1.30)	0.09	1.69 (0.10; 3.28)	0.04
≥1568 kcal/ day	0.57 (-0.36; 1.49)	0.23	-0.20 (-0.86; 0.46)	0.55	-0.92 (-2.37; 0.52)	0.21

[a] The β coefficient (and *P* value) represents the overall treatment effect on the outcome measures over time (adjusted for baseline) and was derived from a generalized estimating equation (GEE) model (coefficient on study group)

Discussion

This study was designed to determine the effects of a dietetic treatment in older, undernourished, community-dwelling individuals. The treatment was provided by regular dietitians working in primary care who received an additional training on treating older, undernourished, individuals. After 6 months, no treatment effect was observed on the primary outcomes body weight, physical performance and handgrip strength, and on the secondary outcomes fat-free mass, energy intake and protein intake.

To our knowledge, this is the first study examining the effect of dietetic treatment alone in older, undernourished, community-dwelling individuals. Previous studies in primary care focused on the effect of a standard prescription of ONS (16). The effect of dietetic treatment alone in older, undernourished individuals was only investigated in a study including hospitalized patients (20). In that study an individualized dietetic treatment consisting of 4 consults, whereby ONS was prescribed if needed, was compared to standard hospital care. A positive treatment effect was shown on the Mini Nutritional Assessment score and on mortality after 6 months follow-up, but not on body weight or nutritional intake. The latter results are in line with our results in a primary care setting.

There are several characteristics of the treatment design, treatment implementation and the participants themselves that could have contributed to the absence of a treatment effect in our study. A component of the treatment design that may have played a role was the duration of follow-up. Previous studies using ONS showed statistically significant positive effects on body weight after 6 months follow-up (36, 37), demonstrating that treatment effects of a nutritional intervention are detectable after this follow-up duration. However, in our study, treatment was completed in 78% of the intervention group and 22% was still in treatment at 6 months based on the information from the dietitians' evaluation form. We cannot exclude that the effects of a dietetic intervention are established later than the effects of ONS and more long-term studies are needed. With respect to the treatment implementation, all participating dietitians received an extensive training about the preferred treatment. A regular primary care dietetic treatment, complemented with additional training, is probably not sufficient to achieve effects in this population when focused on nutrition only. The study population was also quite frail: mean age was high, most participants were chronically undernourished based on a low MUAC, and the majority was suffering from one or more chronic diseases and was using multiple medications. Dietetic treatment only may not have been sufficient to improve nutritional status in frail older persons. Specific characteristics of the participants may also have contributed to the lack of a treatment effect, as not all participants in the intervention group were motivated to follow a treatment or were willing to change their

diet. At baseline, most participants (86%) were aware of the importance of a good nutritional status, but only 36% reported to be willing to receive a specific treatment for undernutrition and 24% reported to be willing to change their diet if needed. Finally, similar to all other studies focusing on the treatment of undernutrition, we cannot ensure that the participants were truly undernourished, as still no golden standard exists. More future studies are required to determine who will benefit from what specific dietetic intervention in order to effectively treat undernutrition in older, community-dwelling individuals. In addition, the effects of a multidisciplinary approach of the often complex situation that may have caused undernutrition should be investigated.

Subgroup analyses showed a statistically significant treatment effect on body weight in individuals with a normal appetite and in those who were physically active at baseline. This probably implies that for individuals with a poor appetite and for those with a low physical activity level other dietetic intervention strategies might be preferred, while for relatively 'healthy' individuals the investigated dietetic treatment might be effective. However, the treatment effect was not found on functional outcome measures in the subgroup analyses. Therefore, the results of the performed subgroup analyses should be interpreted carefully and beneficial effects on functional outcome measures should first be established in future studies before implementing this strategy.

A major strength of this study is the drop-out rate of 13%, which is relatively low compared to other 6-months nutritional intervention studies in older individuals (20, 37, 38), especially when considering the high frailty level of the study sample. Another important strength was the study setting, as the study was conducted using trained dietitians working in a regular primary care setting. This makes the results applicable to the usual care situation.

From the current study we can conclude that dietetic treatment of older, undernourished, community-dwelling individuals as currently provided by trained dietitians in primary care in the Netherlands had no effect on body weight, physical performance, handgrip strength, fat-free mass, energy intake and protein intake after 6 months. A long-term, multidisciplinary approach for successful treatment of undernutrition in primary care should be investigated in future studies.

References

1. Wakimoto P, Block G. Dietary intake, dietary patterns, and changes with age: an epidemiological perspective. J Gerontol A Biol Sci Med Sci 2001;56 Spec No 2:65-80.
2. Meijers JM, Schols JM, van Bokhorst-de van der Schueren MA, Dassen T, Janssen MA, Halfens RJ. Malnutrition prevalence in The Netherlands: results of the annual Dutch national prevalence measurement of care problems. Br J Nutr 2009;101:417-23.
3. Chen CC, Schilling LS, Lyder CH. A concept analysis of malnutrition in the elderly. J Adv Nurs 2001;36:131-42.
4. Hickson M. Malnutrition and ageing. Postgrad Med J 2006;82:2-8.
5. Schilp J, Wijnhoven HA, Deeg DJ, Visser M. Early determinants for the development of undernutrition in an older general population: Longitudinal Aging Study Amsterdam. Br J Nutr 2011;106:708-17.
6. Payette H, Gray-Donald K, Cyr R, Boutier V. Predictors of dietary intake in a functionally dependent elderly population in the community. Am J Public Health 1995;85:677-83.
7. Cereda E, Valzolgher L, Pedrolli C. Mini nutritional assessment is a good predictor of functional status in institutionalised elderly at risk of malnutrition. Clin Nutr 2008;27:700-5.
8. Oliveira MR, Fogaca KC, Leandro-Merhi VA. Nutritional status and functional capacity of hospitalized elderly. Nutr J 2009;8:54.
9. Keller HH, Ostbye T, Goy R. Nutritional risk predicts quality of life in elderly community-living Canadians. J Gerontol A Biol Sci Med Sci 2004;59:68-74.
10. Payette H, Coulombe C, Boutier V, Gray-Donald K. Nutrition risk factors for institutionalization in a free-living functionally dependent elderly population. J Clin Epidemiol 2000;53:579-87.
11. Corrada MM, Kawas CH, Mozaffar F, Paganini-Hill A. Association of body mass index and weight change with all-cause mortality in the elderly. Am J Epidemiol 2006;163:938-49.
12. Locher JL, Roth DL, Ritchie CS, et al. Body mass index, weight loss, and mortality in community-dwelling older adults. J Gerontol A Biol Sci Med Sci 2007;62:1389-92.
13. Payette H, Coulombe C, Boutier V, Gray-Donald K. Weight loss and mortality among free-living frail elders: a prospective study. J Gerontol A Biol Sci Med Sci 1999;54:M440-5.
14. Schilp J, Kruizenga HM, Wijnhoven AHA, et al. High prevalence of undernutrition in Dutch community-dwelling older individuals. Nutrition 2012;28(11-12):1151-6.
15. Elderly people live independently to increasingly older ages. CBS Statline Netherlands, 2011.
16. Milne AC, Potter J, Vivanti A, Avenell A. Protein and energy supplementation in elderly people at risk from malnutrition. Cochrane Database Syst Rev 2009:CD003288.
17. Baldwin C, Parsons TJ. Dietary advice and nutritional supplements in the management of illness-related malnutrition: systematic review. Clin Nutr 2004;23:1267-79.

18. Weekes CE, Emery PW, Elia M. Dietary counselling and food fortification in stable COPD: a randomised trial. Thorax 2009;64:326-31.

19. Ravasco P, Monteiro-Grillo I, Vidal PM, Camilo ME. Dietary counseling improves patient outcomes: a prospective, randomized, controlled trial in colorectal cancer patients undergoing radiotherapy. J Clin Oncol 2005;23:1431-8.

20. Feldblum I, German L, Castel H, Harman-Boehm I, Shahar DR. Individualized nutritional intervention during and after hospitalization: the nutrition intervention study clinical trial. J Am Geriatr Soc 2011;59:10-7.

21. Wijnhoven HA, Schilp J, van Bokhorst-de van der Schueren MA, et al. Development and validation of criteria for determining undernutrition in community-dwelling older men and women: The Short Nutritional Assessment Questionnaire 65+. Clin Nutr 2012;31:351-8.

22. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.

23. Pucci E, Belardinelli N, Borsetti G, Rodriguez D, Signorino M. Information and competency for consent to pharmacologic clinical trials in Alzheimer disease: an empirical analysis in patients and family caregivers. Alzheimer Dis Assoc Disord 2001;15:146-54.

24. Leibbrandt AJ, Kiefte-de Jong JC, Hogenelst MH, Snoek FJ, Weijs PJ. Effects of the PRo-active Interdisciplinary Self-MAnagement (PRISMA, Dutch DESMOND) program on dietary intake in type 2 diabetes outpatients: a pilot study. Clin Nutr 2010;29:199-205.

25. Ishibashi N, Plank LD, Sando K, Hill GL. Optimal protein requirements during the first 2 weeks after the onset of critical illness. Crit Care Med 1998;26:1529-35.

26. Roza AM, Shizgal HM. The Harris Benedict equation reevaluated: resting energy requirements and the body cell mass. Am J Clin Nutr 1984;40:168-82.

27. Sauerwein HP, Strack van Schijndel RJ. Perspective: How to evaluate studies on peri-operative nutrition? Considerations about the definition of optimal nutrition for patients and its key role in the comparison of the results of studies on nutritional intervention. Clin Nutr 2007;26:154-8.

28. Frank E, Dunlop AL. What does a patient's outfit weight? Fam Med 2000;32:595-6.

29. Visser M, Launer LJ, Deurenberg P, Deeg DJ. Total and sports activity in older men and women: relation with body fat distribution. Am J Epidemiol 1997;145:752-61.

30. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49:M85-94.

31. The Netherlands Nutrition Centre. NEVO Dutch food composition table 2006. The Hague, The Netherlands, 2006.

32. Kyle UG, Genton L, Karsegard L, Slosman DO, Pichard C. Single prediction equation for bioelectrical impedance analysis in adults aged 20--94 years. Nutrition 2001;17:248-53.

33. Kyle UG, Genton L, Slosman DO, Pichard C. Fat-free and fat mass percentiles in 5225 healthy subjects aged 15 to 98 years. Nutrition 2001;17:534-41.

34. Milne AC, Avenell A, Potter J. Meta-analysis: protein and energy supplementation in older people. Ann Intern Med 2006;144:37-48.

35. Stel VS, Smit JH, Pluijm SM, Visser M, Deeg DJ, Lips P. Comparison of the LASA Physical Activity Questionnaire with a 7-day diary and pedometer. J Clin Epidemiol 2004;57:252-8.

36. Tidermark J, Ponzer S, Carlsson P, et al. Effects of protein-rich supplementation and nandrolone in lean elderly women with femoral neck fractures. Clin Nutr 2004;23:587-96.

37. Wouters-Wesseling W, Van Hooijdonk C, Wagenaar L, Bindels J, de Groot L, Van Staveren W. The effect of a liquid nutrition supplement on body composition and physical functioning in elderly people. Clin Nutr 2003;22:371-7.

38. Edington J, Barnes R, Bryan F, et al. A prospective randomised controlled trial of nutritional supplementation in malnourished elderly in the community: clinical and health economic outcomes. Clin Nutr 2004;23:195-204.

CHAPTER 6

Is dietetic treatment for undernutrition in older individuals in primary care cost-effective?

Janneke Schilp
Judith E. Bosmans
Hinke M. Kruizenga
Hanneke A.H. Wijnhoven
Marjolein Visser

Submission in preparation

Abstract

Background. Undernutrition in older age is associated with adverse clinical outcomes and high health care costs. This study aimed to evaluate the cost-effectiveness of a dietetic treatment in primary care compared to usual care in older, undernourished, community-dwelling individuals.

Methods. A total of 146 undernourished, independently living older (≥65 years) participants were randomized to receive either dietetic treatment (*N* 72) or usual care (*N* 74). Outcomes were change in kg body weight compared to baseline and Quality Adjusted Life Years (QALYs) after 6 months. Costs were measured from a societal perspective. The main analysis was performed according to the intention-to-treat principle. Multiple imputation was used to impute missing data and bootstrapping was used to estimate uncertainty surrounding cost differences and incremental cost-effectiveness ratios. Cost-effectiveness planes and cost-effectiveness acceptability curves were estimated.

Results. After 6 months, no statistically significant differences were found between the dietetic treatment and usual care group in body weight change (mean difference 0.78 kg, 95% CI -0.26; 1.82), QALYs (mean difference 0.001, 95% CI -0.04; 0.04) and total costs (mean difference €1645, 95% CI -525; 3547). The ICUR for QALYs was not interpretable. The ICER for body weight gain was 2111. The probability that dietetic treatment is cost-effective compared to usual care was 0.78 for a ceiling ratio of €5000 for body weight and 0.06 for a ceiling ratio of €20.000 for QALY.

Conclusion. This study shows that dietetic treatment in older, undernourished, community-dwelling individuals is not cost-effective compared to usual care.

Introduction

Undernutrition is a common condition among older individuals in Western society. In the community, the prevalence of undernutrition varies between 15 and 35% (1, 2), depending on the specific study population and the criteria used to define undernutrition. The absolute number of undernourished, older individuals in primary care is expected to increase due to the ageing of the society (3) and the tendency to live independently at home to increasingly older ages (4). Undernutrition is associated with adverse clinical outcomes such as reduced functional status, poorer quality of life and increased mortality (5-8). Furthermore, undernutrition is shown to be associated with higher general practice consultation rates, higher medication prescription rates and higher hospitalization rates (8-10).

A recent systematic review showed a positive effect of oral nutritional supplements (ONS) on nutritional status in older, undernourished individuals (11). However, much less is known about the effect of treatment including dietetic consults, which is usually provided in the primary care setting. The effect of a dietetic treatment was only studied in hospital in- and outpatients, showing increases in nutritional intake and body weight and a lower mortality risk (12-14).

Considering the high health care costs associated with the presence of undernutrition in the community (9), information is not only needed about the effectiveness of dietetic treatment, but also about its cost-effectiveness. In a cost-effectiveness analysis (CEA) the extra costs of a new intervention strategy are balanced against its extra effects compared to usual care. This information can support policy makers in making resource allocation decisions. In hospitalized patients after discharge, ONS was found to be cost-effective compared to usual care in reducing functional limitations, but not in increasing quality of life and physical activity (15). However, cost-effectiveness studies of dietetic treatment in the community are lacking.

Therefore, the aim of this study was to evaluate the cost-effectiveness of dietetic treatment in primary care compared to usual care in older, undernourished, community-dwelling individuals.

Methods

Design

The economic evaluation was conducted alongside a Randomized Controlled Trial performed in the Netherlands between October 2009 and June 2011, comparing dietetic treatment for undernutrition with usual care: the Nutrition in Primary Care Study (NPCS). The design of the study is summarized here and is extensively described elsewhere (16). The study is in accordance with the Declaration of Helsinki, has been approved by the Ethics Review Board of the VU University Medical Center Amsterdam and is registered at the Dutch Trial Register. Follow-up examinations were performed at 3 and 6 months after the baseline examination. All examinations took place at the participants' home and were executed by a trained researcher or research assistant.

Recruitment and randomization

Participants for the NPCS were recruited in various primary care locations (general practice, home care, outpatient clinic, senior citizen centers, advertisements and pharmacies) by nurses, researchers and research assistants trained to assess undernutrition. Subjects were eligible for the study if they were aged 65 years or older, lived independently and were identified as being undernourished using the following criteria from the Short Nutritional Assessment Questionnaire 65+ ($SNAQ^{65+}$) (17): mid-upper arm circumference (MUAC) <25 cm and/or ≥4 kg self-reported unintentional weight loss within the past six months. MUAC was measured with a measuring tape at the centre point of the left upper-arm to the nearest mm with the arm hanging loosely. Unintentional weight loss was assessed by the following question: 'Have you unintentionally lost 4 kilograms or more within the past 6 months?'.

Subjects were excluded from the study if they were under current dietetic treatment, were diagnosed with dementia, were not living in the vicinity of Amsterdam (where the dietetic treatment was provided), did not speak the Dutch language, or had a MUAC >32 cm. Furthermore, participants with a Mini Mental State Examination Score <18 and those unable to stand on the weighing scale were excluded after the baseline examination.

Randomization allocation was performed at the level of the participants within one day after the baseline examination by a computerized random number generator (http://www.randomization.com) using a 4- and 6-blocked randomization scheme.

All participants were prescribed a combined calcium (1000 mg calcium carbonate) plus vitamin D (800 IU cholecalciferol) supplement by their own general practitioner (if not already being used) during the study. This was done to avoid bias of potential prescription

of vitamin D as part of the dietetic treatment, since research has shown that vitamin D has a positive effect on functional outcome measures (18, 19).

Control group

Participants allocated to the control group received usual care and a standard brochure of the Netherlands Nutrition Centre with general information about healthy eating habits.

Intervention group

Participants allocated to the intervention group were referred to a dietitian, who received a specific training on the treatment of older, undernourished individuals. The intervention treatment was a combination of both face-to-face and telephone consultations. The number of consultations depended on the nutritional situation, needs and desires of the participant. The dietitian provided a personal workbook to each participant to identify specific risk factors that may have led to undernutrition and to choose specific goals of behavioral change to achieve. The dietitians were instructed to aim at adequate nutritional intake by participants, preferably by regular foods and beverages, using motivational interviewing techniques. In case of (continuing) insufficient intake, dietitians were instructed to prescribe additional ONS and/or tube feeding. More information about the dietetic training and treatment can be found elsewhere (16).

Cost measures

The economic evaluation was conducted from a societal perspective. Data on health care utilization were collected over 6 months using two cost diaries, each covering a period of three months. The information on health care utilization was used to calculate costs. Dutch standard costs were used to value resource use (20, 21). Lost productivity costs were not included, because only individuals exceeding the Dutch age of retirement of 65 years were included in the study. Direct healthcare costs included costs of visits to healthcare providers and admissions to a hospital or other institutions. The number of dietetic consultations, with potential prescription of ONS, to intervention participants was recorded by the dietitians on an evaluation form. These forms were used to calculate costs of the dietetic treatment in the intervention group. In case of missing evaluation forms (*N* 7) and for participants in the control group, costs of dietetic treatment and ONS were based on the information provided by the participant in the cost diaries. Medication costs, including the prescribed calcium/vitamin D supplement, and ONS costs were valued using prices of the Royal Dutch Society of Pharmacy (22). Direct non-healthcare costs were

informal care costs (care provided by family, friends or volunteers) and taxi transport costs to healthcare provider or institution.

Clinical outcome measures

The outcomes in the economic evaluation were quality of life and body weight. Quality of life was measured using the EuroQol (EQ-5D), a standardized instrument consisting of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) with three levels (no/some/extreme problems) each (23). The EQ-5D scores were used to calculate utilities for each health state using the Dutch tariff (24). Quality Adjusted Life Years (QALYs) were calculated by multiplying the utilities with the amount of time a patient spent in a particular health state using the area under the curve method. Transitions between health states were linearly interpolated. The maximum QALY score for the 6-months follow-up was 0.50 (6 months of follow-up in perfect health with a utility of 1 divided by 12 months in a year). Body weight was measured without shoes to the nearest 0.5 kg using a calibrated balance beam scale (Seca 761). Adjustments were made for clothing (-1.77 kg for men; -1.13 kg for women) (25) and when necessary adjustments were made for shoes (-0.40 kg for men; -0.28 kg for women) (25) or corset (-1 kg) (26). The change in body weight between the baseline and 6-months examination was calculated.

Statistical analyses

It was estimated that a minimum of 62 participants in each group was needed to detect a statistically significant difference ($\alpha = 0.05$) in body weight of 2.23% (27) after 6 months with 80% power. The main analyses were performed according to the intention-to-treat principle. Multiple imputation by chained equations (predictive mean matching) was used to impute missing cost and effect data. Imputation of cost data was done at the level of cost categories. An imputation model containing important demographic and prognostic variables was used to create five imputed datasets, each of which was analyzed separately. The results of the five analyses were pooled using Rubin's rules (28).

Healthcare utilization rates were calculated based on participants with complete cost data during follow-up. Bias-corrected accelerated bootstrapping with 5000 replications was used to estimate confidence intervals around health care utilization differences. Costs generally have a highly skewed distribution. Therefore, the 'approximate bootstrap confidence' (ABC) algorithm was used to estimate 95% confidence intervals around cost differences (29, 30).

The incremental cost-utility ratio (ICUR) was calculated by dividing the difference in total costs between the two groups by the difference in QALYs between the two groups. The incremental cost-effectiveness ratio (ICER) was calculated by dividing the difference in total costs by the difference in body weight. The ICUR/ICER indicates the additional investments needed for the intervention to gain one extra unit of effect compared to usual care. Non-parametric bootstrapping was used to estimate the uncertainty surrounding the ICUR/ ICER (5000 replications). The bootstrapped cost-effect pairs were plotted on a cost-effectiveness plane (CE plane) (31) and used to estimate cost-effectiveness acceptability (CEA) curves. CEA curves show the probability that the intervention is cost-effective compared to the control treatment for a range of ceiling ratios. The ceiling ratio is defined as the amount of money society is willing to pay to gain one unit of effect (32).

Two sensitivity analyses were performed. In a complete case analysis participants without complete follow-up data on cost and effect measures were excluded (*N* 32). In a per protocol analysis participants in the intervention group who received no or less than 30 minutes dietetic consultation (*N* 8) and participants in the control group who were treated by a dietitian (*N* 5) were excluded.

The multiple imputation was performed using SPSS version 17.0 (SPSS, Chicago, USA) and the cost-effectiveness analyses were done using R statistical software version 2.14.0 (R development Core Team).

Results

The inclusion process and characteristics of participants are extensively described elsewhere and summarized here (16). A total of 146 participants were randomized to the intervention (*N* 72) and control (*N* 74) group and included in the main analysis. The baseline characteristics of the participants are shown in **Table 1**. In the intervention group 10 participants were lost to follow-up due to withdrawal (*N* 5), health problems (*N* 2) or death (*N* 3). In the control group 9 participants were lost to follow-up due to withdrawal (*N* 6) or health problems (*N* 3). Another 13 participants incomplete cost data (*N* 12) or clinical outcome measures (*N* 1). Thus, 114 participants (78%) had complete follow-up data and were included in the complete case analysis. Participants who were lost to follow-up were older at baseline compared to those with complete follow-up (mean age 83.4 versus 80.0 years). No other statistically significant differences in baseline characteristics were found between these groups.

Healthcare utilization

The cost categories and prices included in the economic evaluation are listed in **Table 2**. Also the utilization of health care resources during the study of participants who filled in both cost diaries is presented in **Table 2**. As expected, participants in the intervention group had more hours of dietetic consultations than the control group; 2.4 versus 0.2 hours. Furthermore, the intervention group received more hours professional physical home care during the trial, was more often admitted to a residential home and used a taxi more often compared to the control group. No other statistically significant differences were found.

At baseline, the percentage of participants reporting having used oral nutritional supplements in the past month was 14% in the intervention group and 7% in the control group (P = 0.27). These percentages were respectively 27% and 7% after 3 months (P = 0.01) and 37% and 11% after 6 months (P = 0.001).

Clinical outcomes and costs

Table 3 presents the pooled mean effects and total costs for the intervention and the control group after multiple imputation. The mean number of QALYs was equal in the intervention and control group. Mean body weight increased with 0.25 kg (SD 0.38) in the intervention group and decreased with 0.53 kg (SD 0.37) in the control group, but this difference was not statistically significant.

During the 6 months intervention period, total direct healthcare and non-healthcare costs were not statistically significantly different between the two groups. Primary care costs were the largest contributor to total costs in both groups. The costs of dietetic treatment and oral nutritional supplements were statistically significantly higher in the intervention group compared to the control group. Secondary care costs and medication costs were similar in the intervention and control group.

Table 1. Baseline characteristics.

	N (%)	
Characteristics	**Intervention (*N* 72)**	**Control (*N* 74)**
Women	45 (62.5)	49 (66.2)
Age in years, mean (SD)	80.6 (7.5)	80.5 (7.5)
Home situation		
Living alone	43 (60.6)	53 (71.6)
Living with partner/family	28 (39.4)	21 (28.4)
Aid domestic tasks		
No aid	21 (30.0)	21 (28.4)
Non-professional aid	12 (17.1)	19 (25.7)
Professional aid	37 (52.9)	34 (45.9)
Aid personal care		
No aid	50 (70.4)	53 (71.6)
Non-professional aid	2 (2.8)	2 (2.7)
Professional aid	19 (26.8)	19 (25.7)
$SNAQ^{65+}$ criteria undernutrition		
Weight loss ≥4 kg/ 6 months	23 (31.9)	26 (35.1)
MUAC <25 cm	35 (48.6)	37 (50.0)
Both criteria	14 (19.4)	11 (14.9)
Body weight in kg, mean (SD)	58.0 (11.3)	57.5 (9.9)
Body height in cm, mean (SD)	163.6 (8.8)	162.7 (8.7)
Body Mass Index in kg/m^2, mean (SD)	21.6 (3.1)	21.7 (3.6)
MUAC in cm, mean (SD)	24.8 (3.3)	24.7 (2.6)
Utility (EQ-5D), mean (SD)	0.71 (0.24)	0.68 (0.26)
Use of calcium plus vitamin D supplement	15 (21.1)	13 (17.8)
Number of used medication		
0	5 (6.9)	9 (12.2)
1 – 2	14 (19.4)	18 (24.3)
3 – 4	24 (33.3)	15 (20.3)
≥5	29 (40.3)	32 (43.2)

$SNAQ^{65+}$, Short Nutritional Assessment Questionnaire 65+; MUAC, mid-upper arm circumference; EQ-5D, EuroQol

Table 2. Health care utilization of the intervention and control group in participants with complete cost data during 6 months follow-up.

Type of utilization	Intervention *N* 60	Control *N* 55	Difference (95% CI)	Costs per unit (€) 2009
Direct health care costs				
Primary care				
General practitioner (no. visits)	3.5 (3.9)	2.5 (3.3)	1.0 (-0.3 ; 2.3)	€14 - 43
Dietitian (no. hours)	2.4 (1.4)	0.2 (0.9)	2.2 (1.7 ; 2.6)	€27
Physiotherapist (no. visits)	5.1 (10.5)	8.1 (14.9)	-3.1 (-8.4; 1.5)	€36
Ergo therapist (no. visits)	0.3 (2.1)	0.4 (1.7)	-0.1 (-0.7 ; 0.7)	€22
Speech therapist (no. visits)	0.4 (3.0)	0.5 (4.0)	-0.2 (-1.7 ; 0.9)	€33
Paramedic (no. visits)	0.0 (0.0)	0.3 (2.2)	-0.3 (-0.6 ; 0.2)	- [a]
Social worker (no. visits)	0.0 (0.0)	0.1 (0.6)	-0.1 (-0.3 ; 0.0)	€65
Psychologist (no. visits)	0.0 (0.3)	0.1 (0.7)	-0.1 (-0.4 ; 0.0)	€80
Psychotherapist (no. visits)	0.0 (0.0)	0.3 (1.3)	-0.3 (-0.8 ; 0.0)	€77
Prof. household home care (no. hours)	41.7 (40.9)	33.3 (35.2)	8.3 (-5.7 ; 22.1)	€24
Prof. physical home care (no. hours)	22.5 (46.7)	9.1 (18.8)	13.4 (2.5 ; 28.7)	€48
Secondary care				
Medical specialists (no. visits)	3.9 (4.6)	3.0 (4.2)	0.9 (-0.7 ; 2.5)	€72
Admission hospital (no. days)	2.5 (5.7)	1.3 (6.2)	1.2 (-1.5 ; 3.0)	€457
Admission nursing home (no. days)	0.7 (5.7)	0.6 (4.2)	0.2 (-1.6 ; 2.3)	€238
Admission residential home (no. days)	0.8 (5.4)	0.0 (0.0)	0.8 (0.1 ; 3.5)	€90
Ambulance transportation (no. rides)	0.1 (0.3)	0.0 (0.3)	0.0 (-0.1 ; 0.1)	€262
Medication (no. prescribed at 6 months)	5.0 (3.2)	6.0 (4.2)	-0.8 (-2.1 ; 0.4)	- [b]
ONS (no. units prescribed)	63.3 (117.5)	10.9 (32.8)	58.6 (32.1 – 93.6)	€1.94
Direct non-healthcare costs				
Informal care (no. hours)	8.6 (24.4)	7.0 (19.3)	1.6 (-6.0 ; 10.2)	€12.50
Taxi (no. rides)	2.4 (8.2)	0.4 (1.5)	2.1 (0.5 ; 5.2)	- [c]

[a] Depending on the type of paramedic health care provider; [b] Valued using prices of the Royal Dutch Society of Pharmacy; [c] Taxi costs were determined by asking the amount of rides and costs per ride

Table 3. Pooled mean total effects and costs and difference in mean total effects and costs during 6-months follow-up.

Pooled variables	Mean total effect (SE) Intervention *N* 72	Control *N* 74	Difference (95% CI)
Effects			
QALY	0.36 (0.01)	0.36 (0.01)	0.001 (-0.04 ; 0.04)
Body weight	0.25 (0.38)	-0.53 (0.37)	0.78 (-0.26 ; 1.82)
Costs			
Direct healthcare costs	4778 (777)	3167 (654)	1611 (-533 ; 3475)
Primary care costs[a]	2521 (393)	1880 (230)	641 (-202 ; 1485)
Secondary care costs	1710 (510)	980 (615)	730 (-1124 ; 2155)
Medication costs	410 (63)	280 (59)	130 (-75 ; 326)
ONS costs	136 (30)	27 (9)	109 (57 ; 178)
Direct non-healthcare costs	135 (44)	101 (33)	34 (-61 ; 149)
Total direct costs	4913 (792)	3268 (655)	1645 (-525 ; 3546)

QALY, Quality Adjusted Life Years; ONS, Oral Nutritional Supplements

[a] Include mean dietitian costs: €62 (SE €5) in intervention group and €3 (SE €3) in control group, with €59 (95% CI 46; 70) difference between groups

Cost-utility and cost-effectiveness analyses

Table 4 presents the results of the cost-utility and cost-effectiveness analyses. Due to the small difference in QALYs between the intervention and control group after 6 months, the ICUR was extremely large and not interpretable. Most bootstrapped cost-effect pairs were located in the north east (48%) and north west (46%) quadrants of the CE plane confirming the statistically non-significant differences in costs and effects. The CEA curve indicated that for a ceiling ratio of €20.000 per QALY, the probability that the intervention is cost-effective is approximately 0.06 (figure not shown).

The ICER for body weight gain was 2111. This means that €2111 needs to be invested to gain 1 kg body weight in the intervention group compared to the control group.

Table 4. Results of the cost-utility and cost-effectiveness analyses.

	Sample size		Cost difference (€)	Effect difference	ICUR/ICER	Distribution (%) CE plane*			
Outcome effect	**I**	**C**	**(95% CI)**	**(95% CI)**		**NE**	**SE**	**SW**	**NW**
Intention to treat analysis									
QALY	72	74	1645 (-525 ; 3547)	0.001 (-0.04 ; 0.04)	1153462	48	4	1	46
Body weight	72	74	1645 (-525 ; 3547)	0.78 (-0.26 ; 1.82)	2111	88	6	0	6
Complete cases analysis									
QALY	60	54	1882 (-31 ; 3622)	-0.004 (-0.04 ; 0.04)	-470496	41	2	1	57
Body weight	60	54	1882 (-31 ; 3622)	0.63 (-0.36 ; 1.62)	2973	89	2	0	9
Per protocol analysis									
QALY	64	69	1700 (-380 ; 3573)	0.007 (-0.03 ; 0.05)	257366	59	4	0	36
Body weight	64	69	1700 (-380 ; 3573)	0.79 (-0.21 ; 1.80)	2140	90	5	0	6

I, intervention; C, control; NE, intervention more costly, more effective; SE, intervention less costly, more effective; SW, intervention less costly, less effective; NW, intervention more costly, less effective

Figure 1 shows the CE plane for body weight. Most bootstrapped cost-effect pairs for body weight were located in the north east quadrant (88%), meaning that the intervention was more effective on body weight and associated with higher costs than usual care, although not statistically significantly. The CEA curve (**Figure 2**) shows the probability that the intervention was cost-effective compared to usual care for a range of ceiling ratios. The probability that the intervention was cost-effective compared to usual care is approximately 0.06, 0.13, 0.24, 0.78 or 0.94 if society is willing to invest respectively €0, €500, €1000, €5000, or €20.000, respectively per kg weight gain.

In the complete cases and per protocol analyses, there were also no statistically significant differences in QALYs, body weight, and total costs between the intervention and control group. The results of the cost-utility and cost-effectiveness analyses were similar to the intention-to-treat analysis (Table 4).

Figure 1. Cost-effectiveness plane for the difference in body weight.

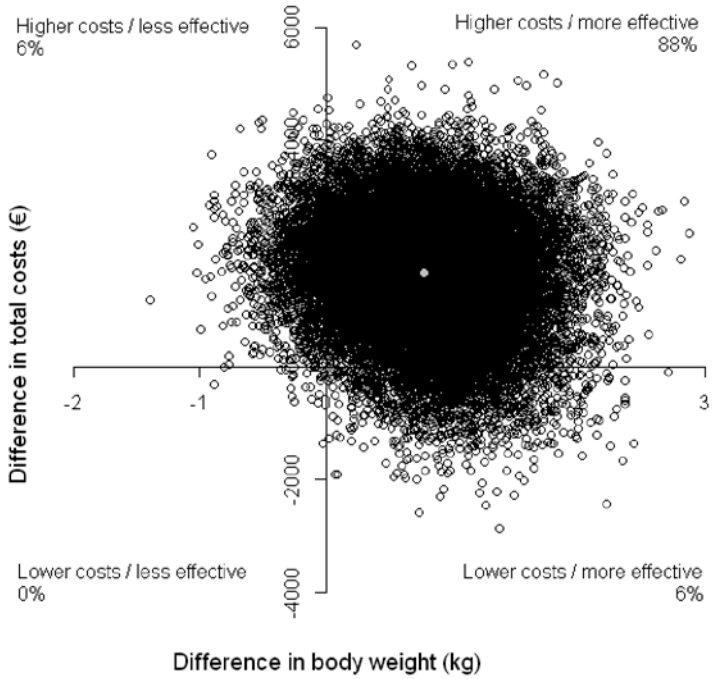
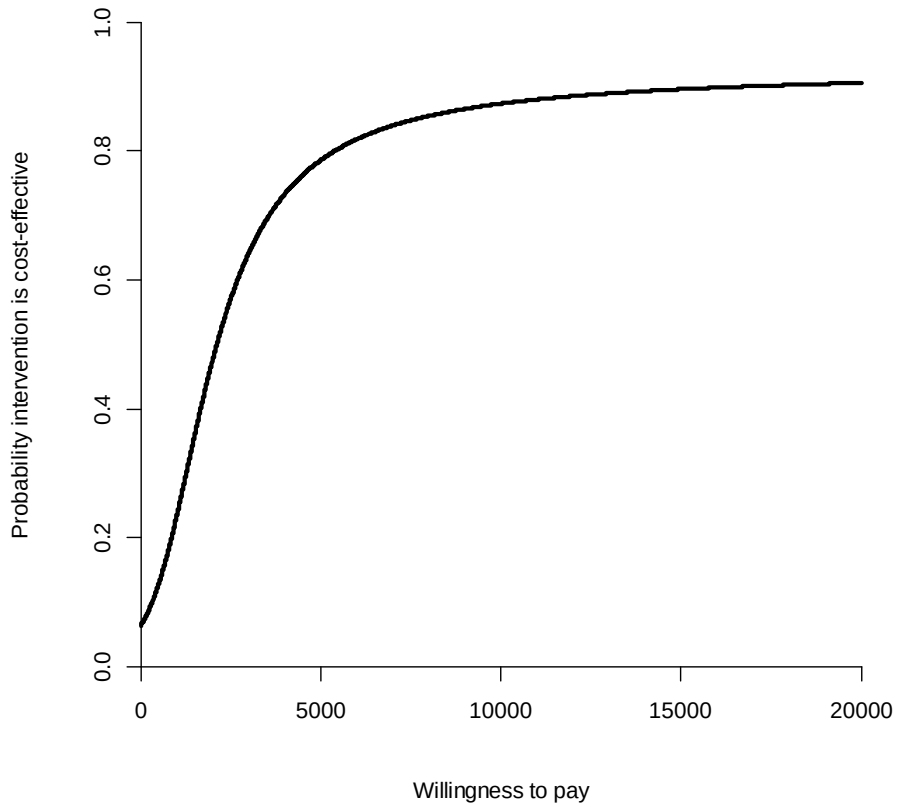


Figure 2. Cost-effectiveness acceptability curve for body weight.



Discussion

To the best of our knowledge, this is the first study that evaluated the cost-effectiveness of a dietetic treatment in primary care compared to usual care in older, undernourished, community-dwelling individuals. No statistically significant differences were found in effects and total costs. Based on the results of the cost-effectiveness analyses we conclude that dietetic treatment as provided in this study was not cost-effective for body weight and quality of life compared to usual care.

A recent study evaluated the cost-effectiveness of ONS use in combination with dietetic consultations to treat undernutrition in hospitalized patients after discharge (15). This study showed that the intervention was cost-effective compared to usual care in decreasing functional limitations, but not in increasing quality of life. However, we

hypothesize that this effect may be due to the calcium/vitamin D supplement that was only provided to the intervention group as part of the treatment, since earlier studies have shown significant effects of these supplements on functional outcome measures (18, 19). By prescribing the calcium/vitamin D supplement to both treatment groups in our study we aimed to evaluate the cost-effectiveness of the dietetic treatment itself. Similar to our study, the intervention was not considered cost-effective with regard to quality of life (also measured with EQ-5D).

In the present study, no statistically significant effect of the intervention was found on body weight gain. A possible explanation for this lack of effect may be the somewhat limited intensity and duration of the treatment. The limited intensity of the treatment is reflected in the total dietetic consultation time, which was 2.4 hours in the intervention group and 0.2 hours in the control group. Possibly more consultation time is needed to achieve an effect on body weight gain. Also, the duration of the follow-up may have been too short. After 6 months follow-up, the dietetic treatment was not completed for one out of five participants in the intervention group.

There was also no effect on quality of life in our study. We hypothesized that improvement of quality of life occurs after body weight gain. An additional logistic regression analysis showed that in the intervention group participants with a stable or gain in body weight after 6 months had a statistically non-significantly 0.03 higher QALY (95% CI -0.004; 0.07, $P = 0.08$) compared to those who lost weight. This trend confirms our hypothesized association between body weight change and quality of life. The follow-up period may have been too short for the intervention to be able to have a positive effect on quality of life. Only a few studies have investigated the effect of a nutritional intervention on quality of life. Two studies with a comparable follow-up period evaluating the use of ONS did also not show statistically significant effects on quality of life in older, undernourished individuals (33, 34).

Participants in the intervention group used professional physical home care more often, were admitted to a residential home more often and used a taxi more often compared to the control group. However, these differences in health care utilization were quite small and, since we cannot explain these differences to be caused by the intervention, were presumably based on chance. Moreover, there was no statistically significant difference in total direct healthcare and non-healthcare costs.

A limitation of this study is that the study was powered to detect differences in body weight, but was underpowered to detect relevant cost differences, which is reflected in the wide confidence intervals around the cost differences. However, this is a common problem in economic evaluations and to solve this problem very large numbers of

participants are needed (35). It may be considered unethical to continue a trial beyond the point at which clinical effectiveness is determined. Another limitation is that information about the number of dietetic consultations and the prescription of ONS was collected from the dietitians participating in the study, while for the control group only self-reported information could be used. An additional analysis was performed to determine the difference in dietetic consultation hours reported by the participant and the hours reported by the dietitian. Participants in the intervention group with both data available were included in this additional analysis (*N* 53). The participants underestimated the amount of dietetic consultation hours with 1.5 hours (SD 1.1). However, the number of participants in the control group who reported to receive treatment from a dietitian during the study was very small (*N* 5) and we do not expect this influences the results significantly. Finally, there is a variety of factors and characteristics associated with the development of undernutrition in older individuals (36). Besides poor nutrition, several medical, psychological, physical and social factors may contribute to the development and progression of undernutrition. These factors were not addressed in our treatment protocol. Probably, more attention has to be paid in future studies to identify and treat these underlying factors in order to treat undernutrition successfully. Hereby, a multidisciplinary approach of the complex situation may be helpful, with involving for example a physiotherapist, social worker, speech therapist or psychologist in the treatment plan.

An important strength of our study is that this is the first study evaluating the cost-effectiveness of dietetic treatment in undernourished older individuals in primary care. The pragmatic design of the study ensures that the results of our study are well applicable to the provision of dietetic treatment in daily practice. The increasing numbers of older individuals with undernutrition living in the community emphasize the need for research in this setting. Information about the cost-effectiveness of dietetic treatment in primary care is important for clinicians and policy makers, who can use this information in making resource allocation decisions.

In conclusion, this study shows that dietetic treatment of older, undernourished, community-dwelling individuals is not cost-effective as compared to usual care. For future studies, we recommend to take into account underlying factors associated with the undernourished condition. Also the intensity and duration of the treatment should probably be prolonged to at least one year in order to positively influence body weight and quality of life.

References

1. Chen CC, Schilling LS, Lyder CH. A concept analysis of malnutrition in the elderly. J Adv Nurs 2001;36:131-42.
2. Schilp J, Kruizenga HM, Wijnhoven AHA, et al. High prevalence of undernutrition in Dutch community-dwelling older individuals. Nutrition 2012;28(11-12):1151-1156.
3. Key figures of the population forecast 2010-2060. CBS Statline Netherlands, 2011.
4. CBS Statline Netherlands. Elderly people live independently to increasingly older ages. http://www.cbs.nl. Accessed at 12 July 2011.
5. Cereda E, Valzolgher L, Pedrolli C. Mini nutritional assessment is a good predictor of functional status in institutionalised elderly at risk of malnutrition. Clin Nutr 2008;27:700-5.
6. Keller HH, Ostbye T, Goy R. Nutritional risk predicts quality of life in elderly community-living Canadians. J Gerontol A Biol Sci Med Sci 2004;59:68-74.
7. Oliveira MR, Fogaca KC, Leandro-Merhi VA. Nutritional status and functional capacity of hospitalized elderly. Nutr J 2009;8:54.
8. Yang Y, Brown CJ, Burgio KL, et al. Undernutrition at baseline and health services utilization and mortality over a 1-year period in older adults receiving Medicare home health services. J Am Med Dir Assoc 2011;12:287-94.
9. Baumeister SE, Fischer B, Doring A, et al. The Geriatric Nutritional Risk Index predicts increased healthcare costs and hospitalization in a cohort of community-dwelling older adults: results from the MONICA/KORA Augsburg cohort study, 1994-2005. Nutrition 2011;27:534-42.
10. Martyn CN, Winter PD, Coles SJ, Edington J. Effect of nutritional status on use of health care resources by patients with chronic disease living in the community. Clin Nutr 1998;17:119-23.
11. Milne AC, Potter J, Vivanti A, Avenell A. Protein and energy supplementation in elderly people at risk from malnutrition. Cochrane Database Syst Rev 2009:CD003288.
12. Weekes CE, Emery PW, Elia M. Dietary counselling and food fortification in stable COPD: a randomised trial. Thorax 2009;64:326-31.
13. Ravasco P, Monteiro-Grillo I, Vidal PM, Camilo ME. Dietary counseling improves patient outcomes: a prospective, randomized, controlled trial in colorectal cancer patients undergoing radiotherapy. J Clin Oncol 2005;23:1431-8.
14. Feldblum I, German L, Castel H, Harman-Boehm I, Shahar DR. Individualized nutritional intervention during and after hospitalization: the nutrition intervention study clinical trial. J Am Geriatr Soc 2011;59:10-7.
15. Neelemaat F, Bosmans JE, Thijs A, Seidell JC, van Bokhorst-de van der Schueren MA. Oral nutritional support in malnourished elderly decreases functional limitations with no extra costs. Clin Nutr 2012;31(2):183-90.

16. Schilp J, Kruizenga HM, Wijnhoven HAH, van Binsbergen JJ, Visser M. Effects of a dietetic treatment in older, undernourished, community-dwelling individuals in primary care: a randomised controlled trial. Eur J Nutr, in revision.

17. Wijnhoven HA, Schilp J, van Bokhorst-de van der Schueren MA, et al. Development and validation of criteria for determining undernutrition in community-dwelling older men and women: The Short Nutritional Assessment Questionnaire 65+. Clin Nutr 2012;31:351-358.

18. Pfeifer M, Begerow B, Minne HW, Suppan K, Fahrleitner-Pammer A, Dobnig H. Effects of a long-term vitamin D and calcium supplementation on falls and parameters of muscle function in community-dwelling older individuals. Osteoporos Int 2009;20:315-22.

19. Zhu K, Austin N, Devine A, Bruce D, Prince RL. A randomized controlled trial of the effects of vitamin D on muscle strength and mobility in older women with vitamin D insufficiency. J Am Geriatr Soc 2010;58:2063-8.

20. Health Care Insurance Board. Handbook for cost studies, methods and guidelines for economic evaluation in health care. Diemen, The Netherlands, 2010 (actualized version).

21. Oostenbrink JB, Koopmanschap MA, Rutten FF. Standardisation of costs: the Dutch Manual for Costing in economic evaluations. Pharmacoeconomics 2002;20:443-54.

22. Z-index. G-standaard. The Hague, The Netherlands, 2009.

23. EuroQol--a new facility for the measurement of health-related quality of life. The EuroQol Group. Health Policy 1990;16:199-208.

24. Lamers LM, Stalmeier PF, McDonnell J, Krabbe PF, van Busschbach JJ. Measuring the quality of life in economic evaluations: the Dutch EQ-5D tariff. Ned Tijdschr Geneeskd 2005;149:1574-8.

25. Frank E, Dunlop AL. What does a patient's outfit weight? Fam Med 2000;32:595-596.

26. Visser M, Launer LJ, Deurenberg P, Deeg DJ. Total and sports activity in older men and women: relation with body fat distribution. Am J Epidemiol 1997;145:752-61.

27. Milne AC, Avenell A, Potter J. Meta-analysis: protein and energy supplementation in older people. Ann Intern Med 2006;144:37-48.

28. Rubin DB. Multiple imputation for nonresponse in surveys. New York: John Wiley & Sons, 1987.

29. Burton A, Billingham LJ, Bryan S. Cost-effectiveness in clinical trials: using multiple imputation to deal with incomplete cost data. Clin Trials 2007;4:154-61.

30. Efron B. Missing data, imputation, and the bootstrap. J Am Stat Assoc 1994;89:463-475.

31. Black WC. The CE plane:a graphic representation of cost-effectiveness.Med Decis Making 1990;10:212-4.

32. Fenwick E, O'Brien BJ, Briggs A. Cost-effectiveness acceptability curves--facts, fallacies and frequently asked questions. Health Econ 2004;13:405-15.

33. Edington J, Barnes R, Bryan F, et al. A prospective randomised controlled trial of nutritional supplementation in malnourished elderly in the community: clinical and health economic outcomes. Clin Nutr 2004;23:195-204.

34. Tidermark J, Ponzer S, Carlsson P, et al. Effects of protein-rich supplementation and nandrolone in lean elderly women with femoral neck fractures. Clin Nutr 2004;23:587-96.

35. Briggs A. Economic evaluation and clinical trials: size matters. Bmj 2000;321:1362-3.

36. Schilp J, Wijnhoven HA, Deeg DJ, Visser M. Early determinants for the development of undernutrition in an older general population: Longitudinal Aging Study Amsterdam. Br J Nutr 2011;106:708-717.

CHAPTER 7

Predictors of future weight loss in undernourished older individuals living in the community

Janneke Schilp
Hinke M. Kruizenga
Hanneke A.H. Wijnhoven
Henrica C.W. de Vet
Martijn W. Heymans
Marjolein Visser

Submission in preparation

Abstract

Background. Undernutrition is a common problem in old age and is characterized by weight loss or underweight. Those who are not able to regain from their weight loss should be identified and probably prioritized to receive an individualized treatment. Aim was to identify predictors of future weight loss in a sample of undernourished, community-dwelling, older individuals.

Methods. Post-hoc analysis of a randomized controlled trial on a dietetic treatment in the community in 126 individuals aged ≥65 years who were assessed as undernourished using the Short Nutritional Assessment Questionnaire 65+. Potential predictors were assessed at baseline. Weight change between baseline and 6-months follow-up was calculated and dichotomized (≥3% loss versus stable or gain).

Results. Twenty-six percent of the study sample lost ≥3% weight in 6 months. Positive predictors for losing ≥3% weight were: poor cognitive status (OR = 13.54, 95% CI 3.39; 54.00), poor physical quality of life (OR = 5.29, 95% CI 0.89; 31.38), receiving household care (OR = 4.05, 95% CI 1.08; 15.15) and a higher BMI (OR = 1.31, 95% CI 1.12; 1.54). The AUC was 0.80 after bootstrapping. The p-value of the Hosmer-Lemeshow test was 0.49, indicating a good fit and the explained variance (R^2) was 0.35.

Conclusion. The prediction model for future weight loss in a sample of undernourished, community-dwelling older individuals has a good discriminative ability, a good fit and a moderate explained variation. This model, including relatively easy to define characteristics, may provide a helpful tool to identify undernourished older individuals at risk for further deterioration of their nutritional status over time.

Introduction

Undernutrition is a serious problem in older individuals in Western society. The prevalence of undernutrition in the community, often based on low weight and/or unintentional weight loss, ranges from 11 to 35% (1, 2), depending on the applied criteria and the investigated study population. The presence of undernutrition has shown to be associated with a reduced functional status (3, 4), a reduced quality of life (5), increased mortality (6, 7) and higher health care costs (8). The causes of undernutrition are extremely diverse and are often interacting with each other. Factors that have been shown to be associated with undernutrition are presence of disease, old age, poor cognitive functioning, poor physical functioning, poor appetite and loneliness (9 - 16). The wide range of factors associated with undernutrition emphasizes the heterogeneity and complexity of the older undernourished population.

Undernutrition is often characterized by weight loss or underweight (17, 18). In older individuals the lost weight is often, but not always, regained. The ability to regain weight after weight loss is decreased with older age (19). Weight cycling was studied in a longitudinal cohort of 2654 community-dwelling individuals aged 70 to 79 year (20). This study showed that from the 489 participants who lost ≥3% weight in one year 30% regained within 3% of their baseline weight in the following year, while 54% continued to lose >3% of their baseline weight (20). Little is known about the individual characteristics contributing to further weight loss in individuals assessed as undernourished. Identifying these individual characteristics is important because this may help in defining high risk groups for further deterioration of the already undernourished condition. These specific groups should be prioritized to receive an individualized treatment to prevent further weight loss. Targeting treatment to these groups is also likely to be more cost-effective as less individuals would need to be treated. Therefore, the aim of this study was to identify predictors of future weight loss in a sample of undernourished, community-dwelling, older individuals.

Methods

Data for this post-hoc analysis were collected within the Nutrition in Primary Care Study (NPCS), a parallel randomized controlled trial performed in the Netherlands. The study was approved by the Ethics Review Board of the VU University Medical Center Amsterdam. Written informed consent was obtained from all participants.

Subjects

Participants of the NPCS were independently living, undernourished individuals aged 65 years and older. Undernutrition was assessed with the Short Nutritional Assessment Questionnaire 65+ (SNAQ^{65+}): mid-upper arm circumference (MUAC) <25 cm, and/or self report of ≥4 kg unintentional weight loss within the past 6 months (21). A total of 146 individuals were included in the study. All examinations took place at the participants' home and were executed by a trained researcher or research assistant using a standardized protocol. More detailed information about the recruitment and study protocol can be found elsewhere (22). For the present study, only participants with a repeated weight assessment at 6 months (*N* 126) were included.

Outcome measure: weight loss

Weight was measured without shoes to the nearest 0.5 kg using a calibrated mechanical scale (Seca 761). Adjustments were made for deviating situations (23, 24). The percentage weight change over 6 months was calculated by dividing the difference between 6-month weight and baseline weight through the baseline weight and multiplying by 100. Weight change was categorized into three categories based on quartiles: 1) loss (≥3% weight loss in 6 months); 2) stable (within 3% weight change in 6 months); and 3) gain (≥3% weight gain in 6 months). In addition, weight change was dichotomized into loss versus stable or gain.

Potential predictors of weight loss

Social characteristics

Education was categorized into low (no education completed, lower general education), medium (lower vocational education, intermediate general education, intermediate vocational education, higher general education) and high (higher vocational education, scientific education) level.

Living situation was categorized into living alone and living together with partner/family/others.

Medical characteristics

The participants were asked whether they received personal and/or household care. Both professional (nurse, alpha, personnel home/ hospital) and informal (partner, family, friend or volunteer) care were included.

The presence (yes/ no) of the following chronic diseases in the past 12 months was reported by the general practitioner of each participant: Diabetes Mellitus, Heart disease, Chronic kidney insufficiency, Colitis ulcerosa/ IBS/ Crohn's disease, Osteoarthritis/ Rheumatoid arthritis, Osteoporosis, Malignity, Parkinson's disease, Hypothyroidie/ Hyperthyroidie, Anxiety disorder /depression and Obstructive Lung Disease (OLD). Four categories were created to define morbidity: 0, 1, 2 and 3 or more chronic diseases.

The number of used medication was determined by having the interviewer check the containers of drugs with prescription the participant was taking in the past two weeks.

Problems with biting and/ or chewing (yes/ no) in the past 12 months were assessed.

Appetite was assessed with the question: 'Last week, I did not feel like eating: my appetite was poor'. The answers 'some or little of the time', 'occasionally or moderate amount of the time' and 'most or all of the time' were categorized as poor appetite and the answer 'rarely or none of the time' as no problems with appetite.

Psychological characteristics

Cognitive functioning was measured with the Mini-Mental State Examination (MMSE) (25). MMSE-scores were ranging from 18 to 30, whereby scores ≤23 were defined as a poor cognitive status (26).

Depressive symptoms were measured with the Dutch translation of the Center for Epidemiologic Studies Depression scale (CES-D) (27), ranging from 0 to 60, whereby scores ≥16 were defined as depressive symptoms (28).

Quality of life was assessed with the SF-12, resulting in a physical component summary (PSC) score and a mental component summary (MCS) score, with scores ranging from 0 (lowest level of health) to 100 (29). Both scores were dichotomized at the average of 50, based on the general US population.

Nutritional status and intake

MUAC was measured with a measuring tape at the centre point (midway between acromion and top of elbow) of the left upper-arm to the nearest mm with the arm hanging loosely.

Unintentional weight loss (yes/ no) was assessed by the question: 'Have you unintentionally lost 4 kilograms or more within the past 6 months?'.

Energy intake and protein intake were calculated from a food diary completed by the participant the day prior to the baseline examination or a 24-hour recall during the baseline examination. Daily energy (kcal) and protein (gram) intake were calculated (30) and expressed per kg weight.

Physical function characteristics

Physical performance was assessed using the Short Physical Performance Battery which consisted of a 4-m walk test, a repeated chair stands test, and a standing balance test (31). The total score ranged from 0 (worst performance) to 12 and was dichotomized at the median score of 7. Additionally, gait speed was calculated from the walk test and dichotomized to the median speed of 0.7 meter/second.

Handgrip strength (kg) was measured twice on each hand. The mean value of the maximum of each hand was used. A grip strength below 85% standard for age and gender was defined as poor handgrip strength (32).

Functional limitations of daily activities were assessed by asking whether the participant had difficulties to perform the following seven activities: walking outside, climbing staircase, getting up and sitting down in a chair, lifting 5 kg, stooping/ crouching/ kneeling, raising arms and grasping/ handling with fingers. A total sum score was calculated ranging from 0 (no limitations) to 24 and dichotomized at the median score of 5. Additionally, all seven individual activity scores were used as dichotomous variables (with/ without limitations).

The frequency and duration of walking outside in the past two weeks was assessed using the validated Longitudinal Aging Study Amsterdam Physical Activity Questionnaire (LAPAQ), and was dichotomized at the median time of 15 minutes per day.

Dietetic treatment characteristics

Participants were asked at baseline if they were willing to receive a specific treatment for undernutrition (yes/ no).

Dichotomous variables were used in the analysis indicating whether a dietetic treatment was provided or oral nutritional supplements (ONS) were prescribed (yes/ no). Also the amount (hours) of dietetic consults and the number of ONS were included in the analysis.

Statistical analysis

Baseline characteristics were evaluated stratified by the three weight change categories. Univariate associations between all potential predictors and ≥3% weight loss (versus stable and gain) were analyzed using logistic regression analysis. Variables associated with ≥3% weight loss ($P < 0.20$) were selected for a multivariate backward stepwise logistic regression analysis to develop a prediction model. If more than one individual functional limitation item was univariately associated with ≥3% weight loss, only the strongest associated item was selected for the multivariate analysis. The variables with the highest p-value were removed one-by-one, until all remaining variables in the prediction model had a P-value < 0.10.

The performance of the prediction model was evaluated by using a Receiver Operating Characteristic (ROC) curve, whereby the area under the curve (AUC) showed the discriminative ability of the model. The internal validation of the model was determined by using bootstrapping techniques (33). A total of 250 random bootstrap samples of equal size were drawn with replacement from the complete dataset. The coefficients of the final regression model were estimated in these bootstrap samples and tested in the original sample. The difference between the regression coefficients in the original sample and bootstrap samples as reflected by the slope index is the measure for the amount of optimism in regression coefficients (34). Slope values normally range from 0 to 1, with a value of 1 meaning no optimism. The slope index was used as a shrinkage method by multiplying the regression coefficients with this slope index to correct for optimism and a new intercept was calculated for these optimism corrected coefficients. This bootstrapping procedure was also used to obtain optimism in the AUC. The goodness-of-fit of the prediction model was verified by the Hosmer-Lemeshow test. A non-significant χ^2 value in this test is indicative of a good model fit. Furthermore, the explained variation of the prediction model was determined with Nagelkerke's R^2 (33), reflecting the proportion of variation in the outcome explained by the predictors in the model.

The analyses were performed using SPSS version 17.0 for Windows (SPSS, Chicago, USA) and R statistical software version 2.14.2 (R development Core Team).

Results

Mean age of the total study sample was 81 years (SD 7.6) and 37% was male. During 6 months, 26% lost ≥3% weight, 48% was stable (within 3% weight change) and 26% gained ≥3%. The baseline characteristics of the individuals in the three weight change categories are shown in **Table 1**.

Table 1. Baseline characteristics of the study sample according to weight change category.

	Weight change categories		
	Loss[a]	Stable[b]	Gain[c]
Characteristics	***N* 33**	***N* 60**	***N* 33**
Demographic and social characteristics			
Male gender, N (%)	11 (33.3)	25 (41.7)	10 (30.3)
Age (y), mean (SD)	81.7 (8.4)	78.8 (7.9)	81.4 (5.8)
Age ≥81.6 y	20 (60.6)	24 (40.0)	19 (57.6)
Low education, N (%)[d]	8 (24.2)	9 (15.8)	5 (15.2)
Medium education, N (%)	22 (66.7)	34 (59.6)	23 (69.7)
High education, N (%)	3 (9.1)	14 (24.6)	5 (15.2)
Living alone, N (%)	22 (66.7)	42 (71.2)	19 (57.6)
Physical characteristics			
Personal care, N (%)	11 (33.3)	14 (23.7)	9 (27.3)
Household care, N (%)	29 (87.9)	38 (64.4)	23 (71.9)
No chronic diseases, N (%)	5 (15.2)	17 (28.3)	6 (18.2)
1 chronic disease, N (%)	15 (45.5)	20 (33.3)	12 (36.4)
2 chronic diseases, N (%)	8 (24.2)	8 (13.3)	9 (27.3)
≥3 chronic diseases, N(%)	5 (15.2)	15 (25.0)	6 (18.2)
Number of used medication, mean (SD)	5.2 (3.0)	4.3 (3.4)	3.7 (2.8)
Problems with biting/chewing, N (%)	6 (18.2)	10 (16.7)	4 (12.1)
Poor appetite, N (%)	13 (39.4)	21 (35.6)	10 (31.3)
Psychological characteristics			
Poor cognitive status, MMSE score ≤23, N (%)	10 (30.3)	3 (5.0)	2 (6.1)
Depressive symptoms, CES-D score ≥16, N (%)	12 (36.4)	21 (35.6)	9 (29.0)
Poor physical quality of life, PCS score <50, N (%)	30 (93.8)	42 (71.2)	27 (81.8)
Poor mental quality of life, MCS score <50, N (%)	12 (37.5)	20 (33.9)	11 (33.3)
Nutritional status and intake			
Body mass index (kg/m^2), mean (SD)	22.9 (2.8)	21.7 (3.3)	20.0 (3.4)
MUAC (cm), mean (SD)	25.4 (2.5)	24.9 (2.9)	23.6 (2.3)
MUAC <25 cm, N (%)	18 (56.3)	39 (66.1)	26 (81.3)
≥4 kg unintentional weight loss in past 6 month, N (%)	17 (51.5)	31 (51.7)	16 (48.5)

Table 1. Continued.

Characteristics	Weight change categories Loss[a] *N* 33	 Stable[b] *N* 60	 Gain[c] *N* 33
Energy intake (kcal/kg), mean (SD)	27.3 (8.1)	29.9 (10.4)	33.1 (16.1)
Protein intake (gram/kg), mean (SD)	1.2 (0.4)	1.2 (0.4)	1.3 (0.8)
Physical function characteristics			
Poor physical performance (score <7), N (%)	20 (60.6)	19 (32.8)	15 (45.5)
Slow gait speed (<0.7 m/s), N (%)	23 (69.7)	23 (40.4)	15 (45.5)
Handgrip strength <100% norm, N (%)	23 (74.2)	38 (65.5)	17 (51.5)
Overall functional limitations (score ≥5), N (%)	20 (60.6)	29 (49.2)	14 (43.8)
Limitations lifting 5 kg, N (%)	25 (75.8)	28 (47.5)	18 (56.3)
Less outdoor walking (<15 min/day), N (%)	18 (54.5)	23 (38.3)	22 (66.7)
Dietetic treatment			
Not willing to receive treatment, N (%)	23 (69.7)	42 (70.0)	19 (57.6)
Total hours dietetic consults, mean (SD)	1.1 (1.7)	1.2 (1.6)	1.7 (1.7)
Received no dietetic treatment, N (%)	17 (58.6)	25 (44.6)	9 (29.0)
Number of ONS, mean (SD)	27.3 (72.1)	39.9 (85.1)	48.8 (115.6)
Received no ONS, N (%)	27 (81.8)	45 (76.3)	23 (71.9)

MMSE, Mini-Mental State Examination; CES-D, Center for Epidemiologic Studies Depression scale; PCS, Physical Component Summary; MCS, Mental Component Summary; MUAC, Mid-upper arm circumference; ONS, Oral Nutritional Supplements

[a] ≥3% weight loss in 6 months; [b] within 3% weight loss or gain in 6 months; [c] ≥3% weight gain in 6 months; [d] low = no education completed, lower general education; medium = lower vocational education, intermediate general education, intermediate vocational education, higher general education; high = higher vocational education, scientific education

The results of the univariate logistic regression analyses are shown in **Table 2**. Household care, poor cognitive status, poor physical quality of life, higher BMI, higher MUAC, overall functional limitations, poor physical performance and slow gait speed were statistically significantly associated with ≥3% weight loss in 6 months. The univariate odds ratios for the individual functional limitation items were: outdoor walking (OR = 2.70, 95% CI 1.19; 6.12), climbing a 15-steps staircase (OR = 2.91, 95% CI 1.22; 6.93), getting up and sitting down in a chair (OR = 2.75, 95% CI 1.21; 6.23) and lifting 5 kg (OR = 3.06, 95% CI 1.25; 7.49). Limitations lifting 5 kg was included in the multivariate model, because of the highest OR and lowest p-value (*P* = 0.02). Regarding individual chronic diseases, diabetes mellitus, obstructive lung disease, malignity, osteoarthritis/ rheumatoid arthritis, osteoporosis and anxiety disorder/ depression were not associated with ≥3% weight loss

in 6 months. Only cardiac disease was associated (OR = 1.91, 95% CI 0.77; 4.75, *P* = 0.17) with ≥3% weight loss in 6 months and included in the multivariate model. Due to missing data on any of the selected characteristics (*N* 3), 123 participants were included in the multivariate backward stepwise analysis.

The final multivariate model after the backward selection procedure is presented in **Table 3**. Positive predictors for losing weight were poor cognitive status, poor physical quality of life, receiving household care and a higher BMI. The ROC curve for this prediction model showed an AUC of 0.82 (95% CI 0.74; 0.89) (**Figure 1**). The multivariate regression coefficients were multiplied with the shrinkage factor (shrinkage factor = 0.83) to correct for optimism and a new intercept (intercept = -8.44) was calculated for these optimism corrected coefficients. Based on the optimism-corrected coefficients of the multivariate logistic regression model, the following prediction rule was constructed:

Logit (weight loss) = -8.4 + 1.2 (household care) + 2.2 (cognitive status) + 1.4 (quality of life PCS-score) + 0.2 (BMI)

With this prediction rule, the probability to lose ≥3% weight in 6 months was calculated for each individual. For example, an individual with household care, a poor cognitive status, a poor physical quality of life and a BMI of 20 had a probability of 76% (*-8.4 + 1.2 * 1+ 2.2 * 1 + 1.4 * 1 + 0.2 * 20)* to lose ≥3% weight in 6 months. The AUC was slightly optimistic with a value of 0.80 after bootstrapping. The Hosmer-Lemeshow test resulted in a p-value of 0.49 and indicated that the model has a good fit (35). The proportion of variation in the outcome explained by the predictors in the model (R^2) was 0.35.

Table 2. Univariate associations between study sample characteristics and ≥3% weight loss in 6 months using logistic regression analyses (*N* 126).

Characteristics	OR[a]	95% CI	P
Demographic and social characteristics			
Male gender	0.83	0.36; 1.91	0.66
Age ≥ 81.6 y	1.79	0.80; 4.02	0.16
Education low (reference)	1.00	-	-
Education medium	0.68	0.25; 1.83	0.44
Education high	0.28	0.06; 1.23	0.09
Living alone	1.02	0.44; 2.36	0.97
Medical characteristics			
Personal care	1.50	0.63; 3.56	0.36
Household care	3.57	1.15; 11.07	0.03
No chronic disease (reference)	1.00	-	-
1 chronic disease	2.16	0.69; 6.78	0.19
2 chronic diseases	2.17	0.60; 7.80	0.24
≥3 chronic diseases	1.10	0.28; 4.33	0.90
Number of used medication	1.12	0.99; 1.26	0.08
Problems with biting/chewing	1.25	0.44; 3.59	0.67
Poor appetite	1.26	0.55; 2.86	0.58
Psychological characteristics			
Poor cognitive status, MMSE score ≤23	7.65	2.38; 24.59	0.001
Depressive symptoms, CES-D score ≥16	1.14	0.50; 2.63	0.75
Poor physical quality of life, PCS score <50	5.00	1.11; 22.57	0.04
Poor mental quality of life, MCS score <50	1.18	0.51; 2.72	0.70
Nutritional status and intake			
Body mass index (kg/m^2)	1.19	1.04; 1.36	0.01
MUAC (cm)	1.13	0.98; 1.31	0.10
≥4 kg unintentional weight loss in past 6 mo	1.04	0.47; 2.30	0.92
Energy intake (kcal/kg), mean (SD)	0.97	0.93; 1.01	0.12
Protein intake (gram/kg)	0.81	0.38; 1.72	0.59
Physical function characteristics			
Poor physical performance (score <7)	2.58	1.14; 5.84	0.02
Slow gait speed (<0.7 m/s)	3.15	1.34; 7.38	0.01
Handgrip strength <100% norm	1.88	0.76; 4.66	0.17
Overall functional limitations (score ≥5)	1.72	0.76; 3.86	0.19
Less outdoor walking (<15 min/day)	1.28	0.58; 2.84	0.54

Table 2. Continued.

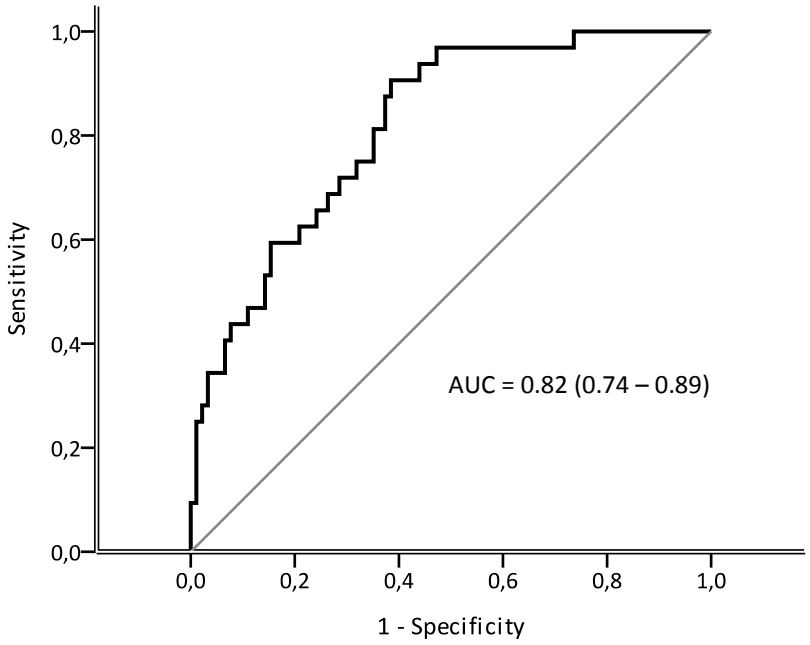
Characteristics	OR[a]	95% CI	P
Dietetic treatment characteristics			
Not willing to receive treatment	1.21	0.51; 2.84	0.67
Total hours dietetic consults	0.89	0.68; 1.17	0.40
Received no dietetic treatment	2.21	0.94; 5.19	0.07
Number of ONS, continuous	1.00	0.99; 1.00	0.40
Received no ONS	1.52	0.56; 4.15	0.41

[a] Weight loss is coded as 1 and stable or gain is reference category

Table 3. Multivariate logistic regression model for predicting ≥3% weight loss in 6 months in older, community-dwelling, undernourished individuals (*N* 123)

Characteristics	OR	95% CI	P
Poor cognitive status, MMSE score ≤23	13.54	3.39; 54.00	<0.001
Poor physical quality of life, PCS score <50	5.29	0.89; 31.38	0.07
Household care, N (%)	4.05	1.08; 15.15	0.04
Body mass index (kg/m^2)	1.31	1.12; 1.54	0.001

Figure 1. Receiver Operator Characteristics (ROC) curve for the prediction model of ≥3% weight loss in 6 months in undernourished older individuals.



Discussion

In this post-hoc analysis in a well-characterized sample of undernourished, community-dwelling older individuals, we developed and validated a prediction model for 6-months future weight loss. The prediction model had a good discriminative ability, a good fit and a moderate explained variation. This model thus can be used to identify undernourished older individuals at risk for further deterioration of their nutritional status over time.

Both poor physical quality of life and poor cognitive functioning were important predictors of future weight loss in our study. Poor quality of life, based on the first part of the Nottingham Health Profile (36) or EuroQol (37, 38), was shown to be associated with the presence of undernutrition in previous studies. Furthermore, previous studies showed that a poor cognitive status was associated with both the risk of developing undernutrition (36) and the presence of undernutrition (9, 39) in older community-dwelling individuals. In addition, weight loss has also been shown to be a predictor of cognitive decline (40, 41).

These results together suggest that older persons with cognitive problems are at increased risk of developing undernutrition as well as subsequent further weight loss.

Older persons receiving household care were also at increased risk of future weight loss. Although no earlier studies have investigated specifically the association between received care and weight loss, home care utilization was shown to be associated with both frailty and disabilities for instrumental activities of daily living in older community-dwelling individuals (42, 43). Receiving home care may therefore be an indicator of frailty and vulnerability in older persons.

Individuals with a higher BMI had a higher risk of weight loss, despite the fact that a loss of ≥3% represents a higher absolute loss of weight in persons with higher BMIs. Comparable results were found for undernourished hospital patients, where patients with higher BMIs were less likely to achieve their energy and protein requirements (44). As weight loss in persons with a higher BMI may be less obvious, health care professionals should be aware of further unintentional weight loss in undernourished individuals with a relatively high BMI. We found evidence for this in our study only for overweight and not obese individuals, as the BMI was normally distributed from 16 to 28 kg/m^2 (mean 21.6 kg/m^2, SD 3.3), with one obese outlier (BMI 32 kg/m^2).

Strengths and limitations

An important strength of our study was the well-characterized sample, including a wide variety of potentially relevant predictors for future weight loss. Thereby, longitudinal data could be used to develop and validate a prediction model for future weight loss, which has not been examined before in older individuals. While several methods are available for executing internal validation, the bootstrapping method we used for internal validation is recommended in literature (34). Although we were not able to test the generalizability of the prediction model in another similar study sample (external validation), there are good indications that internal validation by using bootstrapping generates estimates to be expected in external study samples (34).

Some limitations of our study have to be mentioned. First, the prediction model was developed specifically for community-dwelling undernourished older individuals and its validity for institutionalized or well-nourished older individuals or younger individuals is unknown. Secondly, the model was developed in individuals who completed the weight assessment at 6 months and we cannot exclude attrition bias. However, earlier analyses of the study sample showed no statistically significant differences in medical, physical, psychological, functional and social parameters at study baseline between study

completers and those who discontinued early, except for education level (22). Third, a pre-selection was made for the backward multivariate model based on a P-value < 0.2. This selection was necessary, because the number of variables that could be included in the model was limited due to the relatively small study sample. However, the high AUC of 0.80 after bootstrapping indicates the addition of other variables have improved the prediction model only to a limited extend.

Practical implications

Observational studies have shown that episodes of weight loss are often followed by weight regain in older individuals (20). Treatment for undernutrition should preferably be targeted to those individuals who are likely to experience further weight loss and have a high risk of further deterioration of their nutritional status. The prediction model developed in this study may provide a helpful tool in identifying these individuals. Targeting treatment to these high-risk individuals is likely more cost-efficient than targeting treatment to the whole group of undernourished individuals. Further studies are necessary to investigate the external validity of the prediction model and to investigate whether targeted, nutritional treatment of these high-risk individuals is (cost-)effective.

Conclusion

Our study shows that the risk of losing ≥3% weight in undernourished individuals can be well predicted by relatively easy to define characteristics: poor cognitive status, poor physical quality of life, receiving household care and a higher BMI. More attention should be given by healthcare professionals to undernourished older individuals meeting these characteristics.

References

1. Chen CC, Schilling LS, Lyder CH. A concept analysis of malnutrition in the elderly. J Adv Nurs 2001;36:131-142.
2. Schilp J, Kruizenga HM, Wijnhoven AHA, et al. High prevalence of undernutrition in Dutch community-dwelling older individuals. Nutrition 2012;28(11-12):1151-6.
3. Cereda E, Valzolgher L, Pedrolli C. Mini nutritional assessment is a good predictor of functional status in institutionalised elderly at risk of malnutrition. Clin Nutr 2008;27:700-5.
4. Oliveira MR, Fogaca KC, Leandro-Merhi VA. Nutritional status and functional capacity of hospitalized elderly. Nutr J 2009;8:54.
5. Keller HH, Ostbye T, Goy R. Nutritional risk predicts quality of life in elderly community-living Canadians. J Gerontol A Biol Sci Med Sci 2004;59:68-74.
6. Corrada MM, Kawas CH, Mozaffar F, Paganini-Hill A. Association of body mass index and weight change with all-cause mortality in the elderly. Am J Epidemiol 2006;163:938-49.
7. Locher JL, Roth DL, Ritchie CS, et al. Body mass index, weight loss, and mortality in community-dwelling older adults. J Gerontol A Biol Sci Med Sci 2007;62:1389-92.
8. Baumeister SE, Fischer B, Doring A, et al. The Geriatric Nutritional Risk Index predicts increased healthcare costs and hospitalization in a cohort of community-dwelling older adults: results from the MONICA/KORA Augsburg cohort study, 1994-2005. Nutrition 2011;27:534-42.
9. Fagerstrom C, Palmqvist R, Carlsson J, Hellstrom Y. Malnutrition and cognitive impairment among people 60 years of age and above living in regular housing and in special housing in Sweden: a population-based cohort study. Int J Nurs Stud 2011;48:863-71.
10. Johansson Y, Bachrach-Lindstrom M, Carstensen J, Ek AC. Malnutrition in a home-living older population: prevalence, incidence and risk factors. A prospective study. J Clin Nurs 2009;18:1354-64.
11. Landi F, Russo A, Liperoti R, et al. Anorexia, physical function, and incident disability among the frail elderly population: results from the ilSIRENTE study. J Am Med Dir Assoc 2010;11:268-74.
12. Meijers JM, Schols JM, van Bokhorst-de van der Schueren MA, Dassen T, Janssen MA, Halfens RJ. Malnutrition prevalence in The Netherlands: results of the annual Dutch national prevalence measurement of care problems. Br J Nutr 2009;101:417-23.
13. Payette H, Gray-Donald K, Cyr R, Boutier V. Predictors of dietary intake in a functionally dependent elderly population in the community. Am J Public Health 1995;85:677-83.
14. Schilp J, Wijnhoven HA, Deeg DJ, Visser M. Early determinants for the development of undernutrition in an older general population: Longitudinal Aging Study Amsterdam. Br J Nutr 2011;106:708-17.

15. St-Arnaud-McKenzie D, Payette H, Gray-Donald K. Low physical function predicts either 2-year weight loss or weight gain in healthy community-dwelling older adults. the NuAge Longitudinal Study. J Gerontol A Biol Sci Med Sci 2010;65:1362-8.
16. Torres SJ, McCabe M, Nowson CA. Depression, nutritional risk and eating behaviour in older caregivers. J Nutr Health Aging 2010;14:442-8.
17. Chapman IM. Weight loss in older persons. Med Clin North Am 2011;95:579-93, xi.
18. Hickson M. Malnutrition and ageing. Postgrad Med J 2006;82:2-8.
19. Roberts SB, Fuss P, Heyman MB, et al. Control of food intake in older men. Jama 1994;272:1601-6.
20. Lee JS, Visser M, Tylavsky FA, et al. Weight loss and regain and effects on body composition: the Health, Aging, and Body Composition Study. J Gerontol A Biol Sci Med Sci 2010;65:78-83.
21. Wijnhoven HA, Schilp J, van Bokhorst-de van der Schueren MA, et al. Development and validation of criteria for determining undernutrition in community-dwelling older men and women: The Short Nutritional Assessment Questionnaire 65+. Clin Nutr 2012;31:351-8.
22. Schilp J, Kruizenga HM, Wijnhoven HAH, van Binsbergen JJ, Visser M. Effects of a dietetic treatment in older, undernourished, community-dwelling individuals in primary care: a randomized controlled trial. Eur J Nutr, in revision.
23. Frank E, Dunlop AL. What does a patient's outfit weight? Fam Med 2000;32:595-6.
24. Visser M, Launer LJ, Deurenberg P, Deeg DJ. Total and sports activity in older men and women: relation with body fat distribution. Am J Epidemiol 1997;145:752-61.
25. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.
26. Wind AW, Schellevis FG, van Staveren G, Scholten RP, Jonker C, van Eijk JT. Limitations of the Mini-Mental State Examination in diagnosing dementia in general practice. Int J Geriatr Psychiatry 1997;12:101-8.
27. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Applied Psychological Measurement 1977;1:385-401.
28. Berkman LF, Berkman CS, Kasl S, et al. Depressive symptoms in relation to physical health and functioning in the elderly. Am J Epidemiol 1986;124:372-88.
29. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;34:220-33.
30. The Netherlands Nutrition Centre. NEVO Dutch food composition table 2006. The Hague, The Netherlands, 2006.
31. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49:M85-94.

32. Webb AR, Newman LA, Taylor M, Keogh JB. Hand grip dynamometry as a predictor of postoperative complications reappraisal using age standardized grip strengths. JPEN J Parenter Enteral Nutr 1989;13:30-3.

33. Harrell FE, Jr., Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med 1996;15:361-87.

34. Steyerberg EW, Harrell FE, Jr., Borsboom GJ, Eijkemans MJ, Vergouwe Y, Habbema JD. Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. J Clin Epidemiol 2001;54:774-81.

35. Hosmer DW, Lemeshow S. Applied Logistic Regression. 2nd ed. New York: Wiley, 2000.

36. Johansson L, Sidenvall B, Malmberg B, Christensson L. Who will become malnourished? A prospective study of factors associated with malnutrition in older persons living at home. J Nutr Health Aging 2009;13:855-61.

37. Gombos T, Kertesz K, Csikos A, Soderhamn U, Soderhamn O, Prohaszka Z. Nutritional form for the elderly is a reliable and valid instrument for the determination of undernutrition risk, and it is associated with health-related quality of life. Nutr Res 2008;28:59-65.

38. Kvamme JM, Olsen JA, Florholmen J, Jacobsen BK. Risk of malnutrition and health-related quality of life in community-living elderly men and women: the Tromso study. Qual Life Res 2011;20:575-82.

39. Feldblum I, German L, Castel H, et al. Characteristics of undernourished older medical patients and the identification of predictors for undernutrition status. Nutr J 2007;6:37.

40. Gao S, Nguyen JT, Hendrie HC, et al. Accelerated weight loss and incident dementia in an elderly African-American cohort. J Am Geriatr Soc 2011;59:18-25.

41. Soto ME, Secher M, Gillette-Guyonnet S, et al. Weight loss and rapid cognitive decline in community-dwelling patients with Alzheimer's disease. J Alzheimers Dis 2012;28:647-54.

42. Del Duca GF, Thume E, Hallal PC. Prevalence and factors associated with home care among older adults. Rev Saude Publica 2011;45:113-20.

43. Hoeck S, Francois G, Geerts J, Van der Heyden J, Vandewoude M, Van Hal G. Health-care and home-care utilization among frail elderly persons in Belgium. Eur J Public Health 2011.

44. Leistra E, Willeboordse F, van Bokhorst-de van der Schueren MA, et al. Predictors for achieving protein and energy requirements in undernourished hospital patients. Clin Nutr 2011;30:484-9.

CHAPTER 8

General Discussion

Outline

Recognition and treatment of undernutrition in the Netherlands

The general aim of this thesis was to investigate possibilities for the recognition and treatment of undernutrition in community-dwelling older individuals. In this final chapter the history, present and future will be consecutively presented for the recognition and treatment of undernutrition in the Netherlands.

In the history section significant developments, initiated programs and important activities concerning undernutrition within Dutch clinical practice since the year 2000 will be summarized. This section will provide insight in the progress made regarding the recognition and treatment of undernutrition in the Netherlands. Subsequently, the present findings of this thesis will be synthesized and several methodological considerations will be discussed. Finally, the implications for both future research and clinical practice, regarding recognition and treatment of undernutrition in older community-dwelling individuals, will be described.

Recognition

History

2000 National campaign 'Eat well to get well' An increased awareness of the importance to recognize undernutrition in health care started through a national campaign initiated by the Dutch Dietetic Association. This was the first common activity of dietitians, physicians and nutritionists. The aim of the campaign was to increase awareness for undernutrition in general among health care professionals and in society.

2001 First prevalence data The first Dutch prevalence data on undernutrition were collected in 8529 hospital -, nursing home -, and home care patients, showing a mean prevalence of undernutrition of 12% (1).

2004 Annual prevalence measurement The annual prevalence measurement of undernutrition was initiated in 2004 as part of the National Prevalence Measurement of Care Problems (LPZ) (2). In the home care setting, an increased screening percentage was shown from 16% in 2006 and 52% in 2009, to 68% in 2011 (3). However, across the care settings, often only the measurement of body weight was included in the screening (68%) and for only 29% a validated screening instrument was used (3).

2004 Short Nutritional Assessment Questionnaire (SNAQ) The SNAQ was developed and validated to recognize undernourished hospital patients in an early stage of hospitalization (4).

2005 Dutch Malnutrition Steering Group (DMSG) The DMSG was established. It is a multidisciplinary group of national key members representing various medical disciplines and professional organizations. A website was developed by the DMSG in order to disseminate evidence-based and practice-based knowledge.[1] The website offers developed 'toolkits' for the different care sectors to support implementation of the recognition and treatment of undernutrition.

2006 Hospital project The project 'Early recognition and optimal treatment of undernutrition in hospitals' was started as part of a national care quality improvement campaign. Aim of the project was to implement screening of all hospital patients at admission using the Malnutrition Universal Screening Tool (MUST) or SNAQ instrument and to provide optimal nutritional treatment for undernourished patients. The project started in 6 pilot hospitals and was expanded in the following 3 years to a total of 50 hospitals. In 2009, this project was the most successful ZonMw (Netherlands Organisation for Health Research and Development) project and received an award: the 'pearl of ZonMw'.

2007 Screening performance indicator in hospitals Screening of undernutrition in hospital patients was added as performance indicator (PI) to the national benchmarks on quality of care by the Dutch Health Care Inspectorate (5). Hospitals were required to provide information on the percentage screened patients during hospitalization. The PI resulted in an increasing screening percentage: from 44% in 2008, to 75% in 2009 and 84% in 2010 (6, 7). Dutch translation MNA The Mini Nutritional Assessment (MNA) was translated into Dutch and the translation was validated using a Delphi-procedure.

2008 Nursing/ care homes project The project 'Early detection and treatment of undernutrition in nursing homes and care homes' was initiated by the DMSG and the professional association V&VN (Dutch professional organization of nurses and carers) and started in 6 care homes.

Short Nutritional Assessment Questionnaire for Residential Care ($SNAQ^{RC}$) The $SNAQ^{RC}$ was developed, validated and implemented for the early recognition of undernourished residents in nursing homes and residential homes (8).

[1] *www.stuurgroepondervoeding.nl*

2008 Primary care and home care project The project 'Early recognition and treatment of undernutrition in primary care and home care' was initiated by the DMSG. A total of 125 project leaders, mainly dietitians, were trained during the 3-year project to implement recognition and treatment of undernutrition in their own practice or care organization.

2009 Short Nutritional Assessment Questionnaire 65+ (SNAQ^{65+}) The SNAQ^{65+} was developed and validated to assess undernutrition in community-dwelling older individuals (Chapter 3 of this thesis).

2010 Quality framework responsible care Screening of undernutrition was added as a component of the quality framework responsible care, making risk identification of undernutrition required for patients in nursing homes and patients receiving home care.

National Primary Care Cooperation Agreement Undernutrition The awareness for undernutrition in primary care was enhanced by the introduction of the 'National Primary Care Cooperation Agreement Undernutrition', abbreviated as LESA Undernutrition (in Dutch: Landelijke Eerstelijns Samenwerkings Afspraak Ondervoeding) (9).

2011 Health Council report 'Malnutrition in the elderly' The Health Council of the Netherlands published an advisory report about undernutrition in older individuals (10). An evaluation of screening instruments for older individuals was part of this report. The Health Council concluded that the reproducibility of the evaluated available instruments seems sufficient. However, due to a lack of a golden standard, no assurance can be given about the validity of these instruments.

2012 This thesis As part of the DMSG project 'Early recognition and treatment of undernutrition in primary care and home care', this thesis was completed.

Present: findings of this thesis and methodological considerations

Main findings

Important risk factors for developing undernutrition in community-dwelling older individuals were identified in Chapter 2. We showed in our prospective study that a variety of determinants was associated with the development of undernutrition, ranging from socio-economic, psychological, lifestyle and social factors, to medical and functional factors. Reporting a poor appetite and difficulty climbing stairs were the only remaining determinants in a multivariate model. Older individuals reporting a poor appetite in the

past week had a 1.63 higher risk to develop undernutrition compared to those reporting no problems with appetite. The risk to develop undernutrition was also statistically significantly higher (HR = 1.91) in individuals reporting difficulty climbing stairs compared to individuals reporting no difficulties, but only in those aged 65 to 75 years old.

In Chapter 3, we described the development and validation of a quick and easy-to-apply instrument for assessing (risk of) undernutrition in older individuals in the community: the SNAQ^{65+}. The SNAQ^{65+} was developed using data of the Longitudinal Aging Study Amsterdam (LASA). Its validity was tested by comparing the relationship with mortality using data from the Invecchiare in Chianti (InCHIANTI) study, showing good face validity and moderate predictive validity. The assessment of the SNAQ^{65+} can easily be performed without the need of heavy or expensive equipment and calculation, which is very relevant for the application in the home situation and facilitates its use in general practices. A practical pocket sized version of the SNAQ^{65+} was produced, including a measuring keychain. The SNAQ^{65+} is currently translated into English, German, Spanish, Italian, French and Portuguese. The English version of the SNAQ^{65+} is shown in **Appendix 1** and all translations are available on the international website (www.fightmalnutrition.eu).

Due to the limited knowledge about the number of individuals suffering from undernutrition or who are at risk of undernutrition in the community, we performed a prevalence study using the SNAQ^{65+} (Chapter 4). Three samples of community-dwelling individuals were compared. The prevalence of undernutrition was 35% in patients receiving home care, 12% in general practice patients receiving their influenza vaccination and 11% in a general older population participating in LASA. The prevalence increased with age in general practice patients and in the general older population. In home care patients, no relationship with age was found. Overall, the results showed that undernutrition is a substantial problem in community-dwelling older individuals.

Methodological considerations

Lack of golden standard for undernutrition

The diagnostic accuracy of a developed health measurement instrument is ideally validated against a golden standard. An undernutrition screening instrument lacks a golden standard against which to be developed and validated. Previous undernutrition screening instruments were validated against practice based reference methods of which the value is unknown. A summary of used reference methods for the validation of undernutrition screening instruments applicable to an older population is shown in **Table 1**. For example, instruments were compared with earlier developed instruments (11, 12)

or with nutritional status as evaluated by a physician or dietitian (13-15). An important methodological problem in the development of some instruments is that the same items were included in both the screening instrument and the reference method (4, 8). This will overestimate the agreement between the instrument and the reference method.

Table 1. Overview of available screening instruments for undernutrition in older individuals and the reference methods used to develop these instruments

Instrument	Abbreviation	Reference method
Subjective Global Assessment	SGA (13)	Clinical status evaluated by a physician: routine history taking and physical examination
Mini Nutritional Assessment	MNA (14)	Clinical status evaluated by a physician: based on clinical file and a comprehensive assessment of anthropometrics, biochemical markers and dietary intake
Mini Nutritional Assessment – Short Form	MNA-SF (12)	Full Mini Nutritional Assessment
Nutrition Risk screening 2002	NRS-2002 (11)	Subjective Global Assessment
Malnutrition Universal Screening Tool	MUST (16)	Consensus of an expert group
Seniors in the Community: Risk Evaluation for Eating and Nutrition II	SCREEN II (15)	Nutritional status evaluated by a dietitian: medical/nutritional history, dietary intake and anthropometrics
Short Nutritional Assessment Questionnaire	SNAQ (4)	BMI <18.5 kg/m^2 *and/or* >5% / >10% unintentional weight loss in last month / 6 months
Short Nutritional Assessment Questionnaire Residential Care	SNAQ^{RC} (8)	BMI ≤20 kg/m^2 *and/or* ≥5%/ ≥10% unintentional weight loss in last month / 6 months

We used all-cause mortality as a relevant and clinically useful reference method for the development and validation of the SNAQ^{65+}. This was an unique approach as mortality was not earlier used to develop a screening instrument for undernutrition. It is important to realize that mortality is not a golden standard for undernutrition as people are dying for various reasons other than undernutrition. We therefore only selected anthropometric and other undernutrition-related-items, based on consistency in the literature, which

could potentially be included in the set of criteria to determine undernutrition. More general disease-related items, such as psychological stress or acute disease (e.g. used in the MNA), were not included. Furthermore, we performed an additional analysis to examine the influence of pre-existing illness and smoking. Excluding those with obstructive lung disease, cancer or smoking history resulted in similar hazard ratios. Therefore, it could be concluded that the association between the risk groups and mortality was independent of pre-existing illness or smoking. Despite this careful approach, the validity of the SNAQ^{65+} criteria should be re-evaluated when a golden standard method for undernutrition becomes available in the future or when consensus has been reached regarding a surrogate golden standard.

Determining risk of undernutrition

The SNAQ^{65+} instrument can also be used to identify older persons with an increased risk of developing undernutrition. Mortality was used as reference method for the development of these risk criteria. Ideally, the actual development of undernutrition over time should be defined as reference method to develop the risk criteria. A recently performed analysis in the development sample of the SNAQ^{65+} showed that those defined at the baseline examination as being at risk of undernutrition (reporting a poor appetite as well as difficulty climbing stairs), indeed lost more weight after 3 years of follow-up compared to those defined as not undernourished (-2.1 kg versus -0.9 kg, $P = 0.08$). This is in line with the results of the study presented in Chapter 1. In this study the 9-year incidence of undernutrition was investigated, determined by a low BMI (<20 kg/m^2) and/or unintentional weight loss (≥5% in the last 6 months). This study showed that a poor appetite and difficulty climbing stairs were the only remaining early determinants in a multivariate model. Thus, when the results of these different studies are combined, they provide consistent evidence for the identification of risk criteria for undernutrition.

Principles of health screening

In 1968 Wilson and Jungner formulated 10 general principles of screening for disease for the World Health Organization (17). These principles are shown in **Table 2**. In this paragraph it will be discussed to what extent the screening for undernutrition in community-dwelling older individuals meets these principles.

Table 2. General principles of screening for disease (Wilson & Jungner)

1. The condition sought should be an important health problem.
2. There should be an accepted treatment for patients with recognized disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process and not a 'once and for all' project.

The importance of the problem (principle 1) in older individuals is showed through the high prevalence rates in specific subgroups and large absolute number of undernourished persons living in the community. Until now, no universally accepted treatment is available when undernutrition is assessed (principle 2). Studies regarding the effects of ONS implicates positive results on body weight, but the evidence for the effect on mortality is inconsistent (18). However, the methodological quality of studies concerning the effects of ONS is poor (10). Following the results of this thesis, a dietetic treatment in primary care did not have significant effects in an undernourished older population.

The availability of screening facilities is getting better (principle 3), partly due to the activities of the DMSG, but may still improve especially in primary care. Diagnosing undernutrition is difficult, because a golden standard for undernutrition is still lacking. In practice, the result of screening is often considered as diagnosis. Due to the lack of a golden standard, the recognition of an early symptomatic stage (principle 4) is also difficult, but generally thinness and unintentional weight loss are used to generate attention. We developed the SNAQ^{65+} instrument to assess undernutrition in primary care. The suitability of this instrument (principle 5) is confirmed by the good face validity and moderate predictive validity. The SNAQ^{65+} is now widely being used by primary care providers in the Netherlands. The instrument is very easy and fast to use, and feasible without any problems for the patient (principle 6).

Much is known about the causes and development of undernutrition (principle 7), but there are still some uncertainties as undernutrition is often caused by multiple factors. There is no internationally accepted treatment protocol for undernutrition (principle 8), but some tools are developed to provide direction to care providers, for example the LESA

(19), the national guideline for screening and treatment of undernutrition (20) and the toolkit developed by the DMSG, which is accessible on the website. We showed no cost-effectiveness of a dietetic treatment in primary care (principle 9). Due to the relatively low costs of a dietetic treatment, the costs of the group assigned to the treatment were comparable to the group receiving no treatment. A previous study regarding the cost-effectiveness of ONS in combination with dietetic consultations in hospitalized patients after discharge showed cost-effectiveness on decreasing functional limitations, but not in increasing quality of life (21). Future studies are needed to attain sufficient evidence to meet principle 9. Concerning the last principle, signalling the risk of undernutrition is embedded in the quality framework responsible care for patients in nursing homes and patients receiving home care (principle 10). Screening on undernutrition is not yet a PI in primary care, such as in hospital patients, but the Dutch Healthcare Inspectorate is processing a PI for community-dwelling older individuals.

In conclusion, the principles 1, 5, 6 and 10 are fulfilled for screening of undernutrition and the principles 7 and 8 are partly fulfilled but needs improvements. Until now, the principles 2, 3, 4 and 9 are not realized sufficiently. Despite the lack of an accepted treatment, screening is currently executed in primary care. Therefore, the application of screening and treatment in practice seems to be further than the scientific evidence.

Prevalence of undernutrition

The prevalence of undernutrition, as we showed in Chapter 4, varied between the different primary care locations. The prevalence of undernutrition was higher in those assessed through the home care organization (35%), compared to those assessed through general practices (12%). The prevalence of undernutrition in the Italian sample used for the validation of the $SNAQ^{65+}$ (InCHIANTI) was recently calculated with the $SNAQ^{65+}$criteria for undernutrition. The prevalence in the Italian validation sample was 14%, which was slightly higher compared to the prevalence in the Dutch development sample (11%). The small difference was caused by the higher percentage with a low MUAC in the validation sample (Chapter 3, table 2).

The prevalence shown in our home care sample was relatively high compared to other Dutch data. The prevalence in our home care population was 35%, while the prevalence in the LPZ study was 16% with the LPZ-criteria and 12% with the LASA-criteria (10, 22). As we have earlier discussed in the general introduction (Chapter 1), these differences are mainly explained by the different criteria used for assessing undernutrition. The LPZ-criteria (BMI ≤20 kg/m^2, >6 kg involuntary weight loss / 6 months or >3 kg / 1 month, and reduced nutritional intake) and LASA-criteria (BMI <20 kg/m^2 or ≥5% unintentional weight

loss/ 6 months) for undernutrition were more stringent compared to our criteria (MUAC <25 cm or ≥4 kg unintentional weight loss/ 6 months). In addition, the measured prevalence is also influenced by the specific setting and characteristics of the study sample which may differ between studies. For example, the home care study sample of LPZ was younger compared to our study sample (mean age 76.2 versus 81.8 year). Furthermore, the LPZ-data were collected at one specific day in all patients in various organizations, while data of our home care sample were collected over a longer period of time within one organization and was limited to intake or evaluation consultations. Possibly, the data of our home care sample was collected in a relatively less healthy home care population as these individuals requested home care newly or the care was evaluated again. Certain personal or environmental events or circumstances may have contributed to the need for an intake or evaluation consultation, which might also have influenced the nutritional status.

Thus, a combination of both the difference in criteria and the difference in the study sample may have influenced the measured prevalence of undernutrition. Despite the different prevalence rates in the samples, both studies showed that undernutrition is a significant problem in older individuals receiving home care.

Future: implications for research and clinical practice

Implications for research

We showed that a variety of factors was associated with the development of undernutrition in older individuals. A major challenge for future research is the early detection of those individual risk factors and to investigate possibilities for appropriate prevention strategies. The key to prevention is to identify those at risk of undernutrition and treat modifiable risk factors as early as possible. Especially since the evidence for effective treatment of undernutrition is still limited, more focus on preventive measures is needed.

Implications for clinical practice

A reliable diagnosis of (the risk of) undernutrition is impeded by the lack of a golden consensus standard. The validity of instruments developed to screen on undernutrition is therefore difficult to assure. In practice, the result of screening is often considered as diagnosis. Concerning the lack of a golden standard, currently this practice seems to be the most suitable solution.

The screening is mainly focused on assessing undernutrition and initiating treatment in case of undernutrition. More attention is needed for the screening of those at high risk for developing undernutrition. Thereby, not only nutritional status is important, but also underlying modifiable factors that may contribute to future development of undernutrition. For example, nausea, food shopping problems or dental problems causing biting or chewing difficulties should be identified. The GP and home care personnel could play an important role in this primary prevention of developing undernutrition, but possibilities for other suitable locations should also be investigated. For example, elderly consultation centers or a general practice nurse specialized in the elderly may play an important role in the identification of high risk persons and the identification and treatment of underlying factors contributing to the development of undernutrition. Furthermore, informing older individuals about their increased risk may create a greater awareness in older individuals themselves regarding healthy nutrition in older age and the prevention of involuntary weight loss.

Although an evidence-based treatment is still needed for undernutrition after recognition, a clear identification of factors contributing to the undernourished condition is important to determine what kind of approach is needed. Recently Dutch geriatricians concluded in a Delphi study that undernutrition should be considered a geriatric syndrome, whereby the nutritional status of geriatric patient should be assessed by comprehensive geriatric assessment (19). Although this expert consensus concerns geriatric patients in general, this could probably also be applied to some extent to older individuals in the community. However, given the large amount of community-dwelling older individuals it is practically and financially not possible to perform such a comprehensive geriatric assessment in all older individuals in primary care to assess undernutrition. Nevertheless, a better determination of potential underlying causes of undernutrition by a GP or dietitian and active treatment of these factors should be innovated.

Our prevalence study (Chapter 4) showed that one out of three older (65+) individuals receiving home care and one out of five individuals in the highest age group (85+) of the general community-dwelling population was undernourished. Concerning investment of time and money, it could be useful to investigate possibilities for targeting the screening of undernutrition to these specific risk groups.

Treatment

History

2007 Guideline Perioperative Nutrition A national guideline on perioperative nutrition was developed by The Dutch Institute for Healthcare Improvement CBO (23). This guideline enclosed recommendations and instructions to support the daily practice around the feeding of patients before surgery.

2008 Performance Indicator hospital The treatment of undernutrition became a performance indicator (PI) for hospital patients. To examine the execution of this PI, the intake of protein as a percentage of the requirements at the fourth day of hospital admission is determined for the undernourished patients by the Dutch Healthcare Inspectorate. The percentage undernourished patients with sufficient protein intake (>90% from requirement) slightly increased from 39% in 2008 to 42% in 2009 and 44% in 2010 (24).

2009 Cochrane review nutritional supplements Milne et al. published a meta-analysis on the effects of supplementing ONS in older individuals (18). A positive statistically significant effect was found on body weight and reducing the complication risk. No effects were found on length of hospital stay or muscle strength. A subgroup analysis in undernourished individuals showed an effect on reducing mortality.

Compensation dietary supplementation Based on the results of a validated screening instrument, undernourished patients are eligible for compensation of dietary supplementation through their basic health insurance.

2010 MNI award The Dutch approach of undernutrition received the international **'**MNI Fight Against Malnutrition' award from the European Society for Clinical Nutrition and Metabolism (ESPEN). This award was used to develop an international website.[2]

2011 Health Council report 'Malnutrition in the elderly' The scientific evidence of the effects of treating undernutrition is limited. In contrast to the meta-analysis of Milne et al. (18), the Health Council concluded that the evidence of ONS for the effect on mortality was inconsistent and for the effect on the risk of complications was insufficient. No effect was found for the length of hospital

[2] *www.fightmalnutrition.eu*

stay. No conclusions could be given for other clinically relevant outcome measures (10).

2012 Dietetic treatment in basic health insurance The compensation for dietetic treatment was removed from the basic health insurance of 2012. However, the compensation will be resumed in the basic health insurance next year. This is stated in the preliminary annual plan of the Dutch government.

This thesis Completion of this thesis.

Present: findings of this thesis and methodological considerations

Main findings

The scientific evidence of the effects of treating older undernourished individuals in primary care is limited. Therefore, we performed the first study focusing on the effectiveness and cost-effectiveness of a dietetic treatment alone in primary care in older, undernourished, community-dwelling individuals. The results of this intervention study were presented in Chapter 5 and Chapter 6. A total of 146 older, undernourished and independently living individuals were randomly allocated to either the intervention (*N* 72) or control (*N* 74) group. The intervention consisted of an individualized dietetic treatment in primary care. Both groups were prescribed combined calcium plus vitamin D supplements. After 6 months, no statistically significant differences were found between the intervention and control groups in terms of change in body weight, physical functioning, body composition, nutritional intake and quality of life. Also no difference in total costs between the intervention and control group was found. This was confirmed by the cost-effectiveness planes and cost-effectiveness acceptability curves for body weight and quality of life. Subgroup analyses showed a statistically significant treatment effect on body weight in individuals with a normal appetite and in those who were physically active at baseline.

To investigate which undernourished individuals have the greatest risk of further deterioration of their nutritional status and require treatment, we developed a prediction model for future weight loss in our total study sample in Chapter 7. Positive predictors for losing ≥3% body weight in 6 months after assessment of undernutrition were: poor cognitive status, poor physical quality of life, receiving household care and a higher BMI. The prediction model enables the identification of undernourished older individuals at risk for further deterioration of their nutritional status over time.

Methodological considerations

Randomization

The Nutrition in Primary Care Study (NPCS) was designed as a Randomized Controlled Trial. The primary benefit of randomization is that it eliminates both conscious bias and unconscious bias associated with the selection of a treatment for a specific individual. Without randomization, the researcher or participant may influence the choice of the intervention. Due to the active involvement of the participant in the intervention, blinding of the participant for the intervention assignment was not applicable to our study. Furthermore, those executing the examinations at the participants' home were also not blinded for the assignment. This was not feasible in our study, because questions about the received treatment were also part of the examination. Moreover, blinding the GP for the intervention assignment was also not possible, because they were informed about the participation and assignment and were requested to refer the participant assigned to the intervention group to the dietitian. The provided care of the GP may have been influenced by his/her knowledge about the screening outcome. This could have caused an underestimation of the intervention effect as the control group would have likely been referred to and treated by a dietitian. However, during the six months of the study, only five participants of the control group (7%) were referred to a dietitian by their GP. Excluding these participants in a per protocol analysis, did not influence the conclusions regarding the effectiveness of the intervention.

Study design

Our study focused on the effect of an individualized nutritional intervention performed by a dietitian, which was not earlier studied in this setting. The treatment was provided by regular dietitians within the primary care setting and the results are therefore well applicable to the usual primary care situation. Assuming that improving the nutritional intake by dietetic counseling results in an improvement of the nutritional status, we expected an increase in energy intake and body weight. However, we could not demonstrate these effects in our study. Apparently, a dietetic intervention is not sufficient to achieve an improvement of the nutritional status.

There are several factors concerning the design of the treatment plan, utilization of the treatment and participant characteristics that may have contributed to the absence of a treatment effect in our study. These different factors will be discussed subsequently. We cannot assure which of these factors contributed the most. Possibly, it was a combination of the listed factors that contributed to the lack of effect.

- The treatment plan used in the intervention was based on the results of four meetings with two focus groups consisting of oncology nurses, dietitians (working independently in primary care, home care organization, hospital or nursing home) and dietetic managers. The developed treatment plan is shown in **Appendix 2**. Part of the treatment was a risk profile, consisting of a questionnaire on the presence of predefined risk factors associated with undernutrition. The risk profile was sent to each participants' home and the participant was asked to fill in the questionnaire prior to the first consult. The risk profile is shown in **Appendix 3**. During the first consultation, dietitians were instructed to discuss the risk profile and complete a personal action plan together with the participant. The action plan is shown in **Appendix 4**. During each consecutive consultation, the action plan was discussed with the participant and adjusted to the situation if needed. The content of the treatment was individualized not only depending on the nutritional situation, but also on the specific needs and desires of the participant.

  We did not investigate the effectiveness of the treatment plan itself, by comparing it to a regular used treatment plan. Possibly, the developed treatment plan was not sufficient to improve nutritional status in older undernourished individuals and to show significant results on e.g. energy intake and body weight.

- A motivational interviewing technique was used in the treatment. Although it has been shown that this technique has beneficial effects in a large range of lifestyle problems and diseases (25), as well as in older individuals (26-28), we cannot exclude that this technique might not be the most optimal choice for older, undernourished individuals to achieve dietary behavior change.

- All participating dietitians received a specific training about the treatment of older, undernourished individuals. The dietitians were instructed to utilize the treatment plan as much as possible. A limitation of our study was that we had no insight in the actual achievement and implementation of this plan in their treatment. Therefore, we do not know whether the dietitians implemented and applied the treatment plan, or whether they reverted to their own familiar form of treatment. However, our approach may most correspond to the actual implementation of a dietetic treatment in the regular primary care setting.

- Study participants were actively recruited through assessing undernutrition in a primary care location. We suppose that participants were sometimes in a phase of precontemplation and did not realize the importance of treating their undernourished condition. Several participants included based on a low MUAC told that they had always been thin. An additional analysis showed the effect of the treatment did not

differ between those included based on unintentional weight loss and those included based on a low MUAC. Thereby, the intervention was not more effective in those with recent weight loss or in those with a low MUAC.

- The complexity of the participants may also have contributed to the lack of a treatment effect. A high proportion suffered from one or more chronic diseases (77%), the large majority used multiple medications (90%) and a high percentage experienced depressive symptoms (36%). A reduced nutritional status is often part of a number of problems and diseases in older individuals (29, 30) and is not identified by the older individuals as their most important problem. Performing only a nutritional intervention might not be sufficient to improve the nutritional status. The nutritional intervention should potentially be accompanied by the management of other (health) problems, and especially those problems which may be the underlying cause of undernutrition (e.g. mobility problems, pain, nausea, etc.).

Future: implications for research and clinical practice

Implications for research

Concerning opportunities for future research focusing on the treatment of undernutrition in older individuals in primary care, two possible research approaches will be discussed. The first approach may investigate opportunities for treating underlying problems and factors associated with the undernourished condition and its development, while the second approach investigates the effects of a nutritional treatment.

1. Treating specific, individual, underlying determinants and problems associated with undernutrition may be an effective strategy to prevent the development of undernutrition in those at risk of undernutrition, but may also support the management of undernutrition. Some determinants may be simply treatable by disciplines other than a nutritional intervention. For example, providing food-shopping service in case of food-shopping problems, referral to a dentist when problems with biting or chewing are present, physical therapy in case of physical limitations, or referral to a psychologist or GP in case of depressive symptoms may already result in an improved nutritional status and limits the need for nutritional intervention. Future studies investigating such a multidisciplinary approach in the prevention and treatment of undernutrition are needed.
2. The Health Council concluded that the methodological quality of available studies investigating the effects of supplementation in undernourished older individuals is limited. To achieve a better evaluation of treatment and to improve current treatment,

more high quality research is needed with enough power and duration of follow-up. There is need for a large multicenter study to enable the execution of predefined subgroup analyses for BMI and extent of unintentional weight loss. Scientific evidence of an effective nutritional treatment may support in detecting those who will benefit from a nutritional intervention and therefore have a 'treatable' type of undernutrition. This information could also help in improving the determination of 'true' undernutrition, when assuming that those who improved their nutritional prognosis during a nutritional intervention, were truly undernourished at baseline. Thus, characterizing these individuals afterwards may thereby support in improving the recognition of true undernutrition and potentially the development of a gold standard of undernutrition. This better classification may also result in prevalence rates based on true undernutrition.

A large multicenter study may also enable other subgroup analyses as we showed in our study that clues for effective treatment may be found in particular subgroups (Chapter 5). The intervention was effective on body weight in physically active participants and participants with a normal appetite. Executing subgroup analyses may give insight into identifying specific groups of older undernourished individuals whose nutritional prognoses are most effectively improved by certain treatments. The potential effects of an improved nutritional prognosis should also be investigated in this large multicenter study. Final aim of treatment is to improve functional outcomes and quality of life. Until now, based on available observational studies it is unclear if health problems associated with undernutrition, like impaired functionality or decreased quality of life, are caused by underlying factors such as disease or by the undernourished condition itself.

A final recommendation for all future research related to the prevention or treatment of undernutrition is to include a core set of primary outcome measures in future intervention studies. Better alignment of the methods in future studies will facilitate pooling of data from different studies and the performance of meta-analyses.

Implications for clinical practice

The scientific evidence of the effects of treating undernourished older individuals in primary care is insufficient. Previous studies mostly focused on the effect of a standard prescription of ONS (18). The Health Council performed an analysis containing only RCTs including undernourished participants and meeting certain pre-determined quality criteria (10). The effect of ONS on mortality was inconsistent and the evidence of the effect on the risk of complications was insufficient. No effect of ONS was found for the length of

hospital stay. No conclusions could be given for other clinically relevant outcome measures. The effect of treating undernourished older individuals with a dietetic treatment alone was previously studied only in hospitalized patients (31). An individualized dietetic treatment consisting of 4 consults, whereby ONS was prescribed if needed, was compared to standard hospital care. After 6 months, a positive treatment effect was shown on the subjective assessment part of the Mini Nutritional Assessment score and on mortality. No effect was shown on body weight or nutritional intake. These results in hospitalized patients are comparable to the results of our study in primary care.

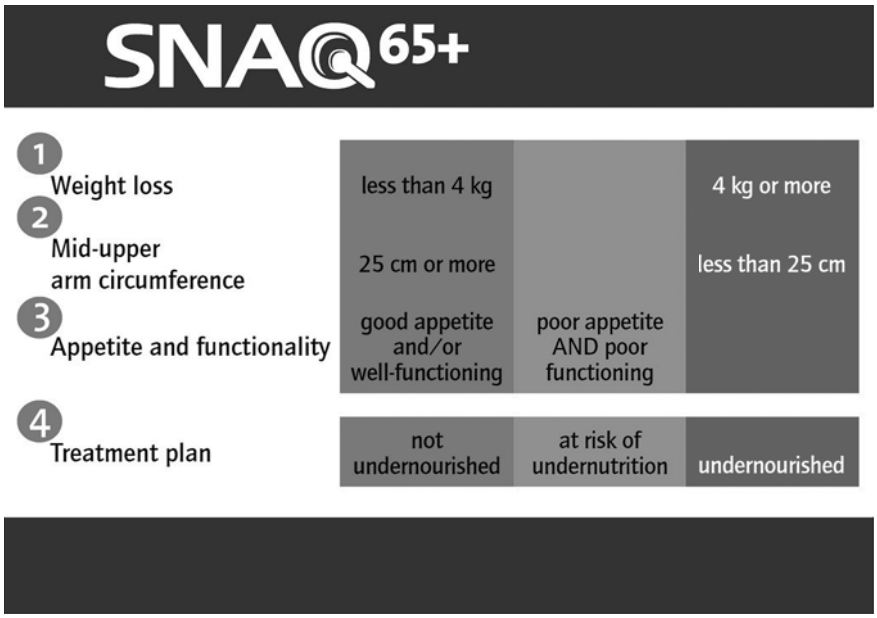
The availability of limited scientific evidence does not implicate that older undernourished individuals should not be treated at all. Although the evidence for treatment with ONS is limited, it may be effective in specific individuals, provided that the compliance is high and supplementation is well controlled by a dietitian. Regularly dietetic counseling is important to achieve a high compliance of ONS, as was concluded in a previous study in hospital patients after discharge (32).

We showed in Chapter 7 that specific characteristics of undernourished individuals contributes to a higher risk of further weight loss and thus further deterioration of their nutritional status. Opportunities in clinical practice of embedding these characteristics in the identification of target groups for treatment, should be investigated.

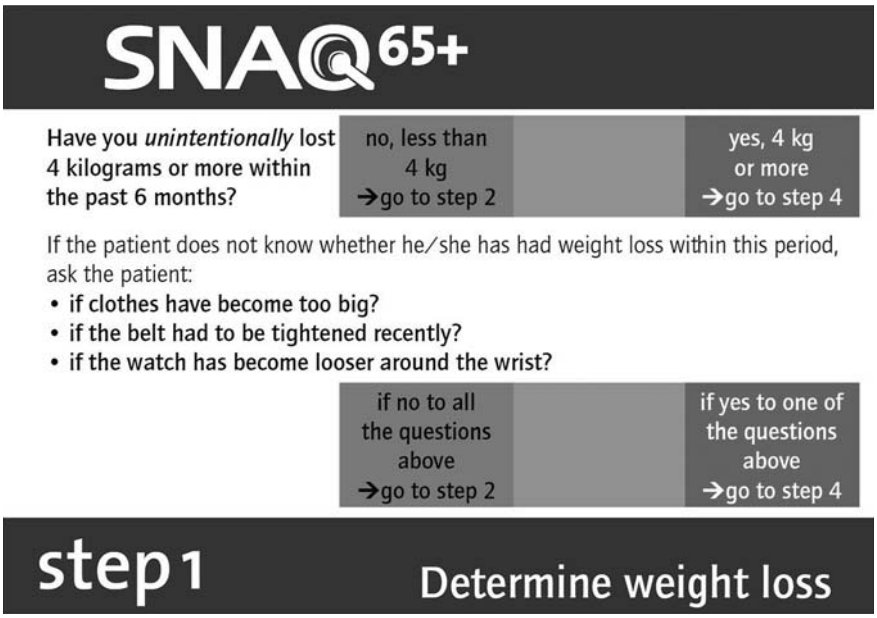
Finally, a major challenge in clinical practice is improving the registration of patient characteristics, provided treatment, compliance, treatment results and drop-out in undernourished older individuals. Collecting and analyzing these data may support better understanding of which treatment elements will be effective in which individuals and will also support the development of intervention studies testing promising treatment strategies.

Appendix 1. SNAQ^{65+}

1.



2.



3.

SNAQ 65+

1. Keep the left arm at a 90° angle with the palm of the hand turned towards the body
2. Determine the centre point between the lateral bone of the shoulder (acromion) and the tip of the elbow (olecranon)
3. Measure the circumference of the left upper arm at the centre point with the arm hanging loosely

25 cm or more →go to step 3		less than 25 cm →go to step 4

step 2 Measure the mid-upper arm circumference

4.

SNAQ 65+

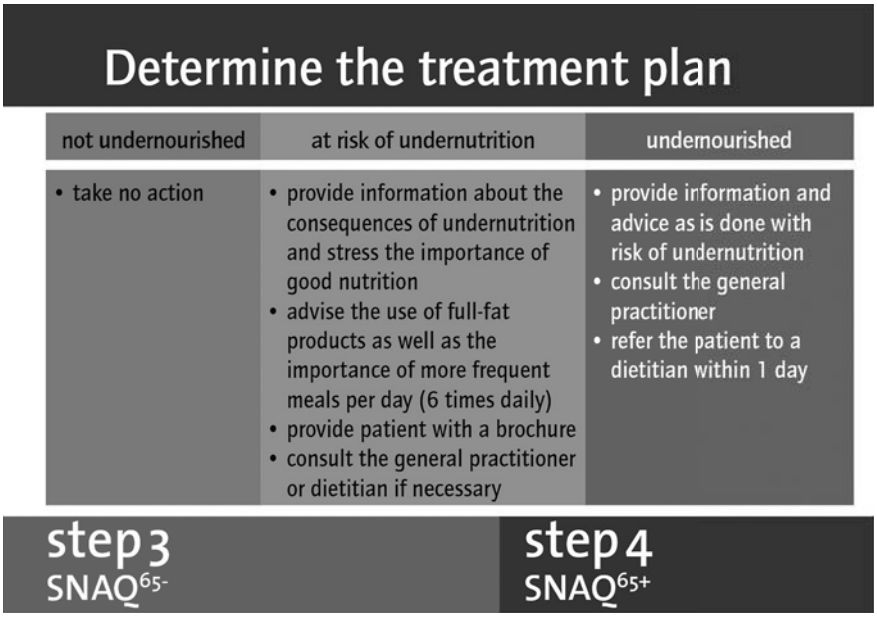
Did you have a poor appetite in the past week?	if no →go to step 4	if yes +	
Can you walk up and down a staircase of 15 steps without resting?	if yes →go to step 4	no →go to step 4*	

If the patient doesn't climb stairs anymore, ask the following question:
Are you able to walk outside for 5 minutes without resting?
or if a patient is wheelchair bound:
Are you able to move your own wheelchair for 5 minutes without resting?

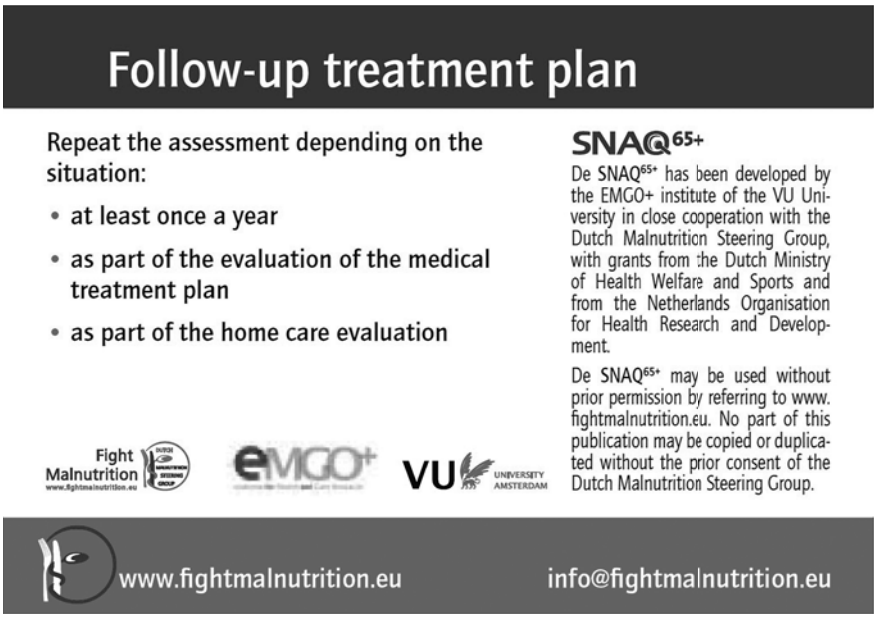
*There is only a risk of undernutrition, if the answers to *both* questions fall within orange

step 3 Assess appetite and functional status

5.


Determine the treatment plan
not undernourished
at risk of undernutrition
undernourished
• take no action
• provide information about the consequences of undernutrition and stress the importance of good nutrition
• advise the use of full-fat products as well as the importance of more frequent meals per day (6 times daily)
• provide patient with a brochure
• consult the general practitioner or dietitian if necessary
• provide information and advice as is done with risk of undernutrition
• consult the general practitioner
• refer the patient to a dietitian within 1 day
step 3
SNAQ65-
step 4
SNAQ65+

6.


Follow-up treatment plan
Repeat the assessment depending on the situation:
• at least once a year
• as part of the evaluation of the medical treatment plan
• as part of the home care evaluation
SNAQ65+
De SNAQ65+ has been developed by the EMGO+ institute of the VU University in close cooperation with the Dutch Malnutrition Steering Group, with grants from the Dutch Ministry of Health Welfare and Sports and from the Netherlands Organisation for Health Research and Development.
De SNAQ65+ may be used without prior permission by referring to www.fightmalnutrition.eu. No part of this publication may be copied or duplicated without the prior consent of the Dutch Malnutrition Steering Group.
Fight Malnutrition
EMGO+
VU UNIVERSITY AMSTERDAM
www.fightmalnutrition.eu
info@fightmalnutrition.eu

Appendix 2. Treatment plan dietitian

The treatment is based on a risk profile (appendix 2) that has been filled out by the patient him/herself. Together with the dietitian the patient discusses his/her risk profile and determines which problems he/she wants to tackle first. The risk profile and the action plan (appendix 3) are also published on this website (www.fightmalnutrition.eu).

This documents describes the possible steps that the dietitian can take to help a patient.

Time schedule

≤1 working day after diagnosis of (the risk of) malnutrition: referral to a dietitian
≤2 working days: assess intake by telephone (explaining risk profile and nutritional diary)
≤5 working days after the telephone contact: plan a consultation
≤2 working days after the consultation: start treatment
≤2-10 working days after the start of treatment: evaluate and adjust (if necessary)

Example of a treatment scheme

These examples are based on the Dutch reimbursement rules for consultations by a dietitian. A patient is reimbursed for a maximum of 4 hours of dietetic consultations per y.

Consultation at the dietitian's office		***Home visit***	
Intake assessment by telephone	15 min	Intake assessment by telephone	15 min
First consultation	45 m	Home visit/ first consultation	45 min
Three follow-up consultations	3 x 15 min	Two follow-up consultations	2 x 30 min
Three contacts by telephone	3 x 5 min	Three contacts by telephone	3 x 5 min
Follow-up consultation after 5 months	15 min	Follow-up consultation after 5 months	30 min
Final consultation after x months	15 min	Final consultation after x months	10 min
Mailing tips and tricks	5 min	Mailing tips and tricks	5 min
Registration and administration	90 min	Registration and administration	90 min
Total	**4 hours**	**Total**	**4½ hours**

Notes:

- Patients lose motivation after approximately 6 months
- The consultations consist of a combination of telephone consultations, face-to-face contact, reminders (letter, e-mail)
- Tips: think of recipes, show patients the advantages of keeping to their dietary advice.

Intake by telephone

- Get an impression of the degree of malnutrition
- Explain the risk profile chart (see the following pages) and nutrition diary
- Make an appointment
- Answer any questions

First consultation

- Personal data
- Medical background (medical diagnoses, medical history, clinical observations by the referring doctor, medical treatment, medication, prognosis, other relevant information)
- Psychosocial data (living situation, education, school, work, ethnicity)
- Reason for referral to the dietitian
- Other referrals (social worker, home care, physiotherapist etc.)
- Check and discuss risk profile:
  - Did you manage to fill out the profile: what struck / impressed you most?
  - Has the patient fillled out the profile in correctly?
  - Discuss any unexpected /abnormal scores
  - Explore any reasons for the unexpected scores
  - Discuss the significance of the problem with the patient
  - Explain the reasons for and consequences of any unexpected / abnormal scores
- Calculate requirements
  - Protein: 1,2 - 1,7 gram/kg/day (in case of overweight, use the weight assigned to BMI 27)
  - Energy: H&B (1984) + 30% extra for activities
  - Give advice about Vitamin D and Calcium (>65 years)
- Take into account the possible risk of the Refeeding Syndrome, especially in patients with very low body weights (BMI <17 kg/m^2) or in patients with involuntary weight loss who have not eaten for the last 7 days.
- Summarise the findings of the risk profile with the patient
- Discuss what the patient would like to do (patient's wishes)
- Which risk factor would the patient like to begin with?
- Give general advice
- Explain the action plan
- Make new appointments

Follow-up consultations

This schedule can be used as a guideline for the dietitian, but must be adapted according to a patient's personal circumstances.

Intake and requirements	Nutritional intervention	Evaluation and next steps
Patient meets 100% of his/ her requirements	Advise a protein and energy enriched diet (if necessary advise oral nutritional supplements)	The patient is asked to monitor his/her own intake and body weight. The patient should contact the dietitian if there are any problems with his/her diet. The dietitian contacts the patient within 10 working days (by telephone).
Patient meets 75-100% of requirements	Advise protein and energy enriched diet (if necessary advise oral nutritional supplements)	The dietitian evaluates intake and monitors body weight within 10 working days. If necessary, he/she will advise starting or continuing oral nutritional supplements.
Patient meets 50-75% of requirements	Advise protein and energy enriched diet and oral nutritional supplements (or tube feeding)	The dietitian evaluates intake and monitors body weight within 5 working days. If necessary he/she will advise starting or continuing tube feeding.
Patient meets <50% of requirements	Advise protein and energy enriched diet combined with tube feeding. Consider complete tube feeding	The dietitian evaluates intake and monitors body weight within 2 working days. He/she will adapt the tube feeding or supplement regimen if necessary.

Check and discuss risk profile:

- Did you manage to fill out the profile: what struck / impressed you most?
- Has the patient filled out the profile in the correctly?
- Discuss any unexpected / abnormal scores
- Explore the reasons for any unexpected / abnormal scores
- Discuss the significance of the problem with the patient
- Explain the reasons for and consequences of any unexpected / abnormal scores

Risk profile

Risk	Points of attention
1. Involuntary weight loss	- Use SNAQ^{65+} or other objective criteria for assessing malnutrition to diagnose any (risk of) malnutrition - Register the present weight and usual weight of the patients, calculate involuntary weight loss - Discuss the consequences of involuntary weight loss with the patient
2. Body weight is too low	- Calculate the optimum body weight (based on BMI: BMI 22-28 ≥65 or BMI 20-25 <65) - Determine the mid arm muscle circumference - If possible determine the FFMI - Discuss the consequences of low body weight with the patient
3. Reduced intake	- Check the specific problems , their seriousness, frequency, and any reason(s) for them - Check if there is a relationship between the problems and the nutritional intake - Check medication(s) if there is nausea - Refer to a dentist if there are dental problems - Consult with a speech therapist if there are swallowing problems
4. Gastrointestinal complaints	- Check the specific problems , their seriousness, frequency and any reason(s) for them - Check if there is a relationship between the problems and the nutritional intake - Check medication(s)
5. Unbalanced diet	- Discuss the nutritional diary with the patient - Is the diary representative of the last month - Discuss any findings about completeness, amounts eaten and altered food intake

Risk	Points of attention
6. Difficulties shopping and cooking (including poverty)	- Check the specific problems , their seriousness, frequency and any reason(s) for them - Check if there is a relationship between the problems and the nutritional intake - Discuss possible solutions (meals on wheals, eating facilities in nearby community homes etc)
7. Other complaints such as tiredness, loneliness, depression, pain	- Check the specific problems , their seriousness, frequency and any reason(s) for them - Check if there is a relationship between the problems and the nutritional intake - Check medication(s), especially in case of pain or depression - Check the pain score in case of pain - Consult with the GP to discuss treatment(s) by other professionals

- Summarise the risk profile with the patient
- Fill out an action plan with the patient
- Ask the patient which issue he/she would like to be dealt with first
- Give initial general advice

Appendix 3. Risk profile

Preparing for your consultation with the dietitian

You have made an appointment with your dietitian. Please fill out the questions on the next page. In addition, please fill out a nutrition diary for two consecutive days.

Filling out the questionnaire

By filling out the questionnaire and the diary, the dietitian can get an impression of your nutritional intake status and any nutrition problems you may have. You will then be able to discuss the questionnaire with the dietitian and together you can make an action plan for treatment.

Circle the answer that applies to you most.

Questionnaire

1. Have you lost weight involuntarily	No	Yes, a little	Yes, quite a lot
2. What do you think about your body weight?	Good	A bit too thin	Far too thin
3. Have you eaten less than normal during the last month? (you can give more than 1 answer)	No	A little less, because of O loss of appetite O nausea O change of taste O chewing problems O swallowing problems O other: ….	Much less, because of O loss of appetite O nausea O change of taste O chewing problems O swallowing problems O other: ….
4. Do you have any gastro-intestinal problems?	Never	Sometimes	Yes
5. Do you think you are eating in a healthy way?	Yes, most of the time	Sometimes	Almost never
6. Do you need help with shopping and cooking?	No	O Yes, with shopping O Yes, with cooking	O Yes, with shopping and cooking
7. Are you tired?	No	Sometimes	Often
8. Do you have pain?	No	Sometimes	Often

Appendix 4. Action plan

Risk profile	Score	Which risk profile would I like to work on?
1. Involuntary weight loss		
2. Present weight		
3. Eating problems		
4. Gastrointestinal problems		
5. Unbalanced menu		
6. Need help with cooking or eating		
7. Tiredness		
8. Pain		
9. Sadness or depression		

How will it help me if I have better nutritional status or if I improve the risk factor that I choose to work on?

-
-
-

What could I do to reach those goals?

-
-
-

My plan: how am I going to do this?

-
-
-

Why might I not succeed?

-
-
-

What can I do to succeed anyway?

-
-
-

How sure am I that I can do this? I need to pick a number on a 10-point scale, 1 meaning that I am not sure I can do it and 10 meaning that I am sure I am going to do it. My number is:

References

1. Kruizenga HM, Wierdsma NJ, van Bokhorst MA, et al. Screening of nutritional status in The Netherlands. Clin Nutr 2003;22:147-52.
2. Meijers JM, Schols JM, van Bokhorst-de van der Schueren MA, Dassen T, Janssen MA, Halfens RJ. Malnutrition prevalence in The Netherlands: results of the Annual Dutch National Prevalence Measurement of Care Problems. Br J Nutr 2008:1-7.
3. Halfens RJG, Meesterberends E, Meijers JMM, Du Moulin MFMT, Van Nie NC, Neyens JCL, Schols JMGA. Rapportage resultaten: Landelijke Prevalentiemeting Zorgproblemen (National Prevalence Measurement of Care Problems). Maastricht University, 2011.
4. Kruizenga HM, Seidell JC, de Vet HC, Wierdsma NJ, van Bokhorst-de van der Schueren MA. Development and validation of a hospital screening tool for malnutrition: the short nutritional assessment questionnaire (SNAQ). Clin.Nutr. 2005;24:75-82.
5. Dutch Health Care Inspectorate, Ministry of Health Welfare and Sports. Performance indicators hospitals, 2010. Utrecht, The Netherlands, 2009:43-49.
6. Halfens RJG, Meijers JMM, Neyens JCL, Offermans MPW. Rapportage resultaten: Landelijke Prevalentiemeting Zorgproblemen (National Prevalence Measurement of Care Problems). Maastricht University, 2008.
7. Halfens RJG, Meijers JMM, Du Moulin MFMT, Van Nie NC, Neyens JCL, Schols JMGA. Rapportage resultaten: Landelijke Prevalentiemeting Zorgproblemen (National Prevalence Measurement of Care Problems). Maastricht University, 2010.
8. Kruizenga HM, de Vet HC, Van Marissing CM, et al. The SNAQ(RC), an easy traffic light system as a first step in the recognition of undernutrition in residential care. J Nutr Health Aging 2010;14:83-9.
9. Van Avendonk MJ, Mensink PA, Drenthen AJ, van Binsbergen JJ. Primary care and public health a natural alliance? The introduction of the guidelines for obesity and undernutrition of the Dutch College of General Practitioners. Fam Pract 2012;29 Suppl 1:i31-i35.
10. Health Council of the Netherlands. Malnutrition in the elderly. The Hague, 2011.
11. Kyle UG, Kossovsky MP, Karsegard VL, Pichard C. Comparison of tools for nutritional assessment and screening at hospital admission: a population study. Clin Nutr 2006;25:409-17.
12. 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 Gerontol A Biol Sci Med Sci 2001;56:M366-72.
13. Detsky AS, McLaughlin JR, Baker JP, et al. What is subjective global assessment of nutritional status? JPEN J Parenter Enteral Nutr 1987;11:8-13.
14. Guigoz Y, Lauque S, Vellas BJ. Identifying the elderly at risk for malnutrition. The Mini Nutritional Assessment. Clin Geriatr Med 2002;18:737-57.
15. Keller HH, Goy R, Kane SL. Validity and reliability of SCREEN II (Seniors in the community: risk evaluation for eating and nutrition, Version II). Eur J Clin Nutr 2005;59:1149-57.

16. Elia M. Screening for malnutrition: a multidisciplinary responsibility. Development and use of the “Malnutrition Universal Screening Tool" (MUST) for adults. Worcester: Malnutrition advisory group (MAG) - a standing committe of BAPEN, 2003.
17. Wilson JM, Jungner YG. Principles and practice of mass screening for disease. Bol Oficina Sanit Panam 1968;65:281-393.
18. Milne AC, Potter J, Vivanti A, Avenell A. Protein and energy supplementation in elderly people at risk from malnutrition. Cochrane Database Syst Rev 2009:CD003288.
19. Van Asselt DZ, van Bokhorst-de van der Schueren MA, van der Cammen TJ, et al. Assessment and treatment of malnutrition in Dutch geriatric practice: consensus through a modified Delphi study. Age Ageing 2012;41:399-404.
20. Dutch Malnutrition Steering Group. Guideline screening and treatment of undernutrition. Amsterdam, 2011.
21. Neelemaat F, Bosmans JE, Thijs A, Seidell JC, van Bokhorst-de van der Schueren MA. Oral nutritional support in malnourished elderly decreases functional limitations with no extra costs. Clin Nutr 2011;31:183-90.
22. Schilp J, Kruizenga HM, Wijnhoven AHA, et al. High prevalence of undernutrition in Dutch community-dwelling older individuals. Nutrition 2012;28(11-12):1151-6.
23. Institute for Healthcare Improvement CBO. Guideline Perioperative Nutrition. Utrecht, The Netherlands, 2007.
24. Dutch Healthcare Inspectorate. Het resultaat telt (It's the result that counts), 2008 - 2010. Utrecht, The Netherlands,
25. Rubak S, Sandbaek A, Lauritzen T, Christensen B. Motivational interviewing: a systematic review and meta-analysis. Br J Gen Pract 2005;55:305-12.
26. Brodie DA, Inoue A, Shaw DG. Motivational interviewing to change quality of life for people with chronic heart failure: a randomised controlled trial. Int J Nurs Stud 2008;45:489-500.
27. Fleming MF, Manwell LB, Barry KL, Adams W, Stauffacher EA. Brief physician advice for alcohol problems in older adults: a randomized community-based trial. J Fam Pract 1999;48:378-84.
28. Bennett JA, Perrin NA, Hanson G, et al. Healthy aging demonstration project: nurse coaching for behavior change in older adults. Res Nurs Health 2005;28:187-97.
29. Chen CC, Schilling LS, Lyder CH. A concept analysis of malnutrition in the elderly. J Adv Nurs 2001;36:131-42.
30. Hickson M. Malnutrition and ageing. Postgrad Med J 2006;82:2-8.
31. Feldblum I, German L, Castel H, Harman-Boehm I, Shahar DR. Individualized nutritional intervention during and after hospitalization: the nutrition intervention study clinical trial. J Am Geriatr Soc 2011;59:10-7.
32. Neelemaat F, Bosmans JE, Thijs A, Seidell JC, van Bokhorst-de van der Schueren MA. Post-discharge nutritional support in malnourished elderly individuals improves functional limitations. J Am Med Dir Assoc 2011;12:295-301.

Summary

Introduction

Due to the aging population, the high proportion of older individuals living independently in the community and the increasing prevalence of undernutrition with age, undernutrition is a significant problem in community-dwelling older individuals. Undernutrition can be defined as "a disorder of nutritional status from reduced nutrient intake or impaired metabolism". A feasible and validated instrument for assessing undernutrition in community-dwelling older individuals is needed. Furthermore, insufficient scientific evidence is available for the treatment of undernourished older individuals in primary care. This thesis describes possibilities for the recognition and treatment of undernutrition in community-dwelling older individuals. The aim was to evaluate the effectiveness and cost-effectiveness of a dietetic treatment in primary care of older individuals assessed as undernourished.

Recognition: main findings

Three studies were performed concerning the recognition of undernutrition. We first identified a variety of determinants associated with the development of undernutrition during a 9-year follow-up in a general older population participating in the Longitudinal Aging Study Amsterdam (LASA) in **Chapter 2**. Those reporting a poor appetite and those with functional limitations (reporting difficulty climbing a staircase) had the highest risk to develop undernutrition in the future. Then we developed and validated a quick and easy-to-apply assessment instrument for undernutrition in the community in **Chapter 3**: the Short Nutritional Assessment Questionnaire 65+ ($SNAQ^{65+}$). With the $SNAQ^{65+}$, a distinction can be made between:

1. *Undernutrition*: mid-upper arm circumference (MUAC) <25 cm *or* ≥4 kg unintentional weight loss within the past 6 months
2. *Risk of undernutrition*: poor appetite in the last week *and* difficulty climbing a staircase
3. *No undernutrition*: other

The hazard ratio for 15-year mortality was 2.22 (95% CI 1.83; 2.69) for the undernourished group (1) and 1.57 (1.22; 2.01) for the group wit risk of undernutrition (2). The area under the curve was 0.55. The $SNAQ^{65+}$ can be easily performed in older community-dwelling individuals and shows good face validity and moderate predictive validity. Subsequently, a prevalence study was performed and described in **Chapter 4** to investigate the extent of the problem of undernutrition in the older community. This study showed that undernutrition is a substantial problem in older individuals in the community. The prevalence of undernutrition, assessed with the $SNAQ^{65+}$, was 35% in patients receiving

home care, 12% in general practice patients during the influenza vaccination and 11% in a general older population. The prevalence of the risk of undernutrition in those three samples was 9%, 2% and 11% respectively. The prevalence of undernutrition increased with age in general practice patients and in the general older population. The prevalence in those aged ≥85 year was 23% in general practice and 21% in the general older population. In home care patients, no relationship with age was found.

Treatment: main findings

The effectiveness of the randomized controlled trial (RCT) of a dietetic treatment in 146 older, undernourished, community-dwelling individuals is described in **Chapter 5**. Participants were randomized to either the intervention or control group. The intervention group (*N* 72) was referred to and treated by a primary care dietitian. The control group (*N* 74) was not referred to a dietitian, but received a standard brochure with general information about healthy eating habits. Both groups were prescribed combined calcium plus vitamin D supplements. After 6 months, no statistically significant effect of the intervention was found on the primary outcomes body weight, physical performance and handgrip strength. Also no treatment effect was found on nutritional intake and body composition. Subgroup analyses showed that the treatment was effective on body weight in physically active participants and in participants with a normal appetite. Furthermore, costs were measured from a societal perspective to evaluate the cost-effectiveness of the dietetic treatment in **Chapter 6**. No statistically significant differences between the intervention and control group were found for the effects on body weight change and QALY, and on total costs. The ICER for body weight gain was 2111, and the ICUR for QALYs was not interpretable. No cost-effectiveness of the treatment was shown.

A post-hoc analysis was performed in **Chapter 7**, including only participants from both the intervention and the control group with a repeated body weight assessment at the 6 month follow-up examination (*N* 126). The aim was to develop a prediction model for future body weight loss. During 6 months follow-up, 26% of the study sample lost ≥3% weight and 26% gained ≥3% weight. Positive predictors for losing ≥3% weight in 6 months were poor cognitive status, poor physical quality of life, receiving household care and a higher BMI. The prediction model may provide a helpful tool in identifying those who are likely to experience further weight loss. Targeting treatment to these high-risk individuals may be more cost-efficient than targeting treatment to the whole group of undernourished individuals, as weight regain has been observed in older persons after a period of weight loss.

Conclusions

We conclude that undernutrition is a prevalent problem in community-dwelling older individuals. A dietetic treatment, as currently provided by trained dietitians in primary care, was not effective or cost-effective on body weight and quality of life. Also no effects were found on physical performance, handgrip strength, nutritional intake and body composition.

Future studies should focus on the early detection of individual risk factors associated with the development of undernutrition and investigate possibilities for appropriate prevention strategies. In clinical practice, more attention is needed for the screening of those at high risk for developing undernutrition and for creating awareness in older individuals themselves for health nutrition and prevention of weight loss. Potential underlying causes of undernutrition should be determined better, followed by active treatment of these factors.

Treating specific, individual, underlying determinants and problems associated with the undernourished condition may be an effective strategy to prevent the development of undernutrition in those at risk of undernutrition and may also support in the management of undernutrition. A large multicenter study is needed to enable the execution of predefined subgroup analyses to detecting those older undernourished individuals who will benefit from nutritional treatment (using supplements and/or ordinary food products). A core set of primary outcome measures should be included in all future studies to facilitate pooling of data and performance of meta-analyses. Another challenge is to improve the registration of patient characteristics, provided treatment and treatment results in clinical practice to support better understanding of which treatment elements will be effective in which individuals.

Samenvatting

Introductie

Gezien de vergrijzende populatie, het hoge percentage thuiswonende ouderen en de toenemende prevalentie van ondervoeding met de leeftijd, is ondervoeding een significant probleem onder thuiswonende ouderen. Ondervoeding kan gedefinieerd worden als “een stoornis in de voedingsstatus door verminderde voedingsinname of beperkt metabolisme”. Er is behoefte aan een eenvoudig te gebruiken en gevalideerd instrument om ondervoeding bij thuiswonende ouderen vast te stellen. Bovendien is er onvoldoende wetenschappelijk bewijs beschikbaar over de behandeling van ondervoede ouderen in de eerstelijnszorg. Dit proefschrift beschrijft mogelijkheden voor herkenning en behandeling van ondervoeding bij thuiswonende ouderen. Het doel was om de effectiviteit en kosteneffectiviteit van de behandeling van ondervoede ouderen door een diëtist in de eerstelijnszorg te evalueren.

Herkenning: belangrijkste bevindingen

Om de herkenning van ondervoeding te onderzoeken zijn drie studies uitgevoerd. Eerst werden in **Hoofdstuk 2** verscheidene determinanten geïdentificeerd die geassocieerd waren met de ontwikkeling van ondervoeding tijdens een follow-up tijd van 9 jaar in een algemene oudere populatie die deelnam aan de Longitudinal Aging Study Amsterdam (LASA). Diegenen met een verminderde eetlust en diegenen met functionele beperkingen (moeite met traplopen) hadden het hoogste risico om in de toekomst ondervoed te raken. Daarna ontwikkelden en valideerden we in **Hoofdstuk 3** een snel en eenvoudig te gebruiken instrument om ondervoeding vast te stellen in de thuissituatie: de Short Nutritional Assessment Questionnaire 65+ ($SNAQ^{65+}$). Met de $SNAQ^{65+}$ kan een onderscheid worden gemaakt tussen:

1. *Ondervoeding*: bovenarmomtrek <25 cm *of* ≥4 kg onbedoeld gewichtsverlies in de laatste 6 maanden
2. *Risico op ondervoeding*: verminderde eetlust in de afgelopen week *en* moeite met traplopen
3. *Niet ondervoed*: anders

De hazard ratio voor 15-jaars sterfte was 2.22 (95% BI 1.83; 2.69) voor de ondervoede groep (1) en 1.57 (1.22; 2.01) voor de risicogroep voor ondervoeding (2). De oppervlakte onder de curve (area under the curve) was 0.55. De $SNAQ^{65+}$ kan eenvoudig worden toegepast bij thuiswonende ouderen en heeft een goede indruksvaliditeit en predictieve validiteit. Vervolgens werd een prevalentie studie uitgevoerd en werd in **Hoofdstuk 4** de omvang van het probleem in de thuissituatie beschreven. Deze studie liet zien dat

ondervoeding een substantieel probleem is onder thuiswonende ouderen. De prevalentie van ondervoeding, vastgesteld met de SNAQ^{65+}, was 35% in de thuiszorg, 12% in huisartspraktijken tijdens de griepvaccinatie en 11% in een algemene oudere populatie. De prevalentie van het risico op ondervoeding in deze populaties was respectievelijk 9%, 2% en 11%. De prevalentie van ondervoeding nam toe met de leeftijd in de huisartspopulatie en in de algemene oudere populatie. Onder diegenen van 85 jaar en ouder was de prevalentie 23% in de huisartspopulatie en 21% in de algemene oudere populatie. In de thuiszorgpopulatie werd geen verband met leeftijd gevonden.

Behandeling: belangrijkste bevindingen

De effectiviteit van de gerandomiseerde trial (RCT) van de dietistische behandeling in 146 ondervoede thuiswonende ouderen werd beschreven in **Hoofdstuk 5**. Deelnemers werden gerandomiseerd naar een interventie- en controlegroep. De interventiegroep (*N* 72) werd doorverwezen en behandeld door een eerstelijns diëtist. De controle groep (*N* 74) werd niet doorverwezen naar een diëtist, maar ontving een algemene folder met informatie over gezonde voedingsgewoonten. Aan beide groepen werden gecombineerde calcium plus vitamine D supplementen voorgeschreven. Na 6 maanden werd geen statistisch significant effect van de interventie gevonden op de primaire uitkomstmaten lichaamsgewicht, fysiek prestatievermogen en knijpkracht. Op voedingsinname en lichaamssamenstelling werd ook geen effect van de behandeling gevonden. Vooraf gedefinieerde subgroep analyses lieten zien dat de behandeling wel effectief was op lichaamsgewicht bij lichamelijk actieve deelnemers en bij deelnemers met een normale eetlust. Verder werden kosten gemeten vanuit een sociaal perspectief om de kosteneffectiviteit van de behandeling te kunnen evalueren in **Hoofdstuk 6**. Er werden geen statisch significante verschillen gevonden tussen de interventie- en controlegroep voor zowel de effecten verandering in lichaamsgewicht en QALY, als de totale kosten. De ICER voor lichaamsgewicht was 2111, en de ICUR voor QALY's was niet te interpreteren. Er werd geen kosteneffectiviteit van de behandeling aangetoond.

In **Hoofdstuk 7** werd een post-hoc analyse uitgevoerd, waarin alleen deelnemers van zowel de interventie- als controlegroep met een meting van het gewicht tijdens de 6-maanden meetronde werden meegenomen (*N* 126). Het doel was om een predictiemodel voor toekomstig gewichtsverlies te ontwikkelen. Gedurende 6 maanden follow-up, viel 26% van de onderzoeksgroep onbedoeld ≥3% af en kwam 26% van de onderzoeksgroep ≥3% aan. Positieve voorspellers voor ≥3% afvallen in 6 maanden waren slechte cognitieve status, slechte fysieke kwaliteit van leven, hulp in het huishouden en een hogere BMI. Het predictiemodel kan een hulpmiddel zijn in het identificeren van diegenen die

waarschijnlijk verder gewicht gaan verliezen. Mogelijk is het kostenefficiënter om de behandeling te richten op deze hoogrisico groep dan de behandeling op de totale groep ondervoede ouderen te richten, omdat herstel van gewicht na een periode van gewichtsverlies eerder al werd aangetoond bij ouderen.

Conclusies

Geconcludeerd kan worden dat ondervoeding een veelvoorkomend probleem is onder thuiswonende ouderen. Een diëtistische behandeling, zoals die op dit moment werd toegepast door getrainde diëtisten in de eerstelijnszorg, was niet effectief of kosteneffectief op lichaamsgewicht en kwaliteit van leven. Er werden ook geen effecten gevonden op fysiek prestatievermogen, knijpkracht, voedingsinname en lichaamssamenstelling.

Toekomstig onderzoek zal zich meer moeten richten op de vroege herkenning van individuele risicofactoren die geassocieerd zijn met de ontwikkeling van ondervoeding en op mogelijkheden voor passende preventie strategieën. In de klinische praktijk moet meer aandacht komen voor de screening van diegenen met een verhoogd risico op het ontwikkelen van ondervoeding en voor de bewustwording van ouderen zelf voor gezonde voeding en preventie van gewichtsverlies. Mogelijke onderliggende oorzaken van ondervoeding moeten beter opgemerkt worden, gevolgd door een actieve behandeling van deze factoren.

Het behandelen van specifieke, individuele, onderliggende determinanten en problemen die gekoppeld zijn aan de ondervoede status, kan een effectieve strategie zijn om de ontwikkeling van ondervoeding te voorkomen bij diegenen met een risico op ondervoeding en kan ook ondersteunen in het behandelen van ondervoeding. Een groot multicenter onderzoek is nodig om de analyse van vooraf bepaalde subroepen mogelijk te maken om te onderzoeken in welke ondervoede ouderen behandelen effectief is (met supplementen en/of normale voedingsproducten). In toekomstige onderzoeken zou een basisset van primaire uitkomstmaten opgenomen moeten worden om de pooling van data en toepassing van meta-analyses mogelijk te maken. Een andere uitdaging is het verbeteren van de registratie van patiëntkarakteristieken, de gegeven behandeling en de behandelresultaten in de klinische praktijk om inzicht te geven in welke behandelonderdelen effectief kunnen zijn bij specifieke individuen.