FACULTY OF HEALTH SCIENCES
DEPARTMENT OF COMMUNITY MEDICINE

Body Mass Index and Risk of Malnutrition in Community-living Elderly Men and Women:

Relationships with Morbidity, Mortality and Health-related Quality of Life.

The Tromsø and HUNT studies

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Community Medicine
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HELSE NORD

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A dissertation for the degree of
Philosophiae Doctor

Contents

Preface: *From clinical practice to epidemiological research*

During my more than 20 years in clinical medicine and gastroenterology, I have met numerous elderly patients with weight loss and who were underweight. For some patients, these problems were symptomatic of a severe disease, such as cancer. For others, however, malnutrition was the missing puzzle piece in a complex case history. In the hospital system, malnutrition and underweight had often gone unrecognised. This fact wakened my interest in malnutrition and Professor Jon Florholmen introduced me to this field.

Most of my elderly patients were from the community of Tromsø, and the Tromsø Population Study had for years explored the health of its inhabitants. The Tromsø 6 survey was in the planning phase when I prepared my PhD project. It is a short distance from the University Hospital in Tromsø to the epidemiological setting at the Department of Community Medicine, where I met Professor Bjarne K Jacobsen. He has a background both in nutritional science and epidemiology. During these last three years, I have had the privilege to more carefully investigate the interesting relationship between nutritional-status and health in the elderly population.

Jan-Magnus Kvamme
Tromsø, March 2011

Acknowledgements

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The HUNT Study (Helseundersøkelsen i Nord Trøndelag) for access to data used in the mortality analyses.

My parents, Astrid and Jan-Ivar, for their interest and commitment. My wife, Brita, for continuous support during the ups and downs throughout the project, and our three children Rasmus, Ragnhild and Ingeborg, for reminding me of the other important aspects of life in this busy period.

Kort norsk sammendrag-Short Norwegian summary

I denne avhandlingen er forholdet mellom *ernæringsstatus* og *sykelighet*, *dødelighet* og *helse-relatert livskvalitet* undersøkt hos hjemmeboende eldre. Avhandlingen er basert på de tre befolkningsundersøkelsene, Tromsø 4 (1994-95), Tromsø 6 (2007-08) og Helseundersøkelsen i Nord-Trøndelag, HUNT 2 (1995-97). Ernæringsstatus er vurdert både ved hjelp av *kroppsmasseindeks* (KMI, kg/m^2), også kjent som BMI, og et spesielt *screeningsverktøy* for underernæring, MUST (Malnutrition Universal Screening Tool).

Vurdert utifra MUST fant vi at 8 % av hjemmeboende eldre hadde middels eller høy risiko for underernæring. Både depressive symptomer, gjennomgått brudd (lårhals), redusert muskelstyrke og dagligrøyking forekom hyppigere hos undervektige (KMI <20 kg/m^2). Redusert fysisk aktivitet og kronisk lungesykdom var vanligere både ved undervekt og fedme (KMI ≥30 kg/m^2) (U-formet relasjon til KMI). Eldre med fedme hadde også økt hyppighet av diabetes og iskemisk hjertesykdom. Helse relatert livskvalitet var redusert ved økende risiko for underernæring, mer hos menn enn hos kvinner. Dødeligheten var økt hos alle med KMI under 25 kg/m^2 og en del av dette kunne forklares av dødelighet på grunn av lungesykdommer. Den laveste dødeligheten fant vi hos de som var overvektige (KMI 25-30 kg/m^2 hos menn og 25-32.5 kg/m^2 hos kvinner). Det var moderat økt dødelighet hos eldre med fedme.

Underernæring utgjør altså en betydelig helserisiko for hjemmeboende eldre og det er viktig å få på plass tiltak som gjør at underernæring oppdages i en tidlig fase. Andre studier har vist at helsetilstanden kan bedres hvis underernæring behandles.

English summary

The elderly population is rapidly growing, and elderly individuals are more vulnerable to nutritional problems than other adults. A number of studies have found evidence for adverse health outcomes in elderly patients at risk of malnutrition. However, much of the previous research has been performed in hospital populations or in groups of elderly patients with specific diagnoses. More population-based studies in this area are therefore needed. Increased understanding of nutrition in elderly individuals can contribute to the identification of individuals at risk of malnutrition at an earlier stage.

Based on data from three large health surveys, we aimed to study the relationship between *nutritional status* and important *health outcomes* in community-living elderly individuals. We first explored the associations between disease burden, social and life style variables in a cross-sectional design based on data from the Tromsø 4 survey (1994-1995) (paper I). We found that fractures (hip), mental distress, reduced muscle strength and current smoking were more prevalent in underweight individuals. Chronic lung disease and reduced physical activity had a U-shaped relation with body mass index (BMI). Diabetes and ischemic heart disease were more prevalent in obese individuals.

In the Tromsø 6 survey (2007-08), we included the Malnutrition Universal Screening Tool (MUST). We found that approximately 8% of this community-living population was at medium or high risk of malnutrition and that 20% was obese (BMI ≥30 kg/m^2). We used a cross-sectional design to explore the association between mental health symptoms and both risk of malnutrition and BMI (paper II). Mental health symptoms were significantly associated with the risk of

malnutrition, and an association was also found for subthreshold mental health symptoms. Quality of Life is an important health aspect for the increasing number of elderly individuals with longer life expectancy. We found a significant reduction in Health-related Quality of Life with an increasing risk of malnutrition, and this was more pronounced in men than in women (paper III). In paper IV, we combined the HUNT 2 (The Nord-Trøndelag Health Study, 1995-97) and Tromsø 4 surveys with the intention of exploring the relationship between BMI categories and both total and cause-specific mortality in a prospective design. We found mortality to be increased in all BMI categories below 25 kg/m^2 and that overweight individuals had the lowest mortality (BMI 25-29.9 kg/m^2 in men and 25-32.4 kg/m^2 in women). A modest increase in mortality was found with increasing BMI among obese men and women. About 40% of the excess mortality in the lower BMI range in men was explained by mortality from respiratory diseases.

This thesis describes increased morbidity, mortality and reduced HRQoL in community-living elderly individuals at risk of malnutrition or with lower BMI. These findings emphasise the importance of nutritional screening, especially in primary care. Previous research has demonstrated that nutritional intervention can reduce adverse health outcomes in elderly at risk of malnutrition.

List of papers

This thesis is based on the following four papers, which are referred to in the text by their Roman numerals:

Paper I

Kvamme J-M, Wilsgaard T, Florholmen J, Jacobsen B K. **Body mass index and disease burden in elderly men and women: The Tromsø Study.**
European Journal of Epidemiology. 2010 Mar; 25 (3):183-93. Epub 2010 Jan 20.

Paper II

Kvamme J-M, Grønli O, Florholmen J, Jacobsen B K. **Risk of malnutrition and mental health symptoms in community living elderly men and women: The Tromsø Study**.
Submitted.

Paper III

Kvamme J-M, Olsen J A, Florholmen J, Jacobsen B K. **Risk of malnutrition and Health related Quality of life in community-living elderly men and women: The Tromsø Study.**
Quality of Life Research. 2011 May;20(4):575-82. Epub 2010 Nov 13.

Paper IV

Kvamme J-M, Holmen J, Wilsgaard T, Florholmen J, Midthjell K, Jacobsen B K. **Body mass index and mortality in elderly men and women: The Tromsø and HUNT studies**.
Journal of Epidemiology & Community Health. 2011 Feb 14. (Epub ahead of print)

Abbreviations

BAPEN - British Society of Parenteral and Enteral Nutrition

BMI - body mass index

CI - confidence interval

CONOR-COhortNORway, a collaboration between several health surveys in Norway

COPD - chronic obstructive pulmonary disease

CVD - cardiovascular diseases

DXA - dual-energy X-ray absorptiometry

EQ-5D index - value attached to an EQ-5D state according to a particular set of weights

EQ VAS - standard vertical visual analogue scale

ESPEN- The European Society for Clinical Nutrition and Metabolism (previously European Society of Parenteral and Enteral Nutrition)

GDS - Geriatric Depression Scale

HR - Hazard ratio

HRQoL - Health-related Quality of life

HUNT - The Health Study of Nord-Trøndelag County, Norway

ICD - International Classification of Diseases

IHD - ischemic heart disease

MNA - Mini nutritional assessment

MUST - Malnutrition Universal Screening Tool

NRS 2002 - Nutritional risk screening 2002

OR - odds ratio

PEM – protein energy malnutrition

SCL-10 - (Hopkins) Symptoms check list-10

S.D. - standard deviation

SPSS - Statistical package for the Social Sciences

WC - waist circumference

WHO - World Health Organization

Definitions

More details can be found in the respective sections indicated by the page number(s).

BMI: body mass index, weight divided by height squared (kg/m^2), page 28 and 47.

Community Living: Present place of residence is a private dwelling as distinct from elderly hospital in-patients or nursing home residents, page 14 and 43.

Older person: individual aged ≥65 years [145, 154], page 15.

Health related Quality of Life: The measurable impact of a person's perception of his or her health and the effect that produces on satisfaction with life and well-being [154], page 19.

Morbidity: from Latin *morbidus*, state of being diseased [154]

Malnutrition: A state in which a deficiency, excess or imbalance of energy, protein and other nutrients causes adverse effects on body form, function and clinical outcome [143], page 14.

Underweight: BMI ≤20 kg /m^2 [143], page 61.

Overweight: BMI 25-29.9 kg/m^2 [164], page 48.

Obesity: BMI ≥30 kg/m^2 [164], page 48.

Sarcopenia: from Greek *sarx* for flesh and *penia* for loss. Loss of muscle mass, muscle endurance and muscle force occurring during aging [118], page 62.

List of tables and figures

1 Introduction

1.1 General Introduction

The elderly population is rapidly growing, and elderly people live longer than ever before. By 2050 it is expected that one in three Europeans will be 60 years of age or older [153]. In Norway, approximately one in seven individuals is 65 years of age or older. The large majority of the elderly population is self-reliant and live in their homes (i.e., community-living). In the city of Tromsø, nursing home residents constitute only about 6% of the population in this age category [24], similar to the Norwegian population as a whole [137]. However, a large portion of health care resources are allocated to the elderly population, and one in three hospital beds is occupied by individuals in this age category [126].

Health is closely related to nutrition, and in comparison to younger adults, elderly individuals are more vulnerable to nutritional problems. There is a large body of evidence supporting the idea that elderly people are at risk for malnutrition [143]. However, many of the studies available have been performed in hospitalised patients and in groups of elderly individuals with specific diseases or conditions. Thus, more *population-based research* is needed in the field of nutritional problems in elderly people, with special attention to the lower BMI categories and elderly individuals at risk for malnutrition. This is the main focus of the present thesis.

There is no universally accepted definition for the term *malnutrition* [143]. The word can be literally translated as "bad nutrition". The following definition has been suggested by Professor M. Elia: "*Malnutrition is defined as a state in which a deficiency, excess or imbalance of energy, protein and other nutrients causes adverse effects on body form, function and clinical outcome*."

[95, 143]. Strictly speaking, this also includes obesity, but, as in most studies of elderly individuals, excess weight is not included in the concept of "risk of malnutrition" used in this thesis. Protein energy malnutrition (PEM) results if an individual's needs for protein and energy are not satisfied by the diet [149], and this corresponds to the malnutrition term used in this thesis. The nutritional screening tool used in two of the included papers was developed to detect PEM [140]. PEM as a term is about to be replaced by an approach to malnutrition that incorporates *inflammatory response* [75] (see section 7.3, page 67 for more details).

Older persons are often defined as individuals aged ≥65 years [145, 154] and this age limit is applied here to define the elderly population.

1.2 Aging and Nutritional status

Concurrent with the epidemic of obesity, malnutrition also seems to be a persistent problem in the affluent parts of the world and is more prevalent in elderly individuals than in other adults [111]. In developed countries, malnutrition is largely related to diseases [143].

A range of physiological and biological changes involved in ageing affect nutritional status and combine to make deficiencies of macro- and micronutrients more common in elderly individuals. Taste and smell, two senses important for the pleasure of eating, are often decreased during aging [65]. This sensory deficit may partly explain reduced appetite, which can, in turn, contribute to malnutrition [101]. Compared to younger adults, elderly individuals have less ability to respond to concurrent underfeeding that may occur in concert with acute diseases [117]. Gut mechanisms, including a delay in gastric emptying that result in early satiety, may also contribute to lowered food intake in elderly individuals [156, 160]. Approximately the same requirements of vitamins and micronutrients should be ingested in a context of reduced food intake [161], a fact that may also contribute to increased risk of micronutrient deficiencies in the elderly.

Generally, body weight and BMI increase during life up to the age of 50-60 years, after which these values level off and slowly decrease in old age [60, 156]. Body composition also changes with advancing age. The relative proportion of adipose tissue is increased and muscle tissue mass, quality, and strength is reduced, with the latter often characterised as *sarcopenia* [156] [118]. There are a number of risk factors for sarcopenia, including malnutrition, low protein intake, several chronic health conditions and the ageing process itself [26]. (See section 7.3, page 62 for further details).

1.3 Morbidity and Nutritional status

Morbidity is increased in the elderly, and it was found in a previous study that 82% of elderly people had one or two chronic health problems and that 65% had two and more chronic health problems [167]. Nutritional status may be closely related to chronic health problems. Most previous studies of associations between BMI and various medical conditions have focused either on the detrimental effect of on obesity [19, 109], adult populations without specific analysis of elderly participants, [3, 110] or selected chronic diseases [20, 56]. A number of studies of primarily hospital populations have found malnutrition to be a common problem in elderly patients with severe or chronic diseases [143]. However, there are fewer population-based studies that examine elderly persons in all BMI categories. Thus, important factors associated with low BMI compared to other BMI categories may not have been identified.

1.4 Mental health and risk of malnutrition

Mental health problems contribute to the increased morbidity in elderly people. Anxiety and depression, often seen as co-morbid conditions with overlapping symptoms [97], are the two most frequently occurring mental health disorders [31]. Malnutrition is also relatively common in elderly individuals and may be associated with mental health, particularly depression [12].

Although several studies have found mental disorders to be a risk factor for involuntary weight loss and malnutrition in geriatric inpatients and outpatients [159], little population-based research has been done on the relationship between the risk of malnutrition and mental health in the elderly.

The relationship between *malnutrition and depression* has been assessed in some previous studies by the Geriatric Depression Scale (GDS) and the Mini Nutritional Assessment (MNA) instrument (table 1).

Authors	**Participants**	**Methods and variables**	**Results**
Johansson et al. 2009 [79]	579 community-living elderly (Sweden)	Prospective study MNA + GDS	Depressive symptoms predictive of malnutrition
Smoliner et al. 2009 [130]	114 nursing home residents (Germany)	Cross-sectional study MNA + GDS	Modest association between depressive symptoms and malnutrition
Cabrera et al. 2007 [18]	267 community-living elderly individuals (Brazil)	Cross-sectional study, MNA and GDS/regular use of antidepressant medicines	Association between depressive symptoms and malnutrition

Abbreviations: MNA, Mini Nutritional Assessment (nutritional screening tool), GDS, Geriatric Depression scale

Table 1 Studies on the relationship between depression/mental health and the risk of malnutrition; non-hospitalised populations.

Johansson et al. found in a Swedish study of 579 community-living elderly individuals that depressive symptoms were predictive of malnutrition [79], a finding that was observed to a larger extent in men than in women. Smoliner et al. examined nursing home residents and found no differences in the mean MNA score between subjects who had depression and those who did not. However, a modest association was demonstrated between malnutrition and depression in a regression analysis [130]. A study of 267 community-living elderly individuals in Brazil [18] showed a positive relationship between malnutrition and depression.

The relationship between *BMI and depressive symptoms* in adults and elderly individuals has in previous studies been assessed with a main focus on higher BMI categories. Limited evidence for an association between obesity and depressive symptoms has been found [5]. Studies restricted to elderly individuals have yielded conflicting results. In one study, obese elderly men were found to have a reduced risk of depression [107], whereas a later study reported an increased risk of depression in obese individuals [125].

Thus, larger studies examining the associations between BMI, the risk of malnutrition and mental health in community-living elderly individuals are needed.

1.5 Health-related quality of life and risk of malnutrition

Quality of Life (QOL) has received increasing attention in recent decades as a measure for comparing the health status of different patient groups and for measuring health outcomes. QOL is not a well-defined term. However, many will argue that most people, at least in the developed world, are familiar with the term and have an intuitive understanding of it [43]. Aristotle (384-

322 BC) described a term (eudemonia) regarded as very close to the modern QOL in his work on ethics (Nicomachean Ethics) [43]. He stated that the meaning of the term *varies* from person to person and *depends on the life situation* of each individual. To differentiate between QOL in a general sense and the need for a more precise definition in clinical medicine, the narrower term, Health Related Quality of Life (HRQoL) is often used. However, this terminology is also not very precisely defined. In Taber's Medical Dictionary (2009) [154], HRQoL is defined as: *"The measurable impact of a person's perception of his or her health and the effect that produces on satisfaction with life and well-being."* This corresponds to the HRQoL term used in this thesis.

Despite the previously mentioned evidence of increased morbidity [88, 143] and mortality (see below) [63, 142] in elderly people at risk of malnutrition, little attention has been given to the ways in which malnutrition affects HRQoL. For the increasing number of elderly individuals with longer life expectancies, not only is the duration of life important, but also the quality of those additional years.

The concept of HRQoL broadens a previous definition of health based on morbidity and mortality to include aspects of health that include subjective assessments of physical, emotional and social functioning [33]. Nutrition may affect both the physical and psychological aspects important for HRQoL [143]. Several reports have found HRQoL to be reduced in obese individuals [77]. In a study of nursing home patients [25] and a smaller, community-based study [81], QOL was reduced in elderly patients at risk of malnutrition.

However, larger, community-based studies evaluating HRQoL in elderly individuals at risk of malnutrition are lacking.

1.6 Body mass index and mortality

The impact of BMI on mortality in the elderly population is still controversial. There is a growing concern regarding the increase in mortality related to obesity [105], whereas mortality associated with underweight has gained less attention.

As reviewed by Heiat (2001) [62], Zamboni (2005) [171], and Janssen (2007) [73], the recommendations of ideal weight for adults [164] seem to be too restrictive for elderly individuals, in whom being moderately overweight is of limited risk with respect to increased mortality. It is not possible in this introduction to present the more than fifty studies included in these review articles, in addition to other BMI-mortality studies. However, some selected studies are presented in table 2 with the intention to include studies also from Scandinavian countries.

Authors	**Participants**	**Design**	**Results Total mortality**	**Results Cause specific mortality**	**Comments**
Waaler 1984 [158]	1 800 000 from Norway	Prospective study based on compulsory X-ray examinations for tuberculosis 1963-65	Marked U-shape between BMI and mortality, lowest mortality 21-25 kg/m^2, somewhat higher in individuals aged ≥65 years	In both men and women 50-64 years of age, highest mortality in the low BMI categories from obstructive lung diseases, tuberculosis, lung and stomach cancer	Cause specific mortality not examined in persons ≥65 years
Dey et al 2001 [29]	2 628 men and women aged 70 years from Sweden	Prospective study, up to 15 years follow up, BMI (quintiles)	Lowest BMI quintile, highest mortality. Lowest mortality in BMI 27-29 kg/m^2 in males and 25-27 kg/m^2 in women (non smoking)	Not explored	

Rissanen 1991 [116]	17 159 women aged 25-79 years (1 437 women aged ≥65 years) from Finland	Prospective, 12 years follow-up	In women aged ≥65 years, mortality varied little with BMI	Thinness seemed to predict deaths from cancer	Deaths from respiratory diseases not explored
Engeland 2003 [38]	2 million men and women, The majority included in 1963-75	Prospective 22 years follow-up	Subgroup analyses, elderly of 70-74 years: in men optimal BMI 24 kg/m^2, and in women, optimal BMI: 25.7 kg/m^2	Not explored	Partly extension of Waaler 1984. Smoking information available for a sub-cohort. Increased risk at low BMI also in non-smokers.
Pischon 2008 [112]	359 387 adults from nine countries in Europe	Prospective 9.7 years follow up	Subgroup analysis of ≥65 years, lowest mortality men BMI 25-26.6 kg/m^2 and women 23.5-25 kg/m^2. Significant increased mortality if BMI <21.0 kg/m^2 (men and women)	Explored in adults, not specifically in elderly: Respiratory disease mortality increased if BMI <23.5 kg/m^2	Several analyses also adjusted for waist hip data.

Table 2 Selected studies on the relationship between BMI and mortality (only studies with measured height and weight). Results reported with primary attention towards the lower BMI categories.

In Norway, the relationship between BMI and mortality was examined early by Waaler (Waaler 1984) based on height and weight data obtained during screening for tuberculosis and with deaths in the period from 1963-1979 [158]. Waaler described a U-shaped relationship between BMI and mortality. In adults, the strongest increase in mortality in the lower BMI categories was found for obstructive lung disease. However, BMI- mortality curves for cause-specific mortality in elderly individuals were not examined. Two large studies with primarily adult participants from several different countries were published in 2008 and 2009. In the first of these studies, the lowest mortality rate was found to be at a BMI of approximately 22.5-25 kg/m^2 for all ages [163]. The second of these studies (Pischon 2008) found the lowest mortality to be at a slightly higher BMI levels (table 2) [112]. Both studies provide several subgroup analyses, but very limited analysis of elderly participants. Dey et al. (Dey 2001) [29] found that overweight elderly, individuals had the lowest mortality, a finding also demonstrated by others [73].

To summarise, a number of studies have found increased mortality in underweight individuals, but this association remains to be fully explained in the elderly population. Thus, more research should be done on the relationship between BMI and mortality (total and cause specific) with special attention to the lower weight categories.

2 Aims of the thesis

There is a need for more population-based research on the relationships between nutritional status and important health outcomes, including morbidity, HRQoL and mortality in elderly people, with special attention to malnutrition and underweight individuals. More specifically, this thesis concentrates on the following questions regarding community living elderly people:

1. How common is the risk of malnutrition and what are the prevalences of the different BMI categories?
2. What are the characteristics and disease burden of elderly people in different BMI categories, specifically the lower BMI categories?

3. What is the association between mental health symptoms and the risk of malnutrition?
4. Is there an association between the risk of malnutrition and impaired HRQoL?
5. What is the relationship between BMI and both total and cause-specific mortality?

3 Subjects

The individuals included in these analyses were participants in the 4^{th} and 6^{th} surveys of the Tromsø Study (Tromsø 4 and Tromsø 6) and the 2^{nd} Nord Trøndelag Health survey (HUNT 2) (see table 3).

	Tromsø 4 1994-95	**HUNT 2** 1995-97	**Tromsø 6** 2007-2008
Paper I	n = 4 259		
Paper II			n = 3 111
Paper III			n = 3 286
Paper IV	n = 16 711		

Table 3 Study participants included in the studies referred to in this thesis (Paper I-IV).

3.1 The Tromsø 4 survey (paper I and IV)

The Tromsø Study is a single-centre, population-based longitudinal study with repeated health surveys of the Tromsø municipality [72]. Tromsø is the largest city in the northern part of Norway, with a population of 68 000. Most inhabitants live on the Tromsø Island (figure 1).

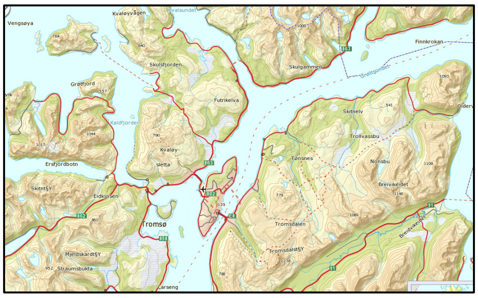


Figure 1 Tromsø Municipality

The fourth cross-sectional health survey of the Tromsø population was conducted in 1994-1995. All community-living inhabitants in the municipality aged 25 years and older were invited to participate, but the present analyses are restricted to participants aged 65 years and older. Nursing home residents were invited, but very few participated. A total of 5 892 subjects in this age group were invited and the study sample consisted of 4 259 persons (72% of the invited). One reminder letter was sent. The participation rate declined with age (table 4). In subjects aged 80 years and older, less than 50% participated.

3.2 The HUNT 2 survey (paper IV)

The Nord Trøndelag Health study (HUNT study) is a large, population-based longitudinal study with repeated health surveys of the county of Nord-Trøndelag. This is a sparsely populated and largely rural county located in the central part of Norway, with 127 000 residents (figure 2). The second Nord-Trøndelag health survey (HUNT 2) was conducted in 1995-97 and has been previously described in more detail [68]. All community-living inhabitants aged 20 years and older were invited to participate in the survey, but only participants aged 65 years and older were included in the study population described in paper IV. A total of 21 946 individuals in this age group were invited and 15 250 participated in the study. One reminder letter was sent. The overall participation rate was rate was 70% and declined with age. In subjects aged 79 years and older, 46% participated. Nursing home residents were invited, but very few participated (45 out of the 15 250 participants were permanent nursing home residents).

Data from the HUNT 2 and the Tromsø 4 surveys were combined for the analyses presented in paper IV. Details about participation by increasing age in the combined cohort are found in table 6. These two surveys had been pre-planned to include the same core questions. Mean BMI, smoking habits and household income in the two regions Nord-Trøndelag and Troms were quite similar [136, 168]. The inhabitants of Tromsø constitute approximately half of the population of the Troms County.

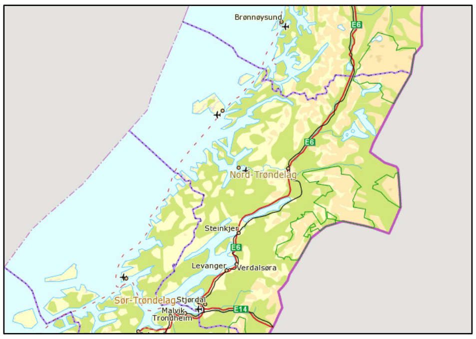


Figure 2 Nord Trøndelag County

3.3 The Tromsø 6 survey (paper II and III)

The Tromsø 6 survey was conducted between October 2007 and December 2008. Invitations were sent to all community-living inhabitants aged 25 to 87 years. One reminder letter was sent. The analyses in this thesis are restricted to individuals aged 65 years and older. A total of 6 098 subjects in this age category were invited and 4 017 subjects (66%) participated in the study. Nursing home residents were also invited, but very few participated (only 8 of the 4 017 participants were permanent nursing home residents). The age distribution of the groups in the invited population, the attending population and the two study samples for papers II and III, respectively, are described in table 5. The two study samples consist of relatively few of the eldest participants, and relatively more women than men were excluded because of missing values.

Age range (years)	Invited, Tromsø 4 *N* Men	Women	Attending, Tromsø 4 *n* (% of invited) Men	Women	Paper 1 Study sample *n* (% of invited) Men	Women
65–69	810	970	691 (85.3)	860 (88.7)	683 (84.3)	841 (86.7)
70–79	1 216	1 548	935 (76.9)	1 240 (80.1)	921 (75.7)	1 215 (78.5)
80–	414	934	214 (51.7)	411 (44.0)	208 (50.2)	391 (41.9)
All	2 440	3 452	1 840 (75.4)	2 511 (72.7)	1 812 (74.3)	2 447 (70.9)

Table 4 Number of invited, attending and included men and women in the Tromsø 4 survey. In the study sample, participants not willing to take part in the research or with missing values for height and/or weight were excluded.

Age range (years)	Invited, Tromsø 6 *N* Men	Women	Attending, Tromsø 6 *n* (% of invited) Men	Women	Paper ll Study sample, *n* (% of invited) SCL10 Men	Women	Paper lll Study sample, *n* (% of invited) HRQoL Men	Women
65–69	1 068	1 054	830 (77.7)	827 (78.4)	721 (67.5)	662 (62.8)	741 (69.4)	690 (65.5)
70–79	1 197	1 456	841 (70.3)	988 (67.9)	698 (58.3)	699 (48.0)	732 (61.2)	748 (51.4)
80–87	492	831	196 (39.8)	335 (40.3)	139 (28.3)	192 (23.1)	159 (32.3)	216 (26.0)
All	2 757	3 341	1 867 (67.8)	2 150 (64.4)	1 558 (56.5)	1 553 (46.5)	1 632 (59.2)	1 654 (49.5)

Table 5 Number of invited, attending and included men and women in the Tromsø 6 survey. In the study samples, participants with missing values for BMI, weight loss, SCL-10 (Paper II) or EQ5D variables (Paper III) were excluded.

Age range (years)	**Invited, Tromsø 4 and HUNT-2** *N*		**Attending, Tromsø 4 and HUNT-2** *n* (% of invited)		**Paper IV Study sample** *n* (% of invited)	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
65–69	3 478	3 786	2 898 (83.3)	3 231 (85.3)	2 635 (75.8)	2 877 (76.0)
70–79	5 990	7 202	4 569 (76.3)	5 529 (76.8)	3 914 (65.3)	4 634 (64.3)
80–	2 694	4 688	1 317 (48.9)	1 971 (42.4)	1 055 (39.2)	1 596 (34.0)
All	12 162	15 676	8 784 (72.2)	10 731 (68.5)	7 604 (62.5)	9 107 (58.1)

Table 6 Number of invited, attending and included men and women in the Tromsø 6 and HUNT 2 surveys combined. In the study sample, participants with a follow-up time below one year (425 participants) and with missing information regarding cause-specific mortality (5 participants) or questionnaire data concerning smoking, marital status or level of education (2 374 participants) were excluded.

3.4 Ethics

All participants gave written, informed consent upon inclusion in the various surveys and had the option of withdrawing from participation after inclusion. All surveys were approved by the regional boards of research ethics and the Data Inspectorate through the Norwegian Social Science Data Services.

4 Methods

4.1 Assessment of Nutritional status

4.1.1 Body Mass index (Paper I-IV)

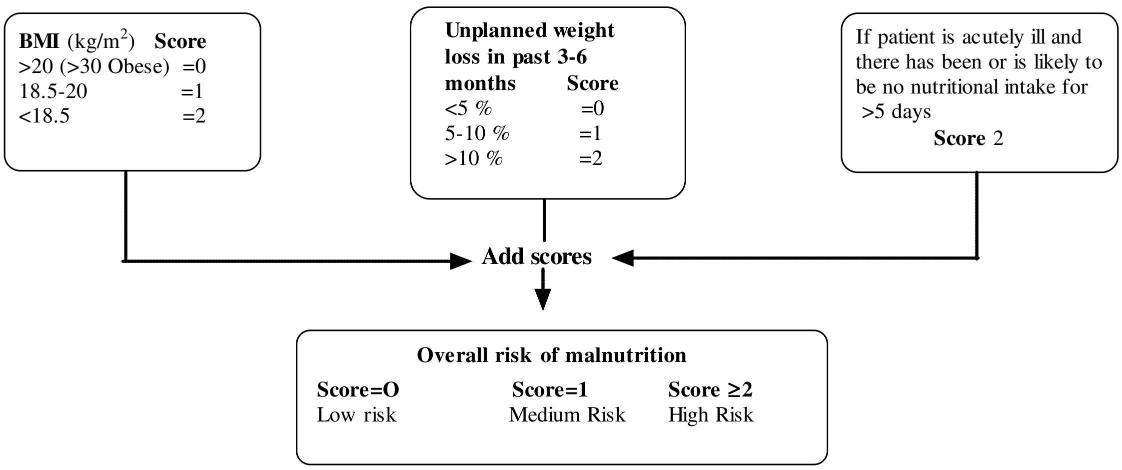
Participants had their weight (kg) and height (cm) measured to the nearest decimal at the research centres. During these measurements, participants wore light clothing and did not wear shoes. BMI was calculated as weight (kg) divided by height (m) squared (kg/m^2).

4.1.2 Waist circumference (Paper IV)

Waist circumference (WC) was measured horizontally to the nearest centimetre at the height of the umbilicus using steel tape. WC was available for all HUNT-2 participants and for all Tromsø participants aged 65-74 as well as for a random sample of participants aged 75-84 years.

4.1.3 Malnutrition Universal Screening Tool (Paper II and III)

The Malnutrition Universal Screening Tool (MUST) was originally developed by the British Society of Parenteral and Enteral Nutrition (www.bapen.org.uk). It includes a grading of both (1) *BMI* and (2) *weight loss* in three categories in addition to (3) an *acute disease* component (figure 3). In the questionnaire used in the Tromsø 6 survey, participants were asked about any involuntary weight loss during the previous six months (and if so, how many kg). Weight loss values were placed in the following groups: below 5%, between 5% and 10% or above 10% of body weight prior to weight loss. The MUST also includes an acute disease component corresponding to no nutritional intake for >5 days, which normally necessitates hospitalisation [36]. As participation in the Tromsø study required the ability to independently visit a research centre, the acute diseases component was set to zero. The weight loss question was slightly modified to indicate a time span of the "last 6 months", but this encompasses the time span of "the past 3-6 months" in the original MUST. The use of the MUST as described in paper II and III has been confirmed by Professor Marinos Elia, who is in charge of the use of the tool on behalf of BAPEN (appendix B).



The "Malnutrition Universal Screening Tool" is reproduced here with the kind permission of BAPEN (British Association for Parenteral and Enteral Nutrition). For further information on 'MUST' and management guidelines, see www.bapen.org.uk.

Figure 3 The Malnutrition Universal Screening Tool (MUST) is composed of a BMI score, a weight-loss score and an acute illness component. The risk of malnutrition can be assessed based on the sum of these scores.

4.2 Data on cancer (Papers I and IV) and marital status (Papers I to IV)

Data concerning cancer history was obtained from the Norwegian Cancer Registry, which is based on mandatory registration. Data on marital status was obtained from the National Population Register.

4.3 Hand grip strength (Paper I)

Grip strength can be used as a measure of overall muscle strength [14] and has found to be an indirect measure of lean body mass [138]. In a representative subgroup of the Tromsø 4 population, grip strength of the non-dominant hand was registered in kilopascals (kPa), with measurements generated by manual compression of an air filled rubber bulb connected to a manometer. A measurement below the median value for each sex was defined as *low* grip strength.

4.4 Assessment of Mortality (Paper IV)

For the assessment of mortality, each participant included in paper IV (Tromsø 4 and HUNT 2 combined) were linked to information from the Norwegian Causes of Death Registry by a personal identification number to identify vital status (dead, alive or emigrated) during the follow-up period. Data concerning both total and cause-specific mortality were available. When we started on the analyses used in paper IV, data concerning cause specific mortality was available up to 31 December 2007, and this date was set as end date of follow up (figure 4). Cause of death in Norway is routinely registered and coded by the Death Registry based on the International Classification of Diseases (ICD), and we noted the underlying cause of death. For deaths up to 1996, ICD version 9 was used and ICD version 10 was used for later years. We applied the European short list for causes of death [42] to identify three main categories of causes of death; cardiovascular diseases (CVD, ICD-9: 390-459, ICD-10: I00-I99), respiratory diseases (ICD-9: 460-519, ICD-10: J00-J98) and cancer (ICD-9: 140-208, ICD-10: C00-C97)).

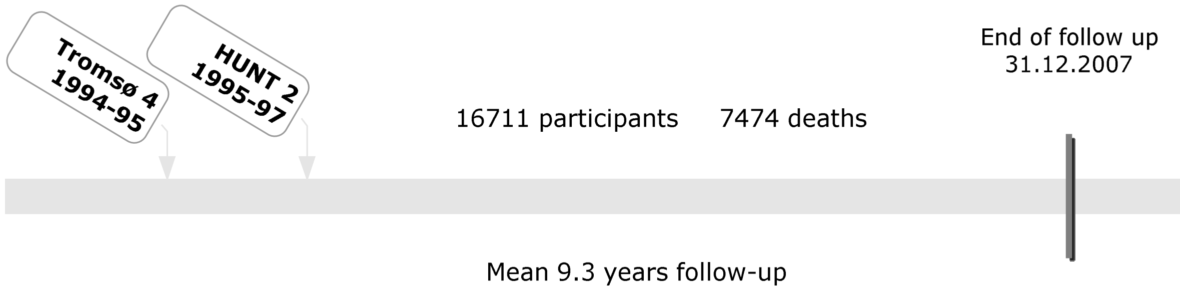


Figure 4 Timeline for the follow-up in paper IV (see 5.4 for details regarding the study).

4.5 Self-administrated Questionnaires (Paper I-IV)

In all three surveys included in this thesis, self-administrated questionnaires (appendix C) were used to obtain information concerning a wide range of diseases and symptoms, smoking habits, alcohol intake, social conditions, education, level of physical activity and other variables. In all surveys, participants were asked to fill in two different questionnaires. The first questionnaire was included with the invitation letter sent by mail to all participants. This questionnaire was intended to be completed at home and collected at the research centre. The second questionnaire was given to the participants upon admittance and was intended to be returned by mail in pre-stamped envelopes. In the HUNT 2 and Tromsø 4 surveys, the second questionnaire was given in different versions for those below and above the age of 70.

In paper I, we selected *symptomatic medical conditions* prevalent in the elderly population that may have a connection to either low weight or obesity according to the literature [55, 143]. The considered conditions were mental distress, hip fracture, asthma or chronic bronchitis, stroke, angina pectoris or myocardial infarction and diabetes mellitus. Cancer was also included, but (as noted above) based on information from the Norwegian cancer registry. Chronic lung disease was defined as asthma or chronic bronchitis, and similarly, ischemic heart disease (IHD) was defined as myocardial infarction or angina pectoris (Paper I and IV).

4.6 Assessment of mental health: CONOR mental health index (Paper I)

In paper I (based on the Tromsø 4 survey), participants' mental health was explored as one of several health conditions. This was done by means of an index based on seven questions concerning different dimensions of mental distress (CONOR Mental Health Index) [134]. The index was developed for use in a cohort including several health surveys in Norway; the COhort NORway (CONOR).This mental distress index was partly modified from the Hopkins Symptom Check List [27] and the General Health Questionnaire (GHQ) [53]. A cut-off value of 2.15 has been proposed to identify persons with significant mental distress [134].

4.7 Assessment of mental health: Symptoms Check List 10 (Paper II)

In paper II (the Tromsø 6 survey), mental health was assessed in greater detail by the Hopkins Symptoms Check List-10 (SCL-10). The SCL-10 has been widely used in epidemiological studies and is a self-administrated instrument that mainly explores symptoms of anxiety and depression [139]. The ten items of the SCL-10 were part of the questionnaire included in the invitation to the Tromsø 6 survey (appendix C).

The SCL-10 questions explored the presence and severity of the following ten symptoms during the preceding week: (1) “Sudden fear without apparent reason”, (2) “Afraid or worried”, (3) “Faintness or dizziness”, (4) “Tense or upset”, (5) “Easily blaming yourself ”, (6) “Sleeplessness”, (7) “Depressed or sad”, (8) “Feeling worthless”, (9) “Feeling that everything is a struggle”, and (10) “Feeling hopelessness with regard to the future”.

Each question was rated on a four-point scale ranging from 1 (not at all) to 4 (extremely). According to a procedure suggested by Strand et al.[139], missing values were replaced by the sample mean value for each item, but questionnaires with three or more missing values were excluded from the analyses. The SCL-10 total score was calculated by dividing the total score by the total number of items (i.e., ten). A higher score indicated more symptoms. We found an acceptable degree of internal consistency for this scale in the study sample in paper II (Cronbach’s alpha = 0.84).

An SCL-10 score of 1.85 has been proposed as the cut-off for predicting diagnosed mental disorders [139], and score values of ≥1.85 in the current study were referred to as *significant symptoms*. To assess the impact of score values below this cut-off, we subdivided the SCL-10 scores in paper II between 1.01 and 1.84 into a lower score category (SCL-10 score 1.01 to 1.39) referred to as *some symptoms*, and a higher score category (SCL-10 score 1.40 to 1.84) referred to as *sub-threshold symptoms*. Individuals with no symptoms (SCL-10 score 1.0) were used for reference in the analyses.

4.8 Assessment of Health Related Quality of Life: EQ-5D (Paper III)

HRQoL (Paper III) was assessed by the EuroQol questionnaire (EQ-5D), which has been developed by a multidisciplinary group of European researchers. This is a standardised non-disease specific instrument consisting of two parts; the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS) [148]. The EQ-5D instrument has been evaluated in a number of studies and has been validated in elderly populations [17, 21].

The EQ-5D describes health in generic terms using five specific dimensions that are important for elderly individuals: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is divided into three levels of severity (no problems, some problems or extreme problems). In the sample described in paper III, few participants reported problems at the most severe level. According to EQ-5D user guide [41], this category was combined with the category of individuals reporting some problems (second level) in the analyses of the various EQ-5D dimensions. The EQ-5D instrument is designed for self-completion and was included as part of the self-administrated questionnaire in the Tromsø 6 survey (appendix C). A single summary EQ-5D index with a maximum score of 1 is obtained by applying a scoring algorithm that assigns weights to each of the possible combinations of health as described by the three levels within each of the five dimensions. We applied the most widely used scoring algorithm, referred to as the UK time-trade-off tariff [32]. Subjects with missing values to any of the five dimensions were excluded from the analyses.

In addition to this indirect health index assigned through a descriptive system, a direct method asks subjects to rate their health on a visual analogue scale (VAS) with a maximum score 100. The endpoints are labelled “Worst imaginable health state” and “Best imaginable health state”.

4.9 Statistical methods

Statistical analyses were performed using the Statistical Package for Social Science (SPSS), versions 15.0 and 17.0 (SPSS Inc, Chicago, Illinois, USA). Means, medians, and proportions (%) were used to describe both baseline characteristics and outcomes, when appropriate. Student’s t-tests were used to analyse differences between mean scores and chi-square test for differences in proportions. Mann-Whitney U test were applied when appropriate. Two sided P-values <0.05 were considered statistically significant. Odds ratio (OR) and hazard ratio (HR) point estimates were reported with 95% confidence intervals. Adjustments were performed for potential confounding variables (see section 6.4, page 57 regarding what was considered confounding). Most analyses were stratified by sex. Logistic regression models were used in papers I-III to assess associations between BMI and/or risk category of malnutrition, and dichotomised chronic diseases, social and lifestyle variables (paper I), SCL-10 score category (paper II), or EQ-5D dimensions (paper III). In the analyses of specific variables, cases with missing values were not included.

In paper III, analysis of covariance was used to obtain age-adjusted mean values for the EQ-5D score. The importance of the differences in EQ-5D scores between malnutrition risk groups was examined by calculating their effect size as the mean difference divided by the standard deviation (SD) of the control group [43]. We evaluated the detected differences against the criteria introduced by Cohen [23] using the standard deviation (SD) of the low-risk category of malnutrition. Effect size values of 0.2 to <0.5, 0.5 to < 0.8, and ≥0.8 were characterised as small, medium and large differences, respectively.

Mortality analyses in paper IV were performed using a Cox proportional hazards regression model. We assessed the proportional hazards assumption of a constant hazard ratio over time by inspecting the log-log survival curves for the various BMI categories.

For logistic regression analyses of the various BMI categories (paper I), we used the BMI category 22.5-24.9 kg/m^2 as a reference because this is the upper normal BMI category according to WHO [164]. In papers II-IV, the BMI category 25-27.4 kg/m^2 was used as reference, as this was the category both with the most participants and with the highest number of deaths (paper IV).

For further details, see the description of data analyses in the various papers.

5 Summaries of papers and main results

In papers I-IV, we explored the relationships between BMI, the risk of malnutrition and morbidity, HRQoL and mortality (figure 5).

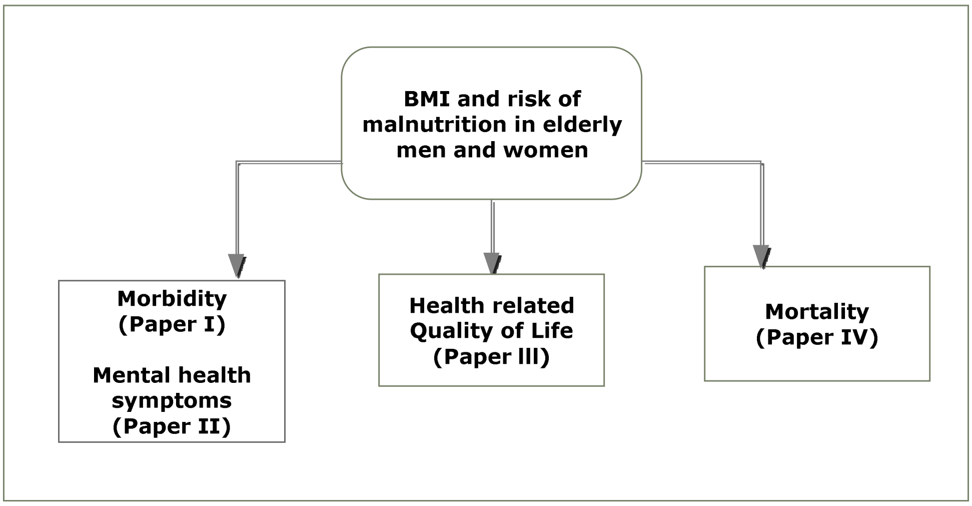


Figure 5 The aspects of health described in papers I through IV.

Paper I identifies the potential risk factors, chronic conditions and diseases associated with different BMI categories. Paper II explores mental health using the SCL-10 score. Another important dimension of life for elderly individuals is HRQoL, which is explored in paper III. Participants examined in papers II and III were classified both according to their BMI and risk of malnutrition. In paper IV, the relationships between the various BMI categories and mortality, the ultimate endpoint, were explored. For more details, see the sections 5.1 to 5.4.

5.1 Paper I

Body mass index and disease burden in elderly men and women: The Tromsø Study

Jan-Magnus Kvamme, Tom Wilsgaard, Jon Florholmen, Bjarne K Jacobsen.

Eur J Epidemiol, 2010: 25(3); 183-193. Epub 2010 Jan 20.

Background: Chronic health problems may be related to body mass index (BMI), but this has been best documented in overweight and obese adults. The primary objective of this study was to identify factors associated with different categories of BMI in community-living elderly men and women, also including the lower categories of BMI.

Methods: In a cross-sectional population survey from the municipality of Tromsø, Norway, we analysed associations between BMI and a wide range of chronic disease conditions, lifestyle and socioeconomic factors. BMI (kg/m^2) was categorised into six groups (<20 kg/m^2, 20.0-22.4 kg/m^2, 22.5-24.9 kg/m^2, 25.0-27.4 kg/m^2, 27.5-29.9 kg/m^2, ≥30.0 kg/m^2). The study included 4 259 non-institutionalised men and women aged 65 years and older.

Results: The overall proportion with BMI <20 kg/m^2 (low weight) was 5.1%, BMI between 25.0 and 29.9 kg/m^2 (overweight) 42.1% and BMI ≥30.0 kg/m^2 (obesity) 16.9%. Obesity was more common in women than in men (21.8% vs. 10.4%). Current smoking, mental distress and hip fractures were more prevalent in the lower BMI categories in both sexes. Asthma or chronic bronchitis and low physical activity exhibited a U-shaped relation to BMI (p-value for a second order term <0.05). Neither single marital status, difficult economy nor lower education was related to underweight, whereas lower education and a difficult economy were related to obesity. Reduced muscle strength was correlated to low weight. Alcohol intake was less frequent in the higher categories of BMI. Diabetes mellitus and ischemic heart disease (IHD) were associated

only with higher BMI categories. Diabetes mellitus was associated with obesity and IHD was associated with overweight and obesity.

Conclusion: These results demonstrate that both low and high BMI are associated with a wide range of prevalent conditions and diseases in community-living elderly individuals. For the clinician, the findings emphasise the importance of nutritional assessment as part of the medical evaluation of elderly patients.

5.2 Paper II

Risk of malnutrition and mental health symptoms in community-living elderly men and women: The Tromsø Study

Jan-Magnus Kvamme, Ole Grønli, Jon Florholmen, Bjarne K Jacobsen. *Submitted*

Background: Little research has been done to examine the relationship between the risk of malnutrition and mental health in community-living elderly individuals. In the present study, we aimed to assess the associations between mental health (particularly anxiety and depression) and both the risk of malnutrition and body mass index (BMI, kg/m^2) in a large sample of elderly men and women from Tromsø, Norway.

Methods: In a cross-sectional survey of 1 558 men and 1 553 women aged 65 to 87 years, the risk of malnutrition was assessed by the Malnutrition Universal Screening Tool (MUST), and mental health was measured using the Symptoms Check List 10 (SCL-10). BMI was categorised into six groups (<20.0 kg/m^2, 20.0-22.4 kg/m^2, 22.5-24.9 kg/m^2, 25.0-27.4 kg/m^2, 27.5-29.9 kg/m^2 , ≥30.0 kg/m^2).

Results: The risk of malnutrition (combining medium and high risk) was found in 5.6% of men and 8.6% of women. Significant mental health symptoms were reported by 3.9% of men and 9.1% of women. In a model adjusted for age, marital status, smoking and education, significant mental health symptoms (SCL-10 score ≥1.85) were positively associated with the risk of malnutrition (odds ratio 3.9 [95% CI 1.7-8.6] in men and 2.5 [95% CI 1.3-4.9] in women), the association was positive also for subthreshold mental health symptoms. For individuals with BMI <20.0 kg/m^2, the adjusted odds ratio for significant mental health symptoms was 2.0 [95% CI 1.0-4.0]. No significant increase in significant mental health symptoms was found in obese individuals.

Conclusions*:* Impaired mental health was strongly associated with the risk of malnutrition in community-living elderly men and women, and this association was also significant for subthreshold mental health symptoms.

5.3 Paper III

Risk of malnutrition and health-related quality of life in community-living elderly men and women: The Tromsø Study

Jan-Magnus Kvamme, Jan Abel Olsen, Jon Florholmen, Bjarne K Jacobsen.

Qual Life Res. 2011 May;20(4):575-582. Epub 2010 Nov 13.

Background: Health-related quality of life (HRQoL) has received increased attention in previous decades as a measure for both comparing health statuses across different patient groups and for measuring health outcomes. However, larger community-based studies evaluating HRQoL in elderly individuals at risk of malnutrition are lacking. In the present study, we aimed to explore the association between risk of malnutrition and HRQoL in community living elderly men and women. The association between body mass index (BMI) and HRQoL was also explored.

Methods: In a cross-sectional population survey including 1 654[1] men and 1 632 women aged ≥ 65 years from the municipality of Tromsø, Norway, we assessed HRQoL by using the EuroQol (EQ-5D) instrument in three risk groups of malnutrition and in different categories of BMI. The Malnutrition Universal Screening Tool (MUST) was used to evaluate the risk of malnutrition.
Results: More women (9.4%) than men (5.5%) were at risk of malnutrition (medium- and high-risk combined). HRQoL was lower in women than in men when assessed by the EQ-5D index and the EQ VAS score. We found a significant reduction in HRQoL with increasing risk of malnutrition, and this was more pronounced in men than in women. The relation between BMI and HRQoL was dome shaped, with the highest HRQoL scores being observed in the 25-27.5 kg/m^2 BMI category although the differences were small between the middle BMI categories.
Conclusions: HRQoL was significantly reduced in elderly men and women at risk of malnutrition. The highest HRQoL was seen in moderately overweight individuals.

5.4 Paper IV

Body mass index and mortality in elderly men and women: The Tromsø and HUNT studies
Jan-Magnus Kvamme, Jostein Holmen, Tom Wilsgaard, Jon Florholmen, Kristian Midthjell, Bjarne K Jacobsen. *J Epidemiol Community Health.* Published online February 14, 2011
Background: The impact of body mass index (BMI, kg/m^2) and waist circumference (WC) on mortality in elderly individuals is controversial, and previous research has largely focused on obesity.
Methods: With special attention to the lower BMI categories, associations between BMI and both total and cause-specific mortality were explored in 7 604 men and 9 107 women aged ≥65 years who participated in the Tromsø 4 survey (1994-95) or the North-Trøndelag Health Study

[1] In the *abstract* of the paper III, the numbers of participating men and women had been interchanged. The correct numbers are 1654 men and 1632 women as written in the table 1 in the main part of the paper.

(HUNT 2 survey) (1995-97). A Cox proportional hazards model adjusted for age, marital status, education, study site and smoking, was used to estimate hazard ratios for mortality in different BMI categories using the BMI range of 25-27.5 kg/m^2 as a reference. The impact of each 2.5 kg/m^2 difference in BMI on mortality (later in this abstract denoted as change in BMI) in individuals with BMI $<$25.0 kg/m^2 and BMI $\geq$25.0 kg/m^2 was also explored. Furthermore, relationships between WC and mortality were assessed.

Results: We identified 7 474 deaths during a mean follow-up period of 9.3 years until 31.12.2007. The lowest mortality was found in the BMI range 25-29.9 kg/m^2 and 25-32.4 kg/m^2 in men and women, respectively. Mortality was increased in all BMI categories below 25 kg/m^2 and was moderately increased in obese individuals. U-shaped relationships were also found between WC and total mortality. When modelling BMI as a continuous variable, we found a 20% increase in mortality per 2.5 kg/m^2 decrease in BMI in the lower BMI range ($<$25 kg/m^2). In the upper BMI range ($\geq$25 kg/m^2), we found a 7 to 9% increase in mortality per 2.5 kg/m^2 increase in BMI. About 40% of the excess mortality in the lower BMI range in men was explained by mortality from respiratory diseases.

Conclusions: BMI below 25 kg/m^2 was in elderly men and women associated with increased mortality. A modest increase in mortality was found with increasing BMI among obese men and women. Overweight individuals (BMI 25-29.9 kg/m^2 in men, 25-32.4 kg/m^2 in women) had the lowest mortality.

6 General Discussion – Methodology

6.1 Selection of populations and study design

Each study included in this thesis is *population-based*, which is important for the generalisability of the results. We aimed at describing populations of *community-living* elderly men and women as distinct from elderly hospital in-patients. Nursing home patients were invited, but attended to a very small degree (8 out of 4 017 participants in the Tromsø 6 survey, and 45 out of 15 250 in the HUNT 2 survey). Consequently, the participants in the included studies may be regarded as community-living individuals.

In papers I-III, we explore associations in a cross-sectional design, which restricts the possibility of making cause-effect conclusions. In paper IV, we used a prospective cohort design, which makes it possible to derive causality-based conclusions.

6.2 Validity

The aim of epidemiological research (e.g., the studies included in this thesis) is to obtain correct and precise results that can be generalised to other populations. The *validity* of a study refers the extent to which this aim is fulfilled. Internal validity concerns the degree to which it is possible to draw conclusions concerning the study population. External validity concerns the degree to which it is possible to apply the results to other populations (i.e., generalisability of the results) [90, 119] (figure 6). Internal validity is regarded as a prerequisite for external validity.

6.3 *Internal validity and bias*

Bias is systematic error that tends to produce results that depart systematically from the true values [71, 93]. Violations of internal validity can be classified into one of the categories *selection bias*, *information bias* or *confounding* (figure 6) [119].

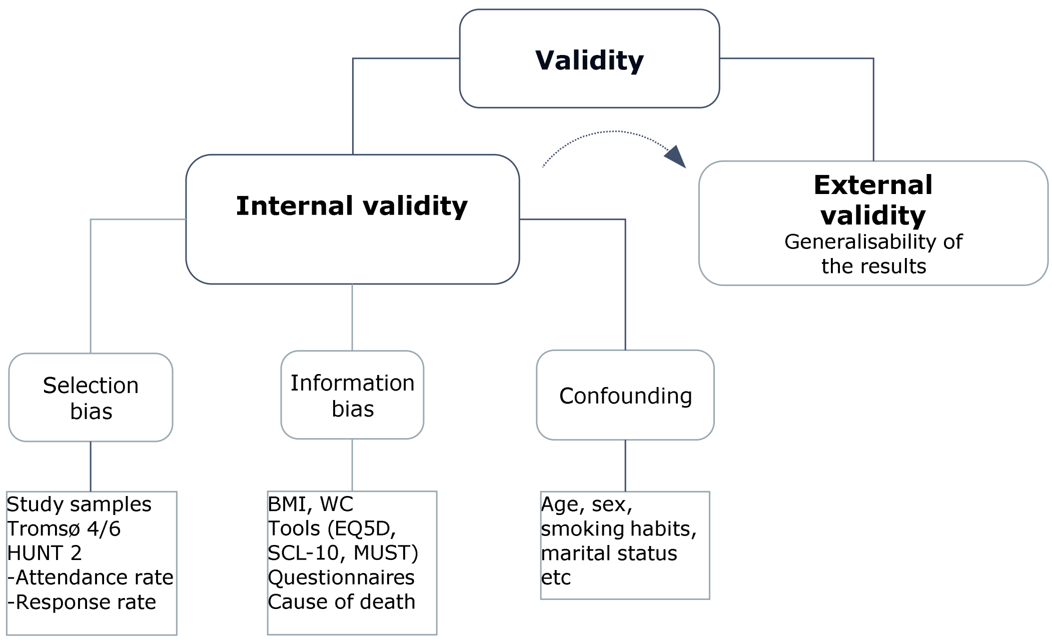


Figure 6 Internal and external validity with examples from the thesis. Internal validity is regarded as a prerequisite for external validity (curved dotted arrow).

6.3.1 Selection bias

Selection bias may arise when the subjects included in the study sample differ from the source population in a way that affects the conclusions [90]. This type of bias arises from participant selection procedures or from factors that influence participation in the study. For selection bias to occur, the association between the independent and dependent variables must be different between study participants and non-participants [123]. The potential for selection bias is somewhat limited by the attendance rates in the included surveys, which were between 65% and 70% (See tables 4 to 6). This may be regarded as relatively high for population-based epidemiological studies. However, there were non-responders for several of the variables, which reduced the size of the study sample by an additional 8-20 percentage points (table 5 and 6).

A precise measurement of the effect of selection bias is not possible, as this would require information regarding the exposure and outcome status for both participants and non-participants. [15]. The only information we have about the non-participants in the Tromsø and HUNT surveys is age and sex. The mean age of the participants included in the study samples was generally lower than for non-attending individuals. In all papers, there was a response rate below 50% for the highest age group (≥80 years).

However, a small study of subjects who selected not to participate in the HUNT 2 survey, was performed shortly after completion of the fieldwork [68]. Among individuals aged ≥70 years reached by phone, *immobility* due to disease and *sufficient follow-up* by the family doctor were reported as important reasons for not participating. In the Tromsø 4 and 6 surveys, immobility was likely more common in non-participating elderly individuals, making it difficult to visit the research centres. Moreover, both decline in cognitive function and dementia are conditions likely to be more prevalent in non-attending individuals and in individuals with missing data on the self-administrated questionnaires. Dementia generally affects 10-20% of the population aged >80 years [37] and is associated with the risk of malnutrition [70]. We do not have data on the prevalence of dementia in the elderly in the Tromsø and HUNT surveys.

The mortality rate in the paper IV cohort was approximately 25% lower than the expected mortality rate based on mortality rates of the entire elderly population of Norway [137]. This result indicates a better general health in participants than in non-participating elderly individuals.

The male to female ratio in paper I (Tromsø 4) was similar in the invited population and in the study population (table 4). However, in Tromsø 6, relatively more women than men had missing values for the EQ-5D and MUST instruments and study sample consisted of almost equal number of men and women (table 5).

In conclusion, we regard it as likely that the non-attending and non-responding elderly men and women were frailer and more prone to both *malnutrition* and *chronic diseases* than the persons who were included in the study samples. Consequently, it is probable that a *selection bias* decreased rather than increased the strength of the observed relations between nutritional status, health conditions and mortality, although this question remains a matter of discussion.

6.3.2 Information bias

Information bias results from a systematic error in the information obtained about study participants [119]. Misclassification errors result when a study subject is placed in the wrong category. Misclassification can be divided into the following categories: (1) Non-differential misclassification results when the proportion of misclassified subjects does not depend on the status of the subjects with respect to other variables (i.e., BMI category or risk category of malnutrition). Height and weight measurements, grip strength and marital status are potential examples of this type of misclassification. (2) Differential misclassification results when the misclassification depends on the status of the subjects with respect to other variables. This could be the case for self-reported diabetes, where obese individuals may have been more likely to have a glucose measurement during visits to their family doctor.

The question of whether the possibility of misclassification is differential with respect to BMI category or risk category of malnutrition, is addressed below in the discussion of the various methods used in this thesis. Overall, we see no indication of serious differential misclassification in the included studies.

Assessment of Nutritional status (Paper I-IV)

Body composition, BMI and Waist circumference

The nutrient and energy balance over the course of a person's life is reflected by his/her body composition. There are four main compartments of the body at the tissue-organ level: (1) adipose tissue, (2) skeletal muscle, (3) visceral organs and (4) skeleton. The latter three compartments are often referred to as the lean tissues or *lean body mass* [66]. A person's body weight represents the sum of all four compartments. Body weight is, however, only an indirect measure of protein mass and energy stores. A change in body weight and BMI is usually regarded as proportional to loss or gain in lean mass and fat mass, but this relationship varies with factors such as gender, age and diseases [66].

BMI is the most widely used measure of weight status. It is simple to calculate and is widely used in clinical settings. The ratio between weight and height used to calculate BMI was first described by Adolphe Quetelet, the Belgian mathematician and statistician, in 1832 [35]. Based on empirical observations, he found the index to be a good measure for height-adjusted weight [114]. The term BMI was first introduced to describe this ratio by Ancel Keys in 1972, based on Framingham data [82]. In the last decades, BMI has been extensively used in epidemiological and clinical research.

Self-reported height and weight have been used in some previous studies of BMI and various health outcomes in elderly individuals, introducing the possibility of error. Trained personnel measured height and weight in each survey included here.

When categorising a variable such as BMI, boundaries can be set at fixed percentiles (e.g., quintiles). An alternative method, used in the present thesis, is to use meaningful category boundaries [120] based on predefined categories, such as those set by the World Health Organization (WHO) [164]. We divided participants into nine categories based on BMI values (<18.5 kg/m^2, 18.5-19.9 kg/m^2, 20.0-22.4 kg/m^2, 22.5-24.9 kg/m^2, 25.0-27.4 kg/m^2, 27.5-29.9 kg/m^2, 30.0-32.4 kg/m^2, 32.5-34.9 kg/m^2 and ≥35 kg/m^2). We included thereby the standard definitions of overweight (BMI 25.0-29.9 kg/m^2) and obesity (BMI ≥30 kg/m^2) (WHO, 2000) [164]. These WHO boundaries are also well established in clinical practise. In some of the analyses, we merged all BMI categories below 20 kg/m^2 and above 30 kg/m^2 due to the limited number of deaths for some of the disease categories. By subdividing the categories between 18.5 and 30 kg/m^2, we were able to describe in more detail the characteristics of the lower-normal BMI categories (18.5 to 25 kg/m^2) and the overweight (25-29.9 kg/m^2) BMI categories.

Repeated measurement of BMI during the follow up period was not performed for the cohort used in the prospective analyses in paper IV. However, for the HUNT cohort, data has been previously published for the time period from HUNT 1 (1984-86) to HUNT 2 (1995-97), which showed that BMI was more stable in individuals aged ≥65 years than for middle-aged and younger individuals [34]. It is not likely that the BMI of elderly participants changed largely during the study period for paper IV (1994-2007). With respect to the middle-aged individuals in the Tromsø cohort [166], high tracking has been demonstrated for BMI (i.e., maintenance of the relative position within a distribution of values in a population over time) [152]).

Several questions can be raised regarding the use of BMI as a measure of nutritional status in elderly individuals. The first question deals with standing height as the divisor component of BMI [51]. During aging, height is gradually reduced (approximately 5 cm from the third to the seventh decade) due to a decrease in thickness of the vertebral body and flattening of the arch of the foot [30]. Height reduction results in an increase in BMI for a given weight. For example, for a person weighing 70 kg, a reduction in height from 1.70 m to 1.65 m will increase BMI from 24.2 to 25.7 kg/m^2. However, this is likely to be more important when BMI values are compared between younger adults and elderly individuals.

A second question is related to how well BMI correlates with body composition and fat mass. BMI is only an indirect measure of body composition. When we include BMI in our analyses, it is usually as a substitute for a measure of fat mass, although lean body mass is also of interest when assessing malnutrition. Advanced methods for the measurement of body composition include Dual-energy X-ray absorptiometry (DXA) [74, 151], but we did not have available DXA measurements for the participants in the respective studies. However, in a large study by Flegal et al. comparing BMI values with DXA measurements in elderly men and women, the Pearson correlation coefficient between BMI and body fat was relatively high (0.72 to 0.76) [46].

A third question with respect to BMI, is related to the change in fat distribution with aging and to what degree this affects BMI. Visceral fat and subcutaneous abdominal fat tend to increase with age [9], and the amount of abdominal fat is likely to be larger at a given BMI in elderly than in younger, adult individuals [155]. In order to assess abdominal obesity, we included *waist circumference* (WC) in the prospective analyses of mortality (paper IV). WC and the waist-hip ratio are both indicators of nutritional status and assess abdominal obesity in particular [50]. WC is easier to interpret as an absolute measure than the waist-hip ratio.

When assessing the relationships between WC and mortality (paper IV), we followed a procedure similar to that described by Flegal et al. [45] and created WC categories that identified similar proportions of participants as each of the nine BMI categories. The WC category equivalent to the 25.0-27.4 kg/m^2 BMI category was used as a reference. We found that in the higher weight categories, WC was not a stronger risk factor for total mortality than BMI. In the lower weight categories, BMI was a stronger risk factor than WC.

Malnutrition Universal Screening Tool (MUST)

When considering the identification of malnutrition, it is common to differentiate between (1) <u>nutritional screening,</u> an initial evaluation and (2) <u>nutritional assessment,</u> a more comprehensive and in-depth evaluation of those considered to be at risk [36]. In larger population-based studies, nutritional screening is the approach that may be used.

The European Society for Clinical Nutrition and Metabolism (ESPEN) has recommended three instruments for nutritional screening, and of these, the MUST is one of the nutritional screening instruments recommended for use in the community [40, 83]. When planning the Tromsø 6 survey (2007-2008), we wanted to include a nutritional screening tool. For use in a large population-based survey, the required tool had to be preferably self-administered and not to extensive. The MUST was chosen because it is relatively brief and the score information can be self-reported. Furthermore, it has been used in a number of previous studies [36] and found to predict both mortality and other clinical outcomes in hospitalised patients [142] and general health status in community-living elderly [98].

The *acute disease component* for the MUST was set to zero because participation in the Tromsø study required the ability to independently visit a research centre. The acute disease component gives a score of two if "*the patient is acutely ill and there has been or is likely to be no nutritional intake for >5 days*" [36]. This criterion is important for detecting well-nourished individuals who in a short time develop a high risk of malnutrition because of acute diseases or accidents. However, even for hospital in-patients, only a small proportion will be so severely affected that this criterion will apply [36].

The terms *face validity* and *content validity* describe to what degree a scale or tool looks reasonable. Face validity deals with whether the instrument seems to evaluate the correct qualities and this is normally based on subjective judgements of groups of experts. Content validity deals with whether the important domains and content are included in the instrument [144]. The present MUST was thoroughly developed by the British Association of Parenteral and Enteral Nutrition [36], which ensured both its face and content validity [115].

Inter-rater reliability deals with the agreement between different raters. In various clinical settings this has been tested for the MUST, with kappa values ranging from 0.9 to 1.0 [36].

Kappa is a measure of agreement above what would be expected by chance, and kappa values ≥ 0.81 are regarded as very high [1].

Due to the lack of a gold standard for determinations of malnutrition, it is challenging to determine the *exact validity* of the nutritional screening tools available [140]. In a study of hospitalised patients from Switzerland [89], the MUST was compared to the Nutritional Risk screening Tool (NRS 2002) [84] and the subjective global assessment (SGA) [28]. The SGA was used as reference. The mean age of the included patients was over 50 years. The sensitivity of the MUST was slightly lower and the positive predictive value was somewhat lower when compared to the more comprehensive NRS 2002. The NRS 2002 also consists of a rating of disease severity and is regarded to be the best tool for use in hospital settings [115]. We considered the NRS 2002 as too extensive for use in a large-scale epidemiological study. Furthermore, in a British study including the SGA and the MUST, the conclusion was that there was a “fair-good” to “excellent” agreement beyond chance between MUST and most other tools studied [140]. Another assessment tool, the Mini Nutritional Assessment (MNA) is intended especially for use in elderly people [83], but the MNA is constructed to be used by health care professionals [57] and is therefore also difficult to use in large epidemiological studies.

In paper II, we correlated the risk of malnutrition with mental health symptoms. Previous studies exploring the associations between these two conditions have used the MNA for the nutritional assessment. However, the MNA includes information about both neuropsychological problems and psychological stress [57]. A positive correlation between the MNA risk score and the symptoms of depression could therefore be anticipated. In this context, we regard it as advantageous to use the MUST, which does not include any component exploring psychological symptoms.

In all the included papers in this thesis, we categorised participants according to BMI. The MUST was included in the Tromsø 6 survey (Papers II and III), whereas this score information was not available for the HUNT 2 and Tromsø 4 surveys (Papers I and IV). However, as BMI is a primary part of the MUST, all participants with BMI $\leq$20 kg/m^2 would have been categorised at medium or high risk according to the MUST.

Assessment of mortality

In Norway, a unique personal identification number is used to link all deaths to the Norwegian Causes of Death Registry. This system covers all deaths except some deaths that occur abroad. In other countries, such as United States, this linking of information is more complicated [157]. After each death, a death certificate is completed by a physician. We used the underlying cause of death, which is defined as "*the disease or injury that initiated the train of morbid events leading directly to death, or the circumstances of the accident or violence which produced the fatal injury*" (WHO) [165]. Autopsy is increasing the precision of the cause-of-death statements [146]. Only 10% of the deaths in elderly people in the Tromsø 4 population were subject to autopsy. This is slightly lower than the 12% average autopsy-rate for all of Norway [146]. Elderly people often have several chronic conditions, a fact that leads to potential difficulties in the diagnosis of the true underlying cause of death. Despite this, the quality of the data from the death registry in Norway is regarded as fairly good [6]. We do not believe it is likely that nutrition status systematically affects the coding of underlying cause of death.

Self-administrated questionnaires

Self-administrated questionnaires are important tools in epidemiological research [122] and were used in the present studies to obtain information regarding lifestyle variables, chronic conditions and diseases. There are several methodological issues related to self-administrated questionnaires. First, self-reported information may be imprecise. Participants may forget portions of their medical history (recall bias), and the fact that cognitive decline is more prevalent in elderly individuals increases this risk. The reported data regarding diseases was not matched with hospital or primary care records. In the case of diabetes, however, a similar question as the one used in the Tromsø 4 survey was validated in the HUNT 2 survey. For this question, a high accordance was found between self-reported and known diabetes in patient records [99]. Several other questions have also been previously validated, mostly in adults but also in elderly individuals. Validations have been found for questions regarding myocardial infarction [150], stroke [39], hip fractures [78] and physical activity [86]. Validation of the two instruments SCL-10 and EQ-5D is reported below.

A second issue related to self-administrated questionnaires is that several diseases may be partly undiagnosed and hence not reported. For example, this is the case for asthma/chronic bronchitis [59] and diabetes [52]. Up to 50% of diabetics are undiagnosed and experience only minor symptoms.

Third, participants may be unwilling to report correct information regarding certain habits, for example alcohol intake or smoking. Alternatively, it is possible that a more anonymous questionnaire will yield more accurate information regarding sensitive life styles issues than personal interviews. In support of this, a large metaanalysis of smoking habits has found a high accuracy for self-reports in most studies [108].

The key question is whether the use of self-administrated questionnaires has biased the results presented in the papers. As discussed, we cannot exclude some bias, but we find it unlikely that the main results are influenced significantly.

Assessment of mental health

CONOR mental health index (Paper I)

Paper I evaluates several diseases, health conditions and mental health, the latter being measured by the CONOR mental health index. This index has been compared with the Hospital Anxiety and Depression Scale [172] and the Hopkins SCL-10 (see below) with a reasonably good agreement also in elderly subjects. A cut-off value of 2.15 has been proposed to identify persons with significant mental distress [134]. The correlation between the CONOR mental health index and the SCL-10 is high (Pearson correlation coefficient 0.82) [134].

Symptoms check list 10 (Paper II)

Paper II deals more specifically with mental health and the risk of malnutrition. For this paper, the SCL-10 instrument was used. The SCL-10 is an abbreviated version of the 25-item Hopkins Symptoms Checklist (SCL-25) [64], which has been validated in different age categories, including a study of elderly individuals in primary care [49]. The SCL-25 was designed to predict both anxiety and depression, but was found to predict depression better than anxiety disorders in a population-based study [127]. The shorter SCL-10 version correlated highly with the SCL-25 version (r=0.97) in a population-based Norwegian study that also included elderly individuals [139]. The SCL-10 has been widely used in epidemiological studies.

Other studies exploring the relationship between nutritional status and mental health have used the geriatric depression scale (GDS). This scale has been more widely used in older individuals and has been recommended for use in primary care [162]. To our knowledge, no study has been performed comparing the SCL-10 and the GDS.

The concept of mental distress has often been used when screening for mental health disorders. Mental distress is regarded as a broader term than mental disorders. Both mental health symptoms [169] and mental distress [133] have previously been used when describing the SCL-10. In paper II, we chose to use the term *mental health symptoms* to describe the score derived from the SCL-10. Depending on the cut-off limits used, the literature indicates that 50-60% of cases detected with instruments similar to SCL-10 actually qualify for a diagnosis of mental disorders based on clinical interviews [139].

The SCL-10 captures symptoms of both anxiety and depression. Depression is more influential in the relationship with nutritional status, but considerable overlap exists between anxiety and depression, and they often appear as co-morbid disorders [87, 97].

Assessment of HRQoL (EQ-5D) (Paper III)

The concept of HRQoL systematically describes the subjective assessment of health and life of each individual. The EQ-5D is a standardised instrument developed to provide a non-disease-specific measure of health status, and this tool is also suitable for use in population based health studies [85, 148]. The Short Form 36 (SF-36) questionnaire for HRQoL assessment is more comprehensive and has a larger evidence base than the EQ-5D [2]. However, in an extensive review of generic, self-assessed health instruments for use in older people [61], the EQ-5D was also found to have good reliability, validity and responsiveness. A later clinical study of women being treated for osteoporosis demonstrated a substantial agreement between the EQ-5D and the SF-36 [17]. A concern in paper III is the high number of missing responses on the visual analogue scale (VAS) portion of the EQ5D instrument. This was the only VAS scale in the Tromsø 6 questionnaire and it seems to have been difficult to interpret for some of the participants. However, there were only minor differences in mean age and BMI between the responders and non-responders to the EQ VAS scale. Therefore, there are no indications that the subjects who did fill in the EQ VAS scale differ in a systematic way from the population who only filled in the other portions of the EQ-5D.

6.4 Confounding

Confounding (from the Latin *confundere*, meaning "to mix together") occurs when the effect of interest is related to, or mixed with, other variables [11]. A confounding variable must be independently associated with the dependent variable, and there must be a statistical association between the confounding variable and the independent variable. Furthermore, the confounder must not be on the causal path between exposure and disease. A confounding variable may result in either an under- or overestimating of the true relationship between the exposure and the outcome variable [71]. Smoking is an example of a confounder in this thesis as it influences both BMI and morbidity/mortality. Smoking is included as a three-level variable (never, ex- and current smoking), at minimum, in the current statistical analyses. Age and sex are very often confounding variables in population-based studies. Most analyses are stratified for sex and all analyses are age adjusted.

One method used to deal with confounding variables, is to *adjust* for the confounding variable in the statistical models. We have done this in most of the analyses. Another method is to *stratify* for the confounding variable. Some of the analyses in paper IV are stratified for smoking.

We aimed to include the most important potential confounders based on prior knowledge. These variables included *marital status* and *educational level* in addition to *age* and *sex. Alcohol intake* and *leisure time physical* activity are two other variables that may be confounders, but there was a high level of missing information for these variables in our samples. In the subgroups in papers II and IV for whom information was available for alcohol and physical activity, we adjusted some of the estimates: In paper II, the analyses of mental health and risk of malnutrition were adjusted for alcohol intake. In paper IV, the analyses of total and cause specific mortality and BMI were adjusted for both alcohol intake and physical activity. Moreover, we included selected *chronic, somatic diseases* (history of cancer, heart attack or stroke) in the analyses in paper II as potentially affecting both mental health and risk of malnutrition. However, it is not possible to account for all possible confounding variables [13], and residual confounding cannot be excluded.

6.5 Other aspects related to methodology

It is self-evident that *food habits* over a long period have affects on the nutritional status in elderly individuals. However, we considered the sparse diet data in the Tromsø 4, 6 and HUNT-2 surveys, but found the information to be insufficient for use in our studies. In general, it may be difficult to obtain valid and reproducible data concerning food habits from self-administered questionnaires [121].

Furthermore, *biochemical data* that could further characterise the individuals at risk of malnutrition, have not been included. For example, blood tests, such as measures of serum albumin levels, have often been regarded as indicative of nutritional status. However, many other conditions affect serum albumin levels, and it is not regarded by most authors as a suitable marker of nutritional status [131, 143]. None of the three nutrition screening tools recommended by the ESPEN require biochemical data [83]. Nevertheless, data on micronutrient deficiencies in the risk groups of malnutrition could have revealed important information.

6.6 External validity

Can the results from this thesis be generalised to other populations of elderly individuals? As previously mentioned, both the Tromsø and HUNT surveys were population-based and had an overall high attendance rate compared to other population studies. Rothman et al. states that "generalization is in large measure a question of whether the factors that distinguish these other groups from studied groups somehow modify the effect in question" [119]. The HUNT and Tromsø studies include populations from both urban and rural areas and may be regarded as relatively homogenous with respect to living conditions and ethnicity. We believe the internal validity to be acceptable and consider it correct to apply the conclusions from this thesis to other Caucasian populations of community-living elderly individuals.

7 General discussion - Results

Detailed discussion of the main results can be found in the respective papers I-IV. We will here concentrate on (1) some general epidemiological aspects, (2) a discussion of the prevalence of the risk of malnutrition, underweight and obesity and (3) some overall results regarding malnutrition, obesity and overweight.

7.1 Epidemiological research in an older population

Elderly people have some characteristics that may complicate epidemiological research. For example, a significant proportion of older people have multiple diseases and conditions, and it may be difficult, if not impossible, to fully identify the *disease burden* in self-administrated questionnaires. The more comprehensive approach used in clinical practice is obviously not possible in larger epidemiological surveys. Memory loss may increase the risk of recall bias. Moreover, the elderly population is diverse, and a substantial proportion in this age group is relatively healthy, self-reliant and has no significant cognitive decline.

Selective survival is also important in the study of elderly individuals. Approximately 83% of all deaths in Norway occur in individuals aged 65 years and older [135]. In a cross-sectional design (paper I-III), we can study disease prevalence but not incidence. For example, if survival after a hip fracture or stroke is influenced by BMI, the relationships between BMI and the prevalence of these conditions in subsequent cross-sectional studies will be affected. For younger adults, who experience lower mortality, this is of less concern than for elderly individuals.

Furthermore, some diseases have such a low prevalence that we are unable to assess their impact on nutritional status with a cross-sectional, population-based design [69]. For example, this may be the case for chronic liver and renal diseases, an examination of which would have required an even larger number of participants than were available for paper I.

7.2 Prevalence of risk of malnutrition, underweight and obesity

By using the MUST, we identified 8% of the study population, 6% of the men and 9% of the women, to be at a medium or high risk of malnutrition (paper III). There were more subjects at medium risk (5% of the population) than at high risk (3%). In a study from the United Kingdom (UK), Margetts et al. used criteria similar to MUST for classifying a representative population of elderly individuals [98]. They found approximately the same proportions of the population to be at medium and high risk. Furthermore, 11% of the study population in the southern UK was at risk of malnutrition (medium and high), a somewhat higher value than observed in our population. The proportion at risk of malnutrition was higher in the northern UK and for all UK about 14%.

Studies using other criteria and screening instruments have found proportions of community-living elderly at risk of malnutrition between 2.5% and 21% [10, 102, 143]. In hospital-populations of elderly individuals, about 40% have been found to be at risk of malnutrition; however both lower and higher prevalence rates have been reported depending on criteria and clinical settings [143, 147].

We found that 5% of the elderly participants in the Tromsø 4 population had BMI values below 20 kg/m^2, which is often regarded as *underweight* [143]. In the Tromsø 6 population, 3% were in this BMI category. The attendance rate was almost similar in these two surveys and the difference may be related to a general increase in BMI. Other population-based studies have found the prevalence of underweight individuals to be approximately 5% in community-living elderly populations [143].

The prevalence of *obesity* (BMI $\geq$30 kg/m^2) was about 17% in the Tromsø 4 survey (1994-95), corresponding to the level found in US populations from the same period [4]. In the more recent Tromsø 6 survey, the proportion of obesity was increased to 20%, a lower increase than has been reported for in some other populations [48, 92].

7.3 Lower BMI categories and individuals at risk of malnutrition

Sarcopenia

The concept of sarcopenia can be regarded as a common approach to partly explain many of the adverse health effects observed in relation to the risk of malnutrition in this thesis. The term sarcopenia comes from Greek "sarx" for flesh and "penia" for loss, and was first stated in 1989 as a description of the loss of muscle mass, muscle endurance and muscle force occurring during aging [118]. Several factors contribute to the process of sarcopenia, including aging, poor nutrition, weight loss, lifestyle and a number of acute and chronic conditions and diseases [26]. These are complex relationships with many contributing elements. A recent review (2009) described sarcopenia as one of the key features of malnutrition occurring also in younger and middle-aged adults at risk of malnutrition [132]. Varying degrees of inflammation are also among the determinants of both sarcopenia and malnutrition [132]. In figure 7, several of our findings related to underweight and the risk of malnutrition are shown in relation to sarcopenia.

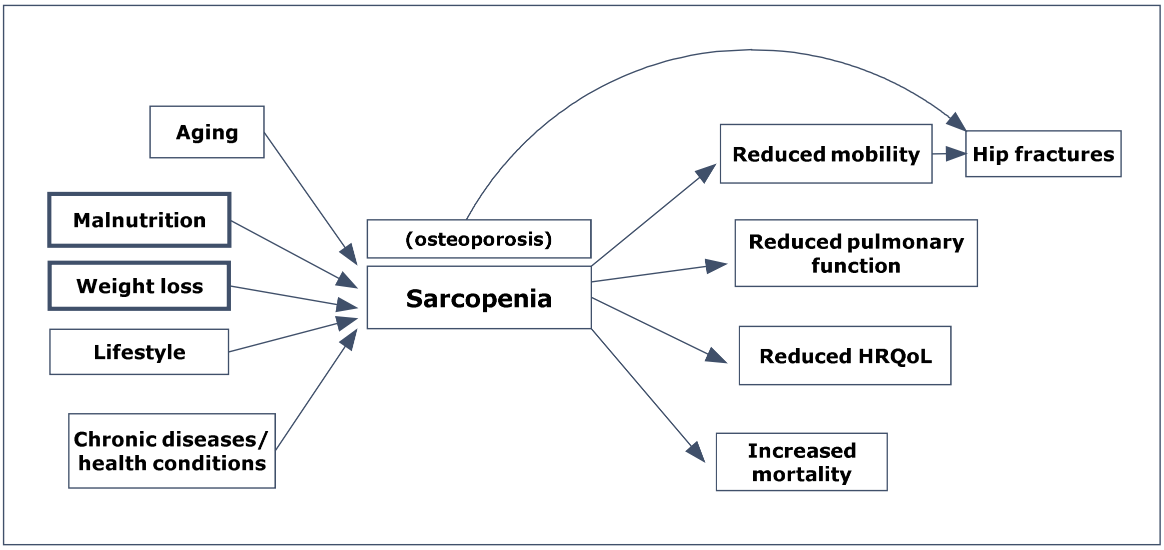


Figure 7 Sarcopenia as a common mechanism for several of the observed relationships (adapted from Cruz-Jentoft et al. [26]).

The consequences of sarcopenia are reduced mobility and increased risk of falls and hip fractures (paper I). Sarcopenia also affects respiratory muscle strength [132], which in turn worsens the course of chronic lung disease and reduces pulmonary function (paper I). Sarcopenia also contributes to reduced HRQoL by exacerbating physical disability (paper III) and to increased mortality, see below (paper IV).

Reduced mental health (depression) is one of the risk factors related to both malnutrition and weight loss (paper II) and may aggravate the process of sarcopenia. An important finding in paper II is the positive association also between sub-threshold mental health symptoms and the risk of malnutrition.

Hip fractures are also associated with osteoporosis (figure 7, curved arrow), and sarcopenia and osteoporosis share several risk factors [113]. Sarcopenia is common in this patient category [44].

Reduced protective padding over the hips may also contribute to the risk of fracture in underweight individuals [129].

Physical disability is increased in the population at risk of malnutrition, with sarcopenia and loss of lean body mass as common features (figure 7). We found self-reported physical activity and muscle strength assessed by isometric dynamometry (hand grip strength) to be reduced in subjects with low BMI (paper I). The mobility dimension of HRQoL was substantially affected in male individuals at risk of malnutrition (paper III). This increased disability as a consequence of malnutrition has also been reported by previous authors [156]**.** The implications of this correlation are important as the burden of care and nursing home admissions for the increasing elderly population is closely related to immobility and function level [80].

Socioeconomic factors

Socioeconomic factors like a difficult economy and lower education were not related to underweight (BMI<20 kg/m^2), but rather to obesity (paper I). It could be assumed that living alone should increase the risk of underweight in elderly individuals. However, in paper I underweight was not related to a single marital status, also when men and women were analysed separately. Our results largely correspond to a study of elderly individuals from the US, finding that a single marital status was not related to malnutrition for any of the categories of participants except black men [94].

Gender differences

More women than men were at risk of malnutrition according to MUST. However, overall, we found similar relationships between BMI, risk of malnutrition and health outcomes in men and women. For HRQoL, we found that although women have a lower general HRQoL, the impact of malnutrition on HRQoL was stronger in men than in women. Research on body composition in older people has demonstrated that during weight loss, men lose more lean mass than fat mass, whereas women lose relatively more fat mass [103]. It is possible that this relatively higher reduction in lean mass can partly explain the stronger impact of malnutrition on HRQoL in men compared to women. Moreover, the BMI range with the lowest mortality extended more to the right in women compared to men, and included BMIs up to 32.5 kg/m^2. This has also been demonstrated in some previous studies [106].

Increased mortality

One of the most striking findings in this thesis is the increased mortality in individuals with a BMI below 25 kg/m^2, including the traditional "normal" BMI range. This challenges the definition of normal weight in this age group. Several previous studies have reported increased mortality among individuals in the lowest BMI categories [58, 62, 73, 163, 171]. Mortality tends to increase when BMI falls below 19-23 kg/m^2. Very few studies of elderly men and women that include information about smoking habits, have been able to demonstrate a significant increase in mortality in the normal weight range of BMI 22.5-24.9 kg/m^2 compared to moderately overweight subjects.

Studies of adult individuals have shown an increased risk of mortality in the lower normal range of BMI 18.5-22.4 kg/m^2 [163]. A proposed explanation for this has been a limited amount of lean mass, a main component of sarcopenia (figure 7) in this BMI range. Preserved lean mass has an important role in different survival and homeostatic mechanisms [96]. Another suggested mechanism has been the lack of protective fat storage in this lower-normal BMI range [96].

Because of the change in body composition with aging, a given BMI represents relatively less lean mass in elderly than in younger, adult individuals. This fact may also partly explain why the BMI range of 22.5-24.9 kg/m^2 was correlated with increased mortality in older age groups.

BMI versus MUST

In this thesis, both BMI and MUST were used to characterise nutritional status. For the participants in the Tromsø 4 and HUNT 2 surveys, only BMI was available. The establishment of a single BMI cut-off for malnutrition in the elderly, as also indicated by data in this thesis, is difficult. From the presented mortality analyses (paper IV), the cut-off could be up to 24.9 kg/m^2, and from the morbidity analyses (paper I), it could be about 20 kg/m^2. Consequently, it may be more appropriate when using BMI, to regard increased health risk across the lower BMI categories as a continuum rather than to use definite cut-offs [74].

Moreover, a single BMI measurement does not take *weight loss* into consideration, which is also an important predictor for sarcopenia [143]. The MUST includes weight loss as one of three components. Weight loss is also part of the screening tools, NRS 2002 and MNA, in addition to other important variables [83]. BMI has been incorporated in all these three screening tools and *underweight* (BMI $\leq$20 kg/m^2) and *risk of malnutrition* classified by one of the tools, overlap to some extent (see page 53). However, the possibility *to correctly identify* individuals at risk of malnutrition is substantial improved by using one of the nutrition screening tools rather than BMI alone [83, 143].

MUST is recommended for use in the community, and our results indicate that it may also be used in epidemiological studies. The papers II and III demonstrated that risk of malnutrition identified according to this tool, was associated with both reduced HRQoL and mental health symptoms. To our knowledge, neither of these two important health measures has been previously explored in relation to MUST in community living elderly individuals.

Unidirectional versus bidirectional relationships

What comes first, malnutrition or disease? In developed countries, malnutrition is largely a problem related to an underlying disease with a direction from disease to malnutrition [76]. However, for several of the observed relationships in this thesis, the direction may be bidirectional, creating *vicious circles* [104]. This may be the case for example for chronic lung disease and depression. Depression may contribute to weight loss, resulting in micronutrient deficiencies that adversely affect mental health. For many malnourished COPD (chronic obstructive pulmonary patients) patients, a vicious circle is created through repeated hospital admissions for acute exacerbations [54].

Mild and acute inflammation

A guideline committee recently proposed disease-related malnutrition to be divided into malnutrition with *mild inflammation* and malnutrition with *acute inflammation* [76]. The participants at risk of malnutrition in the included studies were likely in a state of mild inflammation. During intercurrent hospitalisation due to acute disease, patients enter an acute inflammatory state, resulting in increased loss of lean body mass. It has been shown that hip fracture patients who are malnourished at admission lose additional weight during the course of the disease and are at an increased risk for complications [8]. This is similar to the situation for stroke and other conditions that result in hospital admissions, where intercurrent acute inflammation may aggravate a chronic malnutrition state [104].

Screening and intervention

The purpose of screening is to identify conditions where early detection and intervention improves outcomes [115, 123]. When a person is found to be at risk of malnutrition, an initial assessment for severe underlying disease and reversible conditions, including depressive disorders, should be performed. A multidisciplinary approach to improve nutritional intake should be applied [156]. The nursing home service is important, and some communities will also have access to dietician assessment and counselling for selected patients. Lack of motivation may be a problem for some elderly individuals, and relatives and family should be involved. Eating with others should be encouraged. Some areas have home dinner transport services. The prescription of oral nutritional supplements is beneficial for a large proportion of elderly at risk of malnutrition. Some severely malnourished elderly patients will need hospital admission and tube feeding or parenteral nutrition depending on the clinical setting, may be necessary.

For elderly individuals identified to be at risk of malnutrition, there is clear evidence for the benefits of nutritional support, although most intervention studies have been performed in clinical settings [141]. A Cochrane review from 2007 found a reduction in mortality with the use of nutritional supplements in elderly people when the analysis was limited to studies of undernourished participants (RR 0.79, CI 0.64 to 0.97) [22]. To further reverse loss of muscle mass, nutritional support should preferably be combined with a component of adapted physical exercise [124].

7.4 Obesity

Obesity is associated with serious diseases like diabetes and IHD (paper I), corresponding well with previous studies [3, 109]. This fact likely contributes to the moderately increased mortality observed in men with a BMI ≥30 kg/m^2 and women with a BMI ≥32.5 kg/m^2, respectively (paper IV). Asthma/chronic bronchitis were also more common in obese individuals, an association found in some previous studies [56]. As previously reported [91], obesity seems to be protective against hip fractures (paper I).

From the literature, it is known that obesity is associated with lower limb osteoarthritis [128], a disease not included in the conditions explored in paper I. The joint pain and stiffness caused by osteoarthritis may contribute to the observed reduction in physical activity (paper I) and HRQoL (paper III) in the higher BMI categories. It has recently been shown that a subgroup of obese individuals may be sarcopenic and that sarcopenic-obesity may contribute to physical disability and obesity-related mortality [170].

An interesting result from paper IV is that waist circumference, as a measure of abdominal fat mass, was not a stronger risk factor for mortality than BMI. This finding likely reflects the same basic biology that explains the lack of increased mortality related to the metabolic syndrome in individuals aged 60 years and older, which was recently found in the HUNT 2 survey [67] .

Public health concerns related to obesity in the elderly cannot be ignored based on our results. Obesity is more prevalent than risk of malnutrition also in our population. However, weight reduction in obese elderly is controversial [106]; the documentation of reduced mortality after weight reduction in the elderly population is scarce, although it is clearly indicated in severe cases and in some clinical settings [7].

7.5 Optimal weight for elderly individuals, - overweight?

It was not the primary objective of this work to find the optimal weight for elderly individuals. However, by including all BMI categories we revealed that overweight seems to be favourable for two fundamental health parameters: Mortality (BMI range 25- (30)32.5 kg/m^2) and HRQoL (BMI range 25-27.4 kg/m^2), although the differences in HRQoL were small between the middle BMI categories. Possible explanations for the reduced mortality include a protective effect of fat mass during intercurrent diseases. A recent study of hospitalised elderly patients found that increased fat mass was associated with decreased risk of complications and mortality [16]. Moreover, improved treatment of components of metabolic syndrome [67] and selective survival are also possible explanations. Overweight as the most optimal weight category with regard to mortality, has also been reported by some previous authors [29, 73].

8 Conclusions and implications

8.1 Conclusions

- Risk of malnutrition (moderate and high risk) was found in 8% of the study population, 6% of the men and 9% of the women. Using BMI alone, approximately 5% of participants had a BMI below 20 kg/m^2. Obesity (BMI $\geq$ 30 kg/m^2) was found in 17-20% of the population.
- Increased mental distress, a history of hip fracture, reduced muscle strength and current smoking were associated with low BMI, whereas ischemic heart disease and

diabetes were associated with obesity. Chronic lung disease and a reduced level of physical activity had a U-shaped relation to BMI. Lower education and a difficult economy were associated with high, but not low BMI.

- Mental health symptoms (depression/anxiety) were associated with the risk of malnutrition, and this association was also significant for sub-threshold mental health symptoms.
- HRQoL was significantly reduced with increasing risk of malnutrition and this was more pronounced in men than in women.
- A BMI below 25 kg/m^2 was associated with increased mortality, whereas a moderate increase in mortality was found with increasing BMI among obese men and women. About 40% of the excess mortality in the lower BMI range in men was explained by mortality from respiratory diseases.
- Moderately increased BMI (25-30/32.5 kg/m^2) should not be a concern with regard to mortality in elderly individuals.

These results have several implications with regard to individuals at risk of malnutrition in particular:

8.2 Clinical implications

- **Implementation of screening:** Risk of malnutrition is related to clinical important health conditions in community-living elderly people. Until now, efforts to implement screening systems for malnutrition have been stronger in hospitals than in primary care. Family doctors and community care nurses are more frequently in contact with this age category than health care workers in secondary care. Consequently, further work should be performed to implement screening systems also in primary care. This includes easy access to measurement tools like height and weight scales. (Implementation of nutritional screening is also a potential research issue, see below.)

- **Groups at particular risk of malnutrition**: Elderly individuals with depressive symptoms, chronic lung diseases and functional limitations represent particular risk groups. However, with an 8% risk of malnutrition, all community living elderly individuals should have nutritional screening as part of health examinations.
- **Basic and postgraduate education**: The results of this thesis underscore the importance of increased emphasis on nutritional issues in medical school, nursing schools and postgraduate training. In a study of doctors and nurses working in specialist care, insufficient knowledge was reported as the most common cause of inadequate nutrition practice [100]. It is likely that similar results would have been obtained for primary care physicians.

8.3 Research implications

(Some of these issues have been discussed in previous sections as indicated by the page numbers below)

- **Prospective design; body composition**: Most of the findings in this thesis are from cross-sectional studies and some of them (e.g. the impact of malnutrition on HRQoL) could possibly be tested in a prospective design. This could be done by following the Tromsø cohort into a future Tromsø survey. In such a survey, more precise characterisations of body composition might be available (e.g. DXA measurements of a larger number of the participants) (page 49).

- **Micronutrients**: Micronutrient deficiencies in individuals at risk of malnutrition should be studied in more detail (page 16 and 59).
- **Chronic inflammation**: More detailed characterisations with respect to a chronic inflammatory component in elderly individuals at risk of malnutrition should be performed (e.g. micro CRP could be an option for this purpose) (page 67).
- **Implementation of screening**: More research is needed to find the optimal methods for nutritional screening of patients also in primary care. Furthermore, the impediments for sufficient follow up of patients at risk of malnutrition should be identified.

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10 Appendices A-C

Appendix A

Included papers (I-IV)

Appendix B

Confirmation from Professor M. Elia regarding the use of the MUST tool

Appendix C

Questionnaires used in Tromsø 4, Tromsø 6 and HUNT 2

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RISK FACTORS

Body mass index and disease burden in elderly men and women: The Tromsø Study

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Abstract Chronic health problems may be related to body mass index (BMI, kg/m^2), but this has been best documented in overweight and obese adults. The primary objective of this study was to identify factors associated with different categories of BMI in elderly men and women from the general population, also including the lower categories of BMI. In a cross-sectional population survey from the municipality of Tromsø, Norway we analyzed associations between BMI and a wide range of chronic disease conditions, lifestyle and socioeconomic factors. BMI was categorized into six groups (<20, 20.0–22.4, 22.5–24.9, 25.0–27.4, 27.5–29.9, ≥30.0 kg/m^2). The study included 4,259 men and women aged 65 years and older from the general population. We found low relative weight (BMI < 20 kg/m^2) to be associated with increasing prevalence of mental distress, hip fracture, smoking and low handgrip strength. A U-shaped relation to BMI was found for asthma and chronic bronchitis, poor current health and low physical activity. The higher categories of BMI were associated with low education level, a difficult economical situation, diabetes mellitus and ischemic heart disease. These results demonstrate that both low and high BMI are associated with a wide range of prevalent conditions and diseases in elderly men and women. For the clinician the findings emphasize the importance of nutritional assessment as part of the medical evaluation of elderly patients.

Keywords Body mass index · Elderly · Chronic disease · Life style · Socioeconomic factors · Hand strength

Abbreviations

BMI	Body mass index
COPD	Chronic obstructive pulmonary disease
IHD	Ischemic heart disease
OR	Odds ratio
SD	Standard deviation

Introduction

The elderly population is rapidly growing. By 2050, it is expected that one in three Europeans will be 60 years and older [1]. Chronic health problems are common in later life and may be closely related to nutritional status as reflected by body mass index (BMI).

Most previous studies of associations between BMI and various medical conditions have focused either on the detrimental effect of obesity [2, 3], adult populations without analysis of elderly participants in particular [4, 5], or some selected chronic diseases [6, 7]. A number of studies have found malnourished patients in hospitals or community to be at increased risk of disease [8]. However, there are few population-based studies of elderly persons including all categories of BMI. Thus, important factors associated with low BMI compared to other BMI categories in this age group may not have been identified.

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The primary objective of the present study was to address these problems by exploring relationships between BMI and a wider selection of health-related variables in elderly men and women from the general population, including also the lower range categories of BMI.

Methods

Study population

The Tromsø study is a single centre, population-based longitudinal study with repeated health surveys of the municipality of Tromsø, Norway. The fourth cross-sectional survey of the population was conducted in 1994–1995. All inhabitants in the municipality aged 25 years and more were invited and examined at a research centre. The present analyses are restricted to participants aged 65 years and older. A total of 5,892 subjects in this age group were invited and 4,351 non-institutionalized persons attended the survey. Among them, 92 persons were not willing to take part in research or information concerning height and/or weight was missing. Thus, 2,447 women and 1,812 men with mean age (SD) 73.1 (5.6) and 72.3 (5.9) years, respectively, were included in the analysis. The overall attendance rate was 72%, declining with increasing age (Table 1). In subjects aged <79 years old, 81% attended.

The survey was approved by the regional board of research ethics, and each participating subject gave written informed consent.

Categories of body mass index

Height and weight were measured without shoes in light clothing. BMI was calculated as weight divided by the square of height (kg/m^2).

The BMI was in the main analyses divided into six categories (<20.0, 20.0–22.4, 22.5–24.9, 25.0–27.4, 27.5–29.9, ≥30.0 kg/m^2) and thereby included the WHO (World Health Organization) definitions of low weight (<20 kg/m^2), overweight (25.0–29.9 kg/m^2) and obesity (≥30 kg/m^2) [9].

Table 1 Participation in different age categories of elderly men and women. The Tromsø Study

Age range (years)	No. invited		No. included		Participation rate (%)	
	Men	Women	Men	Women	Men	Women
65–71	1,131	1,310	950	1,127	84.0	86.0
72–78	820	1,089	603	847	73.5	77.8
≥79	489	1,053	259	473	53.0	44.9
Total	2,440	3,452	1,812	2,447	74.3	70.9

Subjects with BMI < 18.5 kg/m^2 and 18.5–19.9 kg/m^2 were merged in the analysis as only 80 subjects were in the former group. Furthermore, in the main tables, we present the results with BMI ≥ 30 kg/m^2 as the top category due to low number of cases of some of the considered clinical conditions in obese subjects. In order to better describe differences across the range of BMI, we divided the 20.0–24.9 kg/m^2 and the 25.0–29.9 kg/m^2 brackets of BMI into two groups, respectively.

The category of BMI < 20 kg/m^2 was in this study classified as low relative weight and included the categories borderline underweight and undernutrition from the ESPEN (European Society of Parenteral and Enteral Nutrition) guidelines for Nutrition Screening [10]. BMI < 20 kg/m^2 has been proposed by several authors as the cut-off value indicating risk of malnutrition in elderly individuals [11, 12].

Medical conditions and lifestyle variables

A self-administrated questionnaire was completed by the participants and included questions across a wide range of diseases and symptoms, smoking habits, intake of alcohol, social conditions, education, financial difficulties and level of physical activity. Detailed information concerning present and past smoking habits were classified into never, previous or current smoking. Age of disease onset was, except for cancer, also self-reported. We calculated the time since diagnosis. Four groups of health-related variables were considered: (1) Specific medical conditions, (2) Self-assessed current health, (3) Social and lifestyle characteristics and (4) Functional level.

We selected nine symptomatic medical conditions prevalent in the elderly population that might have connection to either low weight or obesity [8, 13]. Most of these conditions were self-reported by answering survey questions as "Do you have or have you had….?" The considered conditions were cancer, mental distress, hip fracture, asthma or chronic bronchitis, stroke, angina pectoris or myocardial infarction and diabetes mellitus. We combined asthma and chronic bronchitis in the analysis as a high proportion responded positively for both diseases, and comparable spirometry values in both groups were found in a later evaluation of the same population [14]. Information regarding angina pectoris and previous myocardial infarction were merged into the variable ischemic heart disease (IHD). Data concerning history of cancer was obtained from the Norwegian Cancer Registry. The latter are based on mandatory registration.

The mental health was evaluated by means of an index based on seven questions concerning different dimensions of mental distress [15]. This mental distress index was partly derived from the Hopkins Symptom Check List [16] and the General Health Questionnaire (GHQ) [17]. The index has been compared with the Hospital Anxiety and Depression Scale [18] and Hopkins Symptom Check List with a reasonably good agreement also in elderly subjects. A cut-off value of 2.15 has been proposed to identify persons with significant mental distress [15].

The self-reported overall health was assessed by the question "What is your current state of health?" with the answer categories: Poor, not so good, good and very good. In the analyses, the first two categories were merged (labeled poor), as were the two last categories (labeled good).

Information on marital status was obtained from the National Population Register. Single marital status indicates in our analyses that the respondent has never been married, previously married or is a widow(er). Low educational level was defined as primary school only. Self-reported current economical situation was evaluated with four categories from very good to very difficult and the two lowest categories were categorized as difficult. This question was answered only by subjects aged 70 years and above. Alcohol consumption was low and dichotomized into drinking monthly or more frequently versus a lower consumption.

We defined the participants as having low physically activity if they reported lightly activity (not sweating or out of breath) less than 1 h a week during the past year. Handgrip strength of the non-dominant hand was registered as kilopascal (kPa) generated by manual compression of an air filled rubber bulb connected to a manometer. A measurement below the median value for each sex, respectively, was defined as low. All subjects aged 65–74 and a random sample (8% sample) of those aged 75–84 were eligible for measurement of grip strength and we have data from 74% (2,555/3,473) of these subjects.

Data analysis

In addition to simple descriptive statistics, the difference in the distribution of the BMI groups according to age group or sex (Table 2) was tested with a chi-square test, as were the relationships between the different dependent variables considered and the categories of BMI (Table 3). We calculated odds ratios for the different dichotomized chronic diseases, social and lifestyle factors according to the six different BMI categories using logistic regression (Table 4). The upper-normal category according to WHO [9], BMI 22.5–24.9 kg/m^2, was chosen as the reference category. The estimates were adjusted for sex, age (65–71, 72–78, ≥79 years old) and smoking (current, previous and never smoking). In addition, for each analysis displayed in Table 4, we included, in a separate logistic regression analysis, a cross product terms of sex and BMI to test for interactions by sex. Furthermore, when the results from the logistic regression analysis suggested a non-linear (typically U- or inverse J-shaped) relationship, we tested for a non-linear relation with BMI by including as predictors the BMI-categories (coded 1–6 as a continuous variable) both as a linear term and a second order term. Similarly, when the results from the logistic regression analysis suggested a

Table 2 Prevalence of different categories of BMI in elderly men and women, The Tromsø Study

Age range (years)		65–71	72–78	≥79	All (≥65)
	Men	$n = 950$	$n = 603$	$n = 259$	$n = 1,812$
	Women	$n = 1,127$	$n = 847$	$n = 473$	$n = 2,447$
BMI (kg/m2)					
<18.5	Men	1.2 (11)	2.7 (16)	1.9 (5)	1.8 (32)
	Women	1.5 (17)	2.0 (17)	3.0 (14)	2.0 (48)
18.5–19.9	Men	2.6 (25)	2.8 (17)	4.2 (11)	2.9 (53)
	Women	3.6 (41)	4.0 (34)	1.9 (9)	3.4 (84)
20.0–22.4	Men	12.8 (122)	11.3 (68)	15.1 (39)	12.6 (229)
	Women	11.8 (133)	11.1 (94)	15.4 (73)	12.3 (300)
22.5–24.9	Men	26.0 (247)	23.5 (142)	28.6 (74)	25.5 (463)[a]
	Women	21.9 (247)	22.2 (188)	20.9 (99)	21.8 (534)
25.0–27.4	Men	29.7 (282)	30.3 (183)	31.3 (81)	30.1 (546)[a]
	Women	21.9 (247)	20.8 (176)	21.8 (103)	21.5 (526)
27.5–29.9	Men	15.9 (151)	20.2 (122)	10.8 (28)	16.6 (301)
	Women	16.9 (191)	17.8 (151)	16.9 (80)	17.2 (422)
30.0–32.4	Men	8.9 (85)	6.3 (38)	5.8 (16)	7.7 (139)[a]
	Women	11.6 (131)	11.1 (94)	12.3 (58)	11.6 (283)
≥32.5	Men	2.8 (27)	2.8 (17)	1.9 (5)	2.7 (49)[a]
	Women	10.6 (120)	11.0 (93)	7.8 (37)	10.2 (250)

Numbers are given as % (*n*)

[a] BMI categories with a significant ($P < 0.05$) difference between men and women (Chi-square test)

Table 3 Characteristics of different BMI categories by socioeconomic and lifestyle factors and medical conditions in elderly men and women. The Tromsø Study

Variable	Total No.[a]	Cases % (*n*)	Body Mass Index (kg/m^2)						
			<20.0	20.0–22.4	22.5–24.9	25–27.4	27.5–29.9	≥30.0	P^f
Men (n = 1,812)									
Socioeconomic factors									
Single living	1,811	26.9 (487)	30.6 (26)	22.7 (52)	27.0 (125)	27.5 (150)	25.0 (75)	31.4 (59)	0.39
Lower education	1,804	56.8 (1,025)	60.0 (51)	55.6 (125)	51.5 (237)	60.2 (328)	58.5 (176)	57.4 (108)	0.12
Difficult economy[b]	960	13.5 (130)	19.0 (11)	12.1 (15)	11.9 (29)	13.6 (39)	17.3 (27)	9.8 (9)	0.39
Life style									
Smoking									
Never		14.3 (256)	7.1 (6)	11.1 (25)	17.6 (81)	15.4 (83)	11.0 (32)	15.5 (29)	
Previous	1,785	56.2 (1,004)	34.5 (29)	44.9 (101)	50.1 (230)	59.9 (322)	68.5 (200)	65.2 (122)	<0.001
Current		29.4 (525)	58.3 (49)	44.0 (99)	32.2 (148)	24.7 (133)	20.5 (60)	19.3 (36)	
Alcohol ≥ monthly	1,801	48.5 (874)	37.6 (32)	45.8 (104)	50.7 (232)	49.7 (270)	47.7 (143)	49.5 (93)	0.31
Low physical activity	1,804	28.4 (512)	37.6 (32)	28.9 (66)	24.8 (114)	25.7 (140)	34.1 (102)	31.0 (58)	0.02
Low muscle strength[c]	1,155	48.9 (565)	75.0 (36)	60.9 (84)	49.0 (143)	47.7 (158)	39.0 (83)	45.9 (61)	<0.001
Medical conditions									
Poor current health	1,811	51.1 (925)	70.6 (60)	52.8 (121)	46.4 (215)	47.4 (259)	52.7 (158)	59.6 (112)	<0.001
Mental distress	1,662	5.4 (90)	9.5 (7)	6.1 (13)	4.0 (17)	6.8 (34)	4.0 (11)	4.6 (8)	0.20
Hip fracture	1,349	3.0 (41)	8.6 (5)	1.7 (3)	3.5 (12)	3.7 (15)	1.4 (3)	2.1 (3)	0.06
Asthma/chronic bronchitis[d]	1,439	17.3 (249)	21.3 (13)	20.3 (37)	14.1 (53)	17.6 (76)	16.6 (40)	20.1 (30)	0.37
Stroke	1,800	7.2 (129)	10.7 (9)	5.7 (13)	5.9 (27)	7.9 (43)	7.7 (23)	7.6 (14)	0.52
Ischemic heart disease[e]	1,808	26.2 (474)	14.1 (12)	17.0 (39)	25.5 (118)	27.8 (151)	29.9 (90)	34.2 (64)	<0.001
Diabetes mellitus	1,801	5.6 (100)	3.5 (3)	5.7 (13)	4.8 (22)	3.7 (20)	7.7 (23)	10.2 (19)	0.01
Cancer	1,812	9.8 (178)	14.1 (12)	8.3 (19)	9.5 (44)	10.8 (59)	9.6 (29)	8.0 (15)	0.585
Women (n = 2,447)									
Socioeconomic factors									
Single living	2,443	56.6 (1,383)	64.9 (85)	62.7 (188)	54.8 (292)	55.4 (291)	53.2 (224)	56.8 (303)	0.048
Lower education	2,418	76.0 (1,838)	70.2 (92)	73.2 (218)	72.0 (378)	74.9 (387)	80.2 (336)	80.9 (427)	0.001
Difficult economy[b]	1,280	17.2 (220)	11.6 (8)	18.8 (29)	12.1 (32)	17.1 (49)	17.3 (39)	22.3 (63)	0.037
Life style									
Smoking									
Never		57.8 (1,403)	35.9 (47)	46.1 (137)	57.6 (306)	57.1 (297)	65.6 (275)	64.3 (341)	
Previous	2,428	22.1 (537)	13.0 (17)	21.5 (64)	20.3 (108)	24.2 (126)	22.7 (95)	24.0 (127)	<0.001
Current		20.1 (488)	51.1 (67)	32.3 (96)	22.0 (117)	18.7 (97)	11.7 (49)	11.7 (62)	
Alcohol ≥ monthly	2,432	20.9 (508)	24.2 (32)	25.3 (75)	24.2 (128)	21.0 (110)	17.9 (75)	16.5 (88)	0.006
Low physical activity	2,437	40.5 (987)	45.5 (60)	36.5 (109)	36.2 (192)	36.5 (191)	38.8 (163)	51.1 (272)	<0.001
Low muscle strength[c]	1,400	49.8 (697)	77.8 (56)	50.6 (80)	55.1 (166)	41.0 (126)	43.1 (109)	51.8 (160)	<0.001

Table 3 continued

Variable	Total No.[a]	Cases % (*n*)	Body Mass Index (kg/m²)						
			<20.0	20.0–22.4	22.5–24.9	25–27.4	27.5–29.9	≥30.0	*P*[f]
Medical conditions									
Poor current health	2,444	60.9 (1,488)	65.9 (87)	62.2 (186)	54.1 (289)	57.0 (300)	61.7 (259)	68.9 (367)	<0.001
Mental distress	2,113	11.1 (235)	21.1 (24)	12.8 (33)	12.0 (55)	9.8 (45)	9.2 (33)	9.7 (45)	0.008
Hip fracture	1,575	7.3 (115)	17.5 (14)	9.0 (17)	9.1 (33)	6.8 (23)	5.4 (15)	3.9 (13)	0.001
Asthma/chronic bronchitis[d]	1,670	20.5 (342)	31.5 (28)	18.4 (38)	16.2 (58)	19.0 (68)	18.2 (52)	26.3 (98)	0.001
Stroke	2,432	4.6 (111)	7.6 (10)	4.3 (13)	4.5 (24)	3.1 (16)	5.0 (21)	5.1 (27)	0.300
Ischemic heart disease[e]	2,441	19.2 (468)	16.7 (22)	15.8 (47)	14.6 (78)	20.6 (108)	23.8 (100)	21.3 (113)	0.003
Diabetes mellitus	2,436	6.7 (164)	5.3 (7)	3.7 (11)	6.0 (32)	5.9 (31)	6.2 (26)	10.7 (57)	0.002
Cancer	2,447	8.6 (211)	10.6 (14)	10.0 (30)	8.2 (44)	8.9 (47)	7.8 (33)	8.1 (43)	0.835

Data in each category of BMI are presented as percentages (numbers)

BMI body mass index

[a] Variation in number of subjects included is explained by different response rates on the self administrated questionnaire

[b] Only in participants aged 70 years and older

[c] Handgrip in a subpopulation

[d] At least one of the indicated diseases

[e] At least one of the diseases myocardial infarction and angina pectoris

[f] *P*-value for differences between groups using the chi-square test

Table 4 Adjusted[a] odds ratios (95% confidence interval) for associations between socioeconomic factors, lifestyle, various medical conditions and BMI in elderly men and women. The Tromsø Study

Variable	Body mass index (kg/m^2)						P^e
	<20.0	20.0–22.4	22.5–24.9[b]	25.0–27.4	27.5–29.9	≥30.0	
Socioeconomic factors							
Single living	1.23 (0.89–1.69)	1.04 (0.83–1.32)	1.00	1.04 (0.86–1.26)	0.97 (0.79–1.20)	1.20 (0.98–1.48)	0.37
Lower education	1.00 (0.72–1.37)	1.12 (0.89–1.41)	1.00	1.35 (1.12–1.63)	1.48 (1.20–1.84)	1.59 (1.28–1.99)	<0.001
Difficult economy	1.21 (0.69–2.12)	1.34 (0.87–2.03)	1.00	1.32 (0.93–1.88)	1.54 (1.05–2.25)	1.68 (1.15–2.45)	0.13
Life style							
Current smoking	3.62 (2.65–4.95)	1.72 (1.36–2.17)	1.00	0.73 (0.59–0.90)	0.49 (0.38–0.63)	0.46 (0.35–0.60)	<0.001
Alcohol ≥ monthly	0.72 (0.51–1.02)	0.86 (0.68–1.10)	1.00	0.88 (0.72–1.07)	0.80 (0.64–1.0)	0.72 (0.57–0.91)	0.066
Low physical activity	1.42 (1.04–1.95)	1.04 (0.82–1.32)	1.00	1.05 (0.87–1.28)	1.34 (1.08–1.65)	1.89 (1.53–2.32)	<0.001
Low muscle strength	2.82 (1.78–4.48)	1.12 (0.84–1.49)	1.00	0.73 (0.58–0.92)	0.63 (0.49–0.81)	0.92 (0.72–1.19)	<0.001
Medical conditions							
Poor current health	1.90 (1.38–2.61)	1.32 (1,06–1.64)	1.00	1.09 (0.91–1.29)	1.36 (1.12–1.65)	1.88 (1.54–2.30)	<0.001
Mental distress	1.75 (1.10–2.81)	1.12 (0.75–1.66)	1.00	1.04 (0.74–1.46)	0.85 (0.57–1.27)	0.96 (0.66–1.41)	0.14
Hip fracture	2.04 (1.13–3.69)	0.86 (0.49–1.49)	1.00	0.84 (0.53–1.32)	0.52 (0.29–0.92)	0.44 (0.25–0.80)	<0.001
Asthma/chronic bronchitis[c]	1.79 (1.17–2.73)	1.25 (0.90–1.73)	1.00	1.24 (0.95–1.64)	1.14 (0.83–1.55)	1.80 (1.35–2.40)	0.01
Stroke	1.65 (0.93–2.92)	0.95 (0.58–1.55)	1.00	1.07 (0.73–1.58)	1.21 (0.79–1.85)	1.30 (0.85–2.01)	0.43
Ischemic heart disease[d]	0.75 (0.50–1.13)	0.79 (0.59–1.05)	1.00	1.25 (1.01–1.55)	1.44 (1.14–1.82)	1.46 (1.15–1.85)	<0.001
Diabetes mellitus	0.80 (0.39–1.66)	0.86 (0.52–1.41)	1.00	0.85 (0.57–1.27)	1.18 (0.79–1.78)	1.98 (1.37–2.87)	<0.001
Cancer	1.49 (0.93–2.39)	1.08 (0.75–1.57)	1.00	1.09 (0.81–1.47)	0.94 (0.67–1.32)	0.91 (0.64–1.29)	0.46

BMI body mass index

[a] Adjusted for sex, age and smoking status (current, former and never smoking)

[b] Subjects with 22.5–24.9 kg/m^2 constitute the reference category

[c] At least one of the indicated diseases

[d] At least one of the diseases myocardial infarction and angina pectoris

[e] *P*-value for overall testing of BMI for each variable

linear relationship, we tested for a linear relation with BMI. A two-sided *P*-value <0.05 was considered statistically significant.

Analyses were performed using SPSS statistical software version 15.0 (SPSS Inc, Chicago Illinois. USA).

Results

Prevalence of different BMI categories

The overall proportion with BMI < 20 kg/m^2 (low weight) was 5.1%, BMI 20.0–24.9 kg/m^2 (normal weight) 35.8%, BMI 25.0–29.9 kg/m^2 (overweight) 42.1% and BMI $\geq$ 30.0 kg/m^2 (obesity) 16.9% (Table 2). The distribution of the BMI groups differed significantly between the sexes ($P < 0.001$). Obesity was more common in women than in men (21.8% vs. 10.4%), whereas a comparable proportion of women and men had BMI below 20 kg/m^2, 5.4 and 4.7%, respectively. In women, no significant age difference was seen between BMI categories, whereas in men, indications of an inverse linear relationship between age and BMI was observed ($P = 0.016$).

Lifestyle, socio-economic status and medical conditions

Characteristics of the participants according to BMI category and sex are shown in Table 3. Compared to men, women tended to live alone, have lower education and consume alcohol less frequently. Current and previous smoking was much more prevalent in men than in women.

About 60% of the women and 50% of the men considered their overall current state of health to be poor or not so good. Approximately one in five subjects reported asthma, chronic bronchitis or IHD. The prevalences of mental distress, diabetes mellitus and history of hip fracture, stroke or cancer were between three and eleven percent (Table 3). The median time since the first diagnosis of stroke, hip fracture and cancer was four, 6 and 7 years, respectively.

Current smoking, mental distress and hip fracture were in both sexes more prevalent in the lower BMI categories. Asthma or chronic bronchitis and a poor current health were more frequent both in the lower and higher BMI categories. The higher BMI categories were associated with diabetes mellitus and IHD.

Associations between BMI categories, lifestyle and disease prevalence

Table 4 shows the adjusted associations between BMI and the prevalence of some chronic diseases, social and lifestyle factors. The results for the medical conditions are

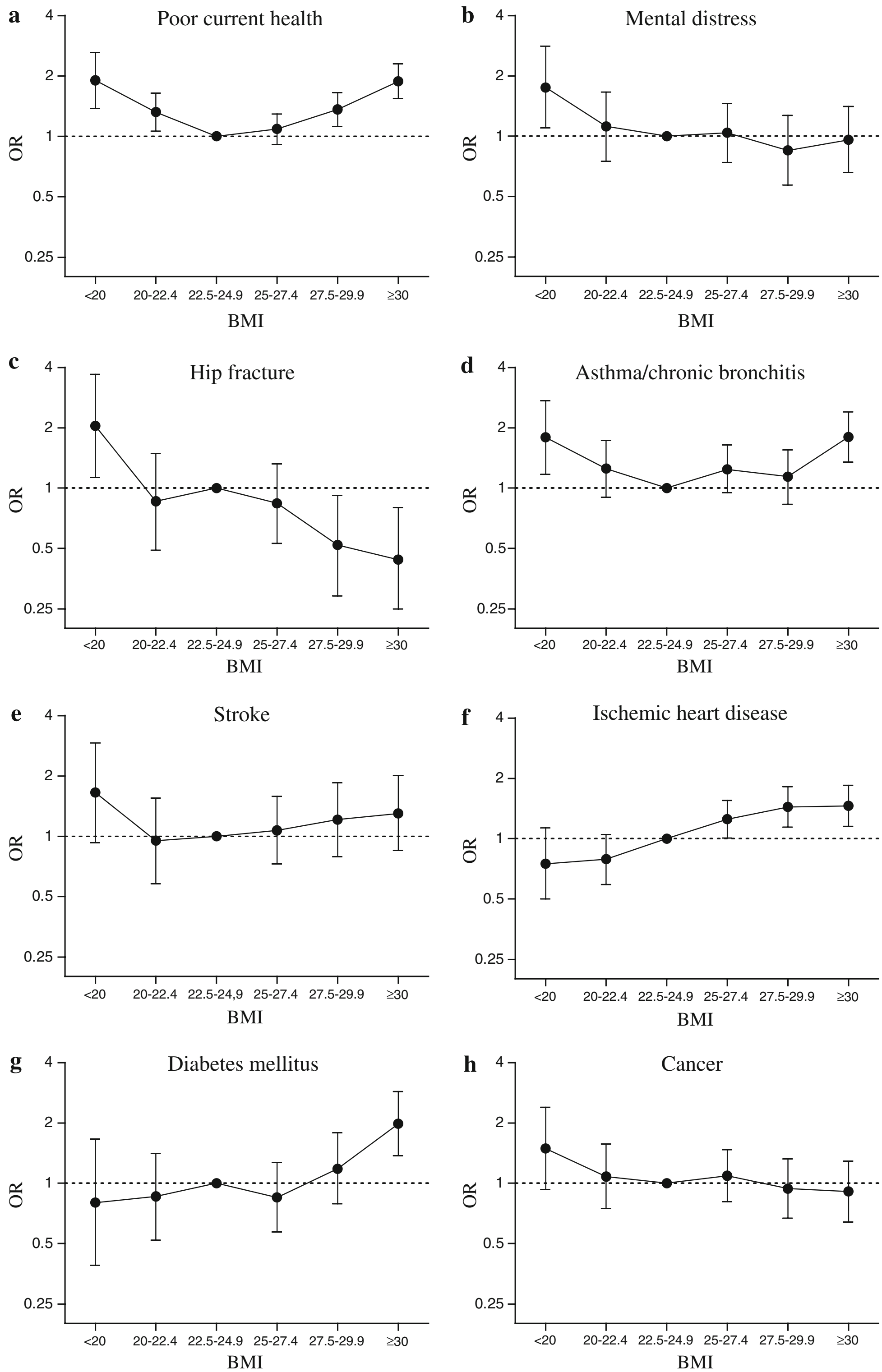

Fig. 1 Adjusted odds ratios for associations between various medical conditions and BMI in elderly men and women (**a**–**h**). Subjects with 22.5–24.9 kg/m^2 constitute the reference category. *Error bars* indicate 95% confidence interval. Adjusted for sex, age and smoking (current, former and never smoking). The Tromsø study

displayed graphically in Fig. 1 as well. The test for interaction by sex was for all variables non-significant (P-values between 0.07 and 0.89) except for hand-grip strength ($P = 0.016$). However, stratified analyses revealed the same overall pattern also for this variable for men and women, and we therefore report the values for men and women combined in Table 4.

Low socioeconomic status was associated with the higher BMI categories. Low physical activity was more common both in the low weight and obese subjects, whereas reduced muscle strength was related to low weight. Current smoking was strongly inversely related to BMI. In Table 4 we give the results for current versus previous and never smokers combined as the results for never and previous smokers were similar.

Diabetes mellitus and IHD were associated only with the higher BMI categories; diabetes mellitus with obesity and IHD both with overweight and obesity. Asthma or chronic bronchitis and a poor current state of health showed a U-shaped relation to BMI (P-value for a second order term <0.05). The prevalence of mental distress and previous hip fracture were both inversely associated with BMI (P-value for linear trend 0.05 and <0.001, respectively). Figure 1e and h, may be suggest that both history of stroke and cancer were related to BMI < 20 kg/m^2, although these associations did not reach statistical significance.

Discussion

The present study points out characteristics of the lower and higher categories of BMI in elderly men and women. The results demonstrate that low weight is associated with fractures, mental distress, and low muscle strength. U-shaped relationships with BMI were found for asthma or chronic bronchitis, low physical activity and a general poor current health. The higher weight categories were associated with IHD and diabetes. Low socioeconomic status was associated with a high BMI. To the best of our knowledge there is no other recent population-based study focusing on all BMI categories assessing a similar wide range of conditions in elderly persons.

The prevalence of low weight (BMI < 20 kg/m^2) was about five percent. This is in accordance with findings from other community based studies [19, 20]. Both overweight and obesity were in this population less frequent than reported in studies of elderly individuals in the U.S. [21] but at the same level as found in a study with data from several European countries [4].

It could be assumed that low socioeconomic status reflected by difficult economy and low education and, should affect food habits adversely and predispose to a lower BMI. A study of elderly admitted patients found education below 12 years to be a risk factor for malnutrition [22]. In the present study, however, neither low education level nor difficult economic situation were related to low BMI. As earlier described in middle aged populations [23], a lower educational level was associated with obesity.

We observed a strong negative impact of current tobacco smoking on BMI. This has also previously been reported [24], and may be explained by increased basal metabolic rate [25] and impairment of smell and taste [26] in smokers.

Alcohol intake was very moderate in this population. Studies of hospital populations with more heavy drinkers have demonstrated a negative impact of alcohol use on nutritional status [27, 28].

Low physical activity, one aspect of physical function, was in this study associated with both low weight and obesity. A similar U-shaped relation between BMI and functional impairment was found in another study of community-dwelling elderly persons using a wider range of assessment techniques [29]. We also found low handgrip strength to be strongly associated with BMI < 20 kg/m^2. Grip strength, important for daily life activities, is a predictor of disability [30] in addition to an indirect measure of lean body mass [31]. Low muscle mass in underweight individuals may explain both a reduced handgrip and a lower level of physical activity. Obesity has also in studies by other authors found to be associated with an impaired functional level [32]. Several mechanisms may explain these findings, including obesity related reduction in flexibility of movement and increased wear and tear on joints [33]. Furthermore, both underweight and obesity may be associated with diseases and conditions which in turn increase the risk of functional impairment [32].

Self assessed current state of health represent an overall subjective perception corresponding well with physicians' assessments and other objective health measures [34]. Compared to the reference group, we found a higher frequency of self-assessed poor health in both the higher and lower categories of BMI including the lower normal category of 20–22.4 kg/m^2. A similar U-shaped relationship was found when a corresponding question was used in a study evaluating obesity among adults in several European countries [4].

We found indications of increased mental distress among participants with BMI below 20 kg/m^2. The symptoms of anxiety and depression are often overlapping, especially in the more minor forms [35] and the index of mental distress used in this study included both set of symptoms. Our findings correspond with results from a study of hospitalized elderly patients evaluating depressive symptoms only [36]. However, a study of non-institutionalized adult and elderly persons found an association of both mood, anxiety and personality disorders to overweight and obesity, but not to underweight [37]. We did not find any association between symptoms of anxiety or depression and the higher categories of BMI.

Hip fracture represents an acute incident often resulting in persistent functional decline [38]. In this study, the median time since the last hip fracture was 6 years and still there was an inverse relation between hip fracture and BMI. This is consistent with other studies [39, 40]. Underweight is a risk factor for osteoporosis [41], which in turn increases the risk of a fall resulting in fracture. One previous study found, even after adjustment for bone mineral density, that underweight was associated with fracture risk [42]. Insufficient protective padding over the hips in underweight individuals is one important mechanism [43].

We found a U-shaped association between chronic bronchitis or asthma and BMI and this relationship was retained when each variable was evaluated separately. These two conditions cover a high proportion of patients with chronic obstructive pulmonary disease (COPD) and there is considerable overlap between the subtypes of COPD [44]. Other community-based studies predominantly in adult and not elderly populations have confirmed an association of COPD to malnutrition and partly to obesity [6, 45].

Pulmonary cachexia, commonly identified by a low BMI, is an aspect of COPD characterized by both loss of muscle mass with or without loss of fat mass [46]. This muscle wasting is not completely understood, but may involve an increase in peripheral muscular vulnerability to oxidative stress [46]. The explanations of underweight in COPD patients further include insufficient nutritional intake because large meals can induce shortness of breath [6]. Additionally, both activity-induced and daily energy expenditure have been found to be increased in many of these patients [47]. There may be several explanations for the observed association between obesity and COPD, including a direct affect on airway calibre through chest wall restriction [6]. A more sedentary lifestyle in obese people may affect breathing pattern and pulmonary function adversely [6].

Diabetes mellitus and IHD were related to obesity, an association well documented in the literature [2, 4] and mainly mediated by an increase in insulin resistance [48]. Earlier studies comparing both adult and elderly populations have found the relative risk associated with overweight for diabetes mellitus [49] and IHD [49, 50] to decline with age. In our study, the risk associated with overweight was even more limited. We found IHD to be the only disease with significantly increased prevalence in the upper overweight category (BMI 27.5–29.9 kg/m^2). More research is needed to define the upper limit of healthy weight in elderly individuals. However, as six out of ten subjects are overweight or obese, affected cases in the upper BMI categories constitute a high number.

Previous studies have shown malnutrition in acute stroke patients to increase the risk of both in-hospital mortality and a poor clinical outcome [51, 52]. In cancer patients, weight loss is often an indication of poor survival [53]. Consequently, survivor bias can explain the lack of significant association found between cancer, stroke and the lower BMI category in this study (Fig 1e, h). As the median time since the first cancer diagnosis was 7 years, the majority of these subjects were long-term survivors.

Our study has several strengths. All elderly men and women in the municipality were invited, the participation rate was high and a wide range of conditions was assessed. BMI values were based on measured rather than self-reported weight and height. Furthermore, including also the lower end of the BMI spectrum, gives important information about underweight individuals.

The use of BMI in an elderly population may be a source of error as body composition is not measured accurately. The relative fat mass is increasing in later life and at a given BMI value, an older person will have a higher proportion of the body as adipose tissue than a younger adult. Nevertheless, BMI is easy to use also in a clinical setting, has a reasonable good correlation with body fat [54], it is reproducible and it is the core measure in several nutrition risk screening instruments [10]. Additionally, most of the variables included in our study are self-reported. This implies a risk of misclassification, but this must be expected to be non-differential in most situations.

The cross-sectional design of this study restricts the possibility of cause-effect conclusions. For some of the variables the expected direction may be from disease or lifestyle variable to BMI category. This is likely for mental distress and smoking. For other medical conditions such as diabetes mellitus and IHD, a high BMI may increase the risk of disease. In some situations, both mechanisms may be of importance, thus creating a vicious circle. It has been shown that hip fracture patients who are malnourished at admission also lose weight during the course of the disease [55].

Conclusions

Our results demonstrate that both low and high BMI are associated with a wide range of prevalent conditions and diseases in elderly men and women. For the clinician this emphasizes the importance of nutritional assessment as part of the medical evaluation of elderly patients. Using BMI alone, a cut off of 20 kg/m^2 identifies a subpopulation at risk in the lower part of the BMI spectrum. At the present time most attention is given to the link between the higher BMI categories and diseases, but our findings suggest that moderate overweight constitutes a relatively small health hazard in this age group.

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Risk of malnutrition is associated with mental health symptoms in community living elderly men and women: The Tromsø Study

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Abstract

Background: Little research has been done on the relationship between malnutrition and mental health in community living elderly individuals. In the present study, we aimed to assess the associations between mental health (particularly anxiety and depression) and both the risk of malnutrition and body mass index (BMI, kg/m^2) in a large sample of elderly men and women from Tromsø, Norway.

Methods: In a cross-sectional survey, with 1558 men and 1553 women aged 65 to 87 years, the risk of malnutrition was assessed by the Malnutrition Universal Screening Tool ('MUST'), and mental health was measured by the Symptoms Check List 10 (SCL-10). BMI was categorised into six groups (< 20.0, 20.0-22.4, 22.5-24.9, 25.0-27.4, 27.5-29.9, ≥ 30.0 kg/m^2).

Results: The risk of malnutrition (combining medium and high risk) was found in 5.6% of the men and 8.6% of the women. Significant mental health symptoms were reported by 3.9% of the men and 9.1% of the women. In a model adjusted for age, marital status, smoking and education, significant mental health symptoms (SCL-10 score ≥ 1.85) were positively associated with the risk of malnutrition (odds ratio 3.9 [95% CI 1.7-8.6] in men and 2.5 [95% CI 1.3-4.9] in women), the association was positive also for subthreshold mental health symptoms. For individuals with BMI < 20.0 the adjusted odds ratio for significant mental health symptoms was 2.0 [95% CI 1.0-4.0].

Conclusions: Impaired mental health was strongly associated with the risk of malnutrition in community living elderly men and women and this association was also significant for subthreshold mental health symptoms.

Background

Mental health problems are among the most prevalent conditions in elderly people. Anxiety and depression, often seen as co-morbid conditions with overlapping symptoms [1], are the two most frequent mental health disorders [2]. Malnutrition is also relatively common in elderly individuals and may be associated with mental health, particularly depression [3].

While several studies have found mental disorders to be a risk factor for involuntary weight loss/malnutrition in geriatric inpatients and outpatients [4], little population-based research has been done on the relationship between risk of malnutrition and mental health in this age group. A study from Sweden found depressive symptoms to predict malnutrition in community living elderly [5], whereas a German study of nursing home residents found no significant difference in the mean malnutrition score between residents with and without depression [6]. Furthermore, studies of the relationship between body mass index (BMI) and depressive symptoms in elderly individuals have yielded conflicting results. In a study from the US, depression in men was found to be inversely associated with body weight [7]. A later study of a multiethnic elderly population found an increased risk of depression with increasing BMI, but the most adverse impact of obesity on depression was found in African Americans [8]. Neither of these studies examined the lower BMI categories in more detail.

In the current study, we therefore aimed to investigate the associations between mental health and both the risk of malnutrition and BMI in a large sample of

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community-living elderly men and women. We hypothesised that there is a positive relationship between impaired mental health and risk of malnutrition and low BMI.

Methods

Study population

Between October 2007 and December 2008, adult inhabitants of the community of Tromsø were invited to participate in a health survey known as the Tromsø Study. In the current analysis, we included data from participants aged 65 to 87 years. All 6098 men and women in this age group were invited, and 4017 (65.9%) completed the survey. Height or weight was not measured in 21 persons and information about weight loss that was required for the determination of malnutrition was missing in 413 persons; in addition, 472 persons omitted data related to smoking, education or mental health symptoms. Therefore, 1558 men and 1553 women (51.0% of the invited individuals) were included in the analysis. The mean age of the participants included in the study sample was lower than that of the non-attending persons, and the mean age was also lower than that of the participants not included in the study sample because of missing values. The BMI of the included participants was not significantly different from that of the non-included participants.

Each participant provided written informed consent, and the survey was approved by the Regional Board of Research Ethics.

Measures

Nutritional screening tool and body mass index

The participants had their weight (kg) and height (cm) measured to the nearest decimal. During these measurements, they were in light clothing and did not wear shoes. BMI was calculated as the weight divided by the square of height (kg/m^2). In a self-administrated questionnaire, the participants were asked for any involuntary weight loss during the last six months (and if so, weight loss in kg). Weight loss was grouped as follows: below 5%, between 5% and 10% or above 10% of their pre-weight-loss body weight.

Based on the BMI and the extent of weight loss, each subject was categorised into low, medium or high risk of malnutrition according to the Malnutrition Universal Screening Tool ('MUST') (Figure 1). The 'MUST' tool is the nutritional screening instrument recommended by the European Society for Clinical Nutrition and Metabolism (ESPEN) for use in the community [9]. Two other nutritional screening tools have been recommended by the ESPEN, the Nutrition Risk Screening 2002 (NRS 2002) and the Mini Nutritional Assessment (MNA). NRS 2002 is mainly intended for use in hospitals. The MNA is constructed to be used by heath care professionals and not for self-administration. Consequently, the MNA is difficult to use in larger epidemiological studies.

The 'MUST' tool was originally developed by the British Society of Parenteral and Enteral Nutrition http://www.bapen.org.uk. It includes an acute disease

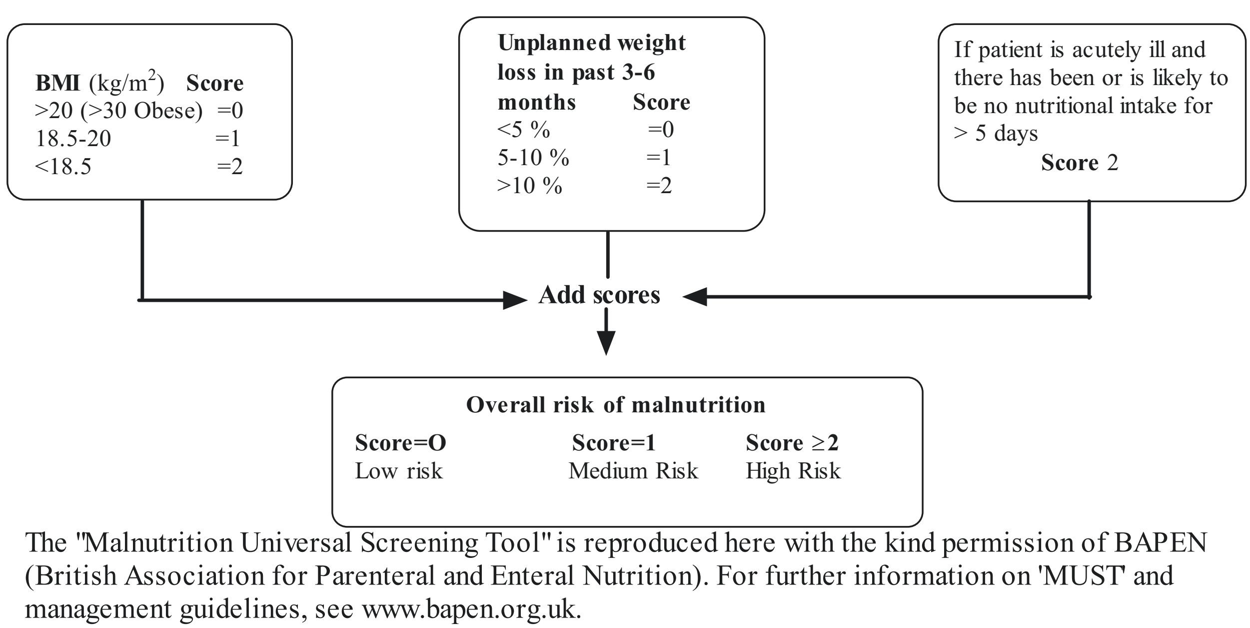

Figure 1 The malnutrition universal screening tool ('MUST') is composed of a BMI score, a weight-loss score and an acute illness component. The risk of malnutrition can be assessed based on the sum of these scores.

Table 1 Baseline characteristics of participating elderly men and women, The Tromsø Study (2007-2008)

	Men (*n* = 1558)	Women (*n* = 1553)	*p*-value
Age in years, Mean (SD)	71.2 (5.3)	72.0 (5.6)	< 0.001[a]
Currently married, % (n)	75.6 (1178)	51.4 (798)	< 0.001[b]
Lower education, % (n)	33.2 (517)	52.9 (822)	< 0.001[b]
Smoking, % (n)			
Never smoked	24.4 (380)	47.8 (743)	< 0.001[b]
Previous smokers	60.6 (944)	38.2 (593)	
Current smokers	15.0 (234)	14.0 (217)	
Alcohol[d] more than once a month, % (n)	57.1 (878)	39.6 (605)	< 0.005[b]
BMI (kg/m^2) Mean (SD)	27.0 (3.6)	27.0 (4.5)	0.69[a]
Risk of malnutrition, % (n)			
Low	94.3 (1470)	91.4 (1419)	0.005[b]
Medium	3.5 (55)	5.5 (85)	
High	2.1 (33)	3.2 (49)	
SCL-10 score Median (interquartile range)	1.10 (1.00-1.30)	1.20 (1.07-1.44)	< 0.001[c]
SCL-10 score ≥ 1.85, % (n)	3.9 (61)	9.1 (142)	< 0.001[b]

[a]t-test, [b]chi-square test, [c]Mann-Whitney U test, [d] *n* is 1538 men and 1526 women (alcohol).

component with no nutritional intake for > 5 days, which normally necessitates hospitalisation [10]. Because participation in this study required the ability to independently visit a research centre, the acute diseases component was set to zero. The weight loss question was slightly modified to state a time span of the "last 6 months", but this encompasses the time span of "the past 3-6 months", as stated in the original 'MUST' tool. In Tables 1 and 2, all three risk categories of malnutrition are described, whereas the medium and high risk categories are combined in the analyses in Figure 2.

BMI was divided into six categories in order to include the World Health Organization definitions of overweight (25.0-29.9 kg/m^2) and obesity (≥ 30 kg/m^2) [11] in addition to the underweight category (< 20 kg/m^2) [9]. We further subdivided the categories between 20 kg/m^2 and 30 kg/m^2 to describe in more detail the lower-normal weight (20.0-22.4 kg/m^2, 22.5-24.9 kg/m^2) and overweight individuals (25.0-27.4 kg/m^2, 27.5-29.9 kg/m^2).

Assessment of mental health symptoms

Mental health status was assessed by the Hopkins Symptoms Check List-10 (SCL-10), which has been widely used in epidemiological studies. The SCL-10 is a self-administrated instrument that mainly explores symptoms of anxiety and depression [12]. The ten items of the SCL-10 were part of the questionnaire that was included in the invitation to the survey. The questionnaire was completed by participants at home and handed in at the study centre.

The SCL-10 questions explored the presence and severity of the following ten symptoms during the preceding week: (1) "Sudden fear without apparent reason", (2) "Afraid or worried", (3) "Faintness or dizziness", (4) "Tense or upset", (5) "Easily blaming yourself ", (6) "Sleeplessness", (7) "Depressed or sad", (8) "Feeling worthless", (9) "Feeling that everything is a struggle", and (10) "Feeling hopelessness with regard to the future".

Each question was rated on a four-point scale ranging from 1 (not at all) to 4 (extremely). Missing values were replaced by the sample mean value for each item, but questionnaires with three or more missing values were excluded from the analyses. The average SCL-10 score was calculated according to Strand et al [12] by dividing the total score by the total number of items (score ranging between 1.0 and 4.0). A higher score value indicated more symptoms. We found an acceptable degree of internal consistency for the scale in this sample (Cronbach's alpha 0.84).

Table 2 The SCL-10 score[a] according to risk categories of malnutrition in elderly men and women, The Tromsø Study (2007-2008)

	Men (*n* = 1558)			Women (*n* = 1553)		
Risk of malnutrition	n	**SCL-10 score**	*p*-value[b]	n	**SCL-10 score**	*p*-value[b]
Low	1470	1.10 (1.0-1.30)		1419	1.20 (1.05-1.40)	
Medium	55	1.13 (1.10-1.40)	< 0.001	85	1.30 (1.10-1.65)	< 0.001
High	33	1.36 (1.05-1.56)		49	1.40 (1.13-1.70)	

[a]Median (IQ range), [b]Kruskal Wallis test.

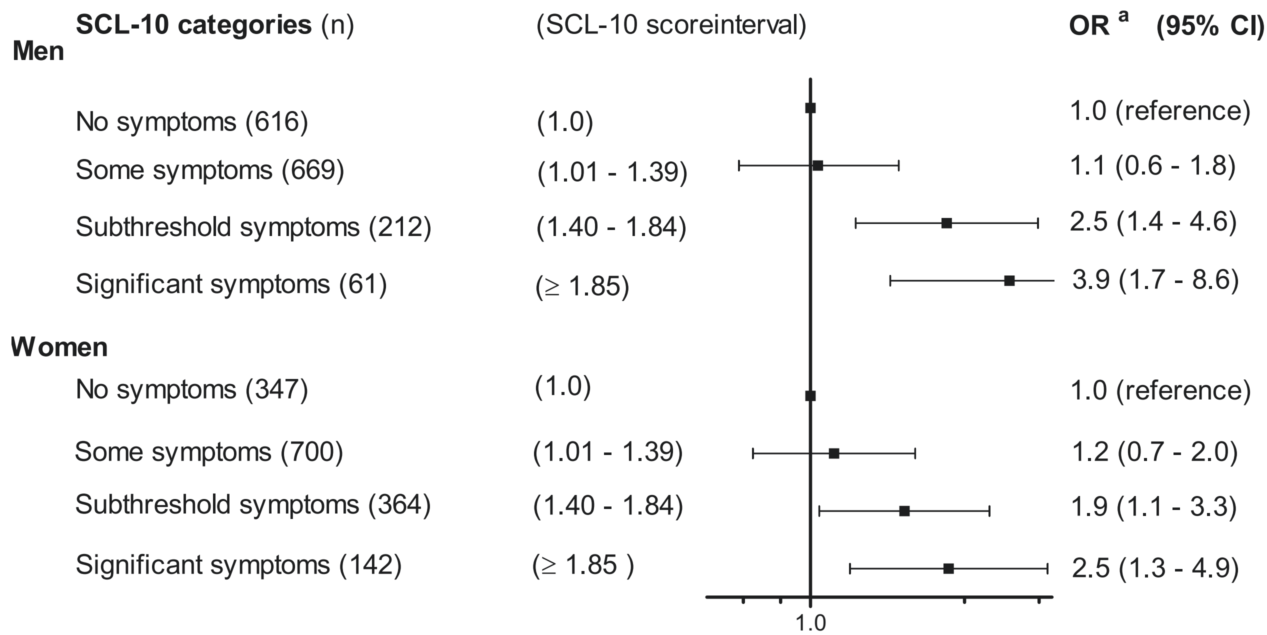

Figure 2 Odds ratio for the association between mental health problems (in four categories) and the risk of malnutrition (combining medium and high risk) in 1558 elderly men and 1553 elderly women, The Tromsø Study. [a]Adjusted for age, smoking, marital status and educational level.

The SCL-10 is an abbreviated version of the 25-item Hopkins Symptoms Checklist (SCL-25) [13], which has been validated in different age categories, including elderly individuals [14]. The SCL-25 was designed to predict both anxiety and depression but was found to predict depression better than anxiety disorders in a population-based study [15]. The shorter SCL-10 version correlated highly with the SCL-25 version (r = 0.97) in a population-based Norwegian study that also included elderly individuals [12]. Depending on the cut-off limits used, the literature indicates that 50-60% of cases detected with these instruments are individuals who actually qualify for a diagnosis of mental disorders based on clinical interviews [12].

An SCL-10 score of 1.85 has been proposed as the cut-off for predicting diagnosed mental disorders [12], and score values of ≥ 1.85 in the current study were referred to as *significant symptoms*. To assess the impact of score values below this cut-off, we subdivided the SCL-10 scores between 1.01 and 1.84 into a lower score category (SCL-10 score 1.01 to 1.39) referred to as *some symptoms* and a higher score category (SCL-10 score 1.40 to 1.84) referred to as *subthreshold symptoms*. The individuals with no symptoms (SCL-10 score 1.0) constituted the reference category (Figure 2).

Other variables

Information regarding age and marital status was obtained from Statistics, Norway. Details regarding educational background, household income, smoking habits and other disease variables were obtained from self-administrated questionnaires. Household income was dichotomised into above and below Norwegian Kroner 300 000. Lower education was defined as primary school only. Alcohol use was relatively infrequent and was dichotomised into drinking more than once a month versus a lower consumption. Smoking habits were divided into three categories (never, previous or current smoking).

Data analysis

The SCL-10 score was analysed as both a dichotomised variable and a continuous variable. The score was positively skewed and we therefore reported the median SCL-10 values with 25 - 75% interquartile (IQ) range in Tables 1 and 2. The Mann Whitney U or Kruskal Wallis test was used to test the differences in SCL-10 score between the groups. Differences in baseline variables between men and women were analysed using the Chi-square test and t-test (Table 1). The associations between the SCL-10 categories and the risk of malnutrition were analysed using logistic regression (Figure 2). The SCL-10 category with no symptoms (1.0) was used as reference. The odds ratio (OR) estimates were adjusted for potential confounders (age, marital status, smoking and educational level). The analysis of the relationship between the risk of malnutrition and the SCL-10 score was stratified by gender. The Chi-square test and logistic regression (table 3) were used to analyse the

Table 3 The proportion of subjects with SCL-10 score ≥ 1.85 and odds ratio (95% confidence interval) for the association between SCL-10 score ≥ 1.85 and BMI in elderly men and women[b], The Tromsø study (2007-2008)

BMI categories	SCL-10 score ≥ 1.85 % (proportions)	OR (95% CI) for SCL-10 score ≥ 1.85	
		Adjusted for age and sex	Multivariable adjusted[a]
< 20.0	15.2 (12/79)	2.3 (1.1-4.5)	2.0 (1.0-4.0)
20.0-22.4	5.2 (16/308)	0.8 (0.4-1.4)	0.8 (0.4-1.4)
22.5-24.9	6.7 (42/631)	1.1 (0.7-1.8)	1.1 (0.7-1.7)
25.0-27.4	5.6 (45/803)	1.0 Reference	1.0 Reference
27.5-29.9	6.5 (42/646)	1.1 (0.7-1.8)	1.1 (0.7-1.7)
≥ 30.0	7.1 (46/644)	1.2 (0.8-1.8)	1.2 (0.8-1.9)

[a] Adjusted for sex, age, educational level, marital status and smoking status, [b]n = 3111.

relationship between the six BMI categories and the proportion of the participants with an SCL-10 score ≥ 1.85. In the regression analysis, the BMI category with the highest number of participants was used as reference. Data from men and women were pooled in this analysis due to the low expected numbers in some BMI groups in sex-stratified analyses.

Two sided p-values < 0.05 were considered statistically significant. The analyses were performed using SPSS statistical software version 17.0 (SPSS inc., Chicago, Illinois, USA).

Results

Baseline characteristics of the 1558 men and 1553 women included in the analyses are shown in Table 1. The mean age was 71.2 years in men and 72.0 years in women. Compared to men, women were more likely to be single and have a lower level of education, and a smaller proportion had a history of smoking. Mean BMI was 27.0 kg/m^2 in both genders. Risk of malnutrition (combining medium and high risk) was found in 7.1% (222/3112) of the participants, which included 5.6% (88/1558) of men and 8.6% (134/1553) of women. The SCL-10 score was higher in women (median 1.20) than in men (median 1.10) (p < 0.001) and was higher in persons aged ≥ 75 years old than in persons aged 65 to 74 years old, which indicates more symptoms of anxiety and depression in women and in the oldest participants. Significant mental health problems (SCL-10 score ≥ 1.85) were found in 3.9% (61/1558) of men and 9.1% (142/1553) of women.

Mental health and the risk of malnutrition

The SCL-10 score was significantly associated with an increased risk of malnutrition in both men and women (Table 2). The results suggest a relatively stronger relationship between the risk of malnutrition and the median SCL-10 score in men than in women.

In men who were at risk of malnutrition (combining medium and high risk), 11.4% (10/88) had significant SCL-10 symptoms; the corresponding percentage in women was 16.4% (22/134). In Figure 2, the strength of the associations between the SCL-10 score categories and the risk of malnutrition is further explored using a logistic regression analysis. In both men and women, significant SCL-10 symptoms were strongly associated with the risk of malnutrition; the odds ratio was 3.9 (95% CI 1.7-8.6) in men and 2.5 (95% CI 1.3-4.9) in women. Also, for the subthreshold symptoms (SCL-10 score 1.40 to 1.84), a statistically significant association with the risk of malnutrition was found. A test for linear trends across the SCL-10 score categories was statistically significant for both genders (p < 0.001 in men and p = 0.01 in women). However, the difference between the genders with regard to the strength of the relationship (Figure 2) was not statistically significant (p = 0.4). The odds ratio estimates were adjusted for age, marital status, smoking habits and educational level. Individuals reporting no SCL-10 symptoms (score 1) constituted the reference category.

In three separate sets of analyses, we also adjusted for the impact of alcohol use (more or less frequent than once a month), chronic somatic diseases (history of cancer, heart attack or stroke) or household economy. However, none of these three variables had a significant impact on the relationship between the SCL-10 score and the risk of malnutrition (data not shown).

Mental health and BMI

We also assessed the relationship between various BMI categories and the proportion of individuals (men and women) with significant SCL-10 symptoms (SCL-10 score ≥ 1.85). The highest proportion with significant SCL-10 symptoms (15.2%, 12/79) was found in participants with BMI < 20.0 kg/m^2 (Table 3). In obese participants (BMI ≥ 30.0 kg/m^2) the corresponding proportion was not significantly increased. A chi-square test for the model was statistically significant (p = 0.03).

The strength of the associations between the BMI categories and a SCL-10 score ≥ 1.85 is further explored using a logistic regression analysis (Table 3). The multivariable adjusted odds ratio estimate for the lowest BMI category (< 20.0 kg/m^2) was 2.0 (95% CI 1.0-4.0) compared to the reference category of BMI 25-27.4 kg/m^2.

Discussion

In this study, we found that mental health symptoms were strongly associated with the risk of malnutrition in elderly individuals. Both the risk of malnutrition and mental health symptoms were more prevalent in women than in men. To our knowledge, this is the largest population-based study that explored the relationship between the risk of malnutrition and mental health in elderly individuals.

Some previous studies in this area have utilised the Geriatric Depression Scale (GDS) and the Mini Nutritional Assessment (MNA) instrument for the assessment of the relationship between depression and malnutrition. A Swedish study of 579 community-living elderly people found that depressive symptoms were predictive of malnutrition [5]; this was observed to a larger extent in men than in women. The relationship between depression and malnutrition in nursing home residents was investigated in a German study, and no differences was found in the mean MNA score between subjects who had depression and those who did not. However, a modest association was demonstrated between malnutrition and depression in a regression analysis [6]. A study of 267 community-living elderly in Brazil [16] showed a positive relationship between malnutrition and depression.

We believe the 'MUST' tool used in the current study has an advantage over the MNA with regards to the associations explored. The MNA has been validated in a number of studies of elderly individuals, but it includes information about both neuropsychological problems and psychological stress [17]. A positive correlation between the MNA risk score and the symptoms of depression could therefore be anticipated. The 'MUST' tool does not include any component that explores mental health. This is the first study to use either the 'MUST' tool or the SCL-10 the assessment of the relationship between risk of malnutrition and mental health.

Increased risk of malnutrition (combining medium and high risk) was found in 7.1% of the individuals in the current sample. In previous studies of community-living elderly individuals, prevalence rates for the risk of malnutrition varied from 2.5% to 21% [18-21]. This variation in prevalence may reflect the use of different criteria both to define malnutrition and differences in sample selections.

In accordance with former studies on adult and elderly individuals, we found that women had more mental health symptoms than men [22]. This gender difference is not fully understood but may to some extent be explained by an underreporting of depressive symptoms by male individuals [23].

Mental health may be assessed by both a categorical approach, which considers diagnoses that are based on a distinct cut-off, and a dimensional approach, which considers symptoms along a continuum. The latter approach also takes into account subthreshold symptoms of anxiety and depression, which may also adversely affect daily life [24,25]. The present study revealed statistically significant associations using both a categorical and a more dimensional approach.

Somatic diseases, especially stroke, myocardial infarction and cancer, represent risk factors for depressive symptoms in elderly individuals [26]. Somatic diseases may also increase the risk of malnutrition [21]. However, adjusting for the history of these three important somatic diseases did not affect the conclusions of the current study.

Individuals with BMI < 20.0 kg/m^2 had a two to three times higher prevalence of significant mental health symptoms (table 3) and the corresponding adjusted OR was 2.0 and of borderline significance ($p = 0.06$) (table 3). Obesity (BMI >30.0) was not associated with more mental health symptoms. Previous studies have reported both a decreased [7] and an increased risk [8] of depression in obese elderly individuals. However, the lower BMI categories were not specifically examined in these two studies.

The Tromsø study included participants from both urban and rural areas although the majority live in the city centre. Our results may not be generalised to all other elderly populations as both living conditions and health care organisation differ between countries. However, we believe that it is likely that similar relationships are present in other similar community living elderly Western populations.

As discussed above, this study has several strengths as well as some potential limitations. First, the SCL-10 captures symptoms of both anxiety and depression, although depression is more influential in the relationship with nutritional status. However, considerable overlap exists between anxiety and depression, which often appear as co-morbid disorders [1,27].

Second, eating disorders were not assessed in this study. In a recent review of eating disorders in the elderly, depression was described as the most important co morbid condition. However, the prevalence of eating disorders is low in the elderly population [28].

Third, the study sample that exhibited valid values for the SCL-10-score and the 'MUST' score represented 52% of the target population. Thus, selection bias may be a concern. However, it is likely that the elderly men and women who did not complete the survey or omitted key information were frailer, more cognitive impaired and more prone to both malnutrition and impaired mental health than the persons who were included in the study sample.

Fourth, by using 1.85 as the cut-off for the SCL-10 score yielded significant mental health problems of 4.2% in men and 9.8% in women, which may be an underestimation. In elderly people, the prevalence of major depression is 1 to 4%, the prevalence of minor depression is 4 to 13% [26] and the prevalence of anxiety is 3.2% to 14.2% [29]. The cut-off of 1.85 for the SCL-10 score was adopted from previous studies that describe the SCL-10 [12] and has not been compared to clinical diagnostic interviews in community-living elderly men or women. However, the main purpose of the current study was not to describe the prevalence of mental health problems but to determine the relationship between impaired mental health and nutritional status.

Fifth, there was no screening of cognitive decline in this study. Mild cognitive impairment can be present a long time before dementia is identified and this might be associated with malnutrition and symptoms of anxiety and depression. However, participants had to both independently visit a research centre and accomplish a detailed self administrated questionnaire. This reduces the risk of cognitive impairment among participants included in the study population.

The current study also demonstrated a significant association between subthreshold mental health symptoms and the risk of malnutrition. Several reports have described other adverse health effects that are related to subthreshold mental health symptoms in elderly individuals [30,31]. The cut-off for the SCL-10 used in the current study identified 13.6% of men and 22.4% of women with subthreshold symptoms. This corresponds well with the 20.2% of older women identified with subthreshold depression in a recent study that used the Center for Epidemiological Studies Scale for Depression (CES-D) [32].

The cross-sectional design hampers conclusions about the directionality of the associations. The most important is probably the influence of depression on appetite and food intake. This can lead to weight loss and increase the risk of malnutrition. In the Diagnostic and Statistical Manual of Mental Disorders [33], both weight gain and weight loss are among the diagnostic criteria for depression. In contrast, malnutrition may also be associated with micronutrient deficiencies that adversely affect mental health. Inadequate intake of nutrients and energy may lead to deficiency of folic acid, thiamine or cobalamin [34] which might worsen mental health symptoms. A recent study that evaluated the impact of weight change alone in elderly people found that weight loss predicted an increase in depressive symptoms [35]. Hence, a bidirectional relationship between the risk of malnutrition and mental health symptoms may be present and result in a vicious circle over time in affected individuals.

Conclusions

Impaired mental health was strongly associated with the risk of malnutrition in community living elderly men and women and this association was also significant for subthreshold mental health symptoms. For the clinical practitioner, our results on the one hand highlight the need for nutritional screening of elderly people presenting with mental health symptoms. Both in somatic and psychiatric settings, nutrition have often been neglected [3,36]. Screening for malnutrition can easily be performed by the use of instruments like the 'MUST' tool. On the other hand, mental health symptoms should also be included in the assessment of elderly people who are at risk of malnutrition.

Conflict of interests

The authors declare that they have no conflicts of interests.

Abbreviations

BMI: Body Mass Index; IQ: interquartile; MUST: Malnutrition Universal Screening Tool; OR: odds ratio; SCL-10: Symptoms Check List 10.

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Authors' contributions

JMK, JF, OG and BKJ were responsible for the initial design of the study. JMK did the analyses and wrote the first draft of the paper. BKJ contributed to the analyses, interpretation of the results and the review of the drafts. All authors contributed to the interpretation of the data and review of the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Risk of malnutrition and health-related quality of life in community-living elderly men and women: The Tromsø study

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Abstract
Purpose To explore the association between risk of malnutrition as well as current body mass index (BMI) and health-related quality of life (HRQoL) in elderly men and women from the general population.
Methods In a cross-sectional population survey including 1,632 men and 1,654 women aged 65 to 87 years from the municipality of Tromsø, Norway, we assessed HRQoL by using the EuroQol (EQ-5D) instrument in three risk groups of malnutrition and in different categories of BMI. The Malnutrition Universal Screening Tool ('MUST') was used to evaluate the risk of malnutrition.
Results We found a significant reduction in HRQoL with an increasing risk of malnutrition, and this was more pronounced in men than in women. The relationship between BMI and HRQoL was dome shaped, with the highest score values in the BMI category being 25–27.5 kg/m^2.
Conclusions HRQoL was significantly reduced in elderly men and women at risk of malnutrition. The highest HRQoL was seen in moderately overweight individuals.

Keywords HRQoL · EQ-5D · Body mass index · Elderly · Malnutrition universal screening tool · Nutrition assessment

Abbreviations

HRQoL	Health-related quality of life
BMI	Body mass index
MUST	Malnutrition universal screening tool
EQ-5D	EuroQol-5D
EQ-5D index	Value attached to an EQ-5D state according to a particular set of weights
EQ VAS	Standard vertical visual analogue scale
CI	Confidence interval
SD	Standard deviation

Introduction

Malnutrition and being underweight are persisting problems also in the affluent parts of the world and is more prevalent in the elderly than in other adult individuals [1]. In developed countries, malnutrition is largely related to diseases [2]. Throughout the previous decades, health-related quality of life (HRQoL) has received increased attention as a measure for comparing health statuses across different patient groups and for measuring health outcomes. While recent studies reveal strong evidence of increased morbidity [2, 3] and mortality [4, 5] in underweight elderly people, little attention has been given to the ways in which malnutrition affect HRQoL. Not only is the quantity of life, calculated in years, important for the increasing number of elderly individuals with longer life expectancies, but the quality of life is important as well.

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The concept of HRQoL broadens a previous definition of health based on morbidity and mortality to include aspects such as subjective assessment of physical, emotional and social functioning [6]. Nutrition may affect both physical and psychological aspects important for HRQoL [2]. Several reports have found HRQoL to be reduced in obese individuals [7]. In a study of nursing home patients [8] and a smaller community-based study [9], quality of life was reduced in the elderly at risk of malnutrition. However, larger community-based studies evaluating HRQoL in the elderly at risk of malnutrition are lacking.

The purpose of the present study was to explore the association between risk of malnutrition, categories of body mass index and HRQoL in community-living elderly men and women using the EuroQol (EQ-5D) instrument [10].

Methods

Population for the study

The Tromsø Study is a health survey of the population of Tromsø, a medium-sized town in Norway. The 6th cross-sectional survey was conducted between October 2007 and December 2008. All independently living inhabitants aged 65 to 87 years (6,098) were invited, of which 4,017 (66%) participated by going to a study center for data collection. After exclusions (21 persons because height or weight had not been measured due to various disabilities, 412 persons because of missing weight loss information and additionally 298 persons due to lack of response to the EQ-5D health state descriptive system), 3,286 subjects (i.e., 54% of the eligible subjects) were included in the analyses of the EQ-5D-index. The second part of the EQ-5D exercise (the EQ VAS scale) had 1,306 respondents.

The regional board of research ethics approved the survey, and each participant gave written informed consent prior to inclusion in the study.

Nutritional screening tool and body mass index

At the study center, the participants, who were instructed to wear no shoes and light clothing, had their weight (kg) and height (cm) measured to the nearest decimal using a Jenix DS-102 stadiometer (Dong Sahn Jenix Co., Ltd., Seoul, Korea). Body mass index (BMI) was calculated as weight divided by the square of height (kg/m^2). The participants were asked in a self-administrated questionnaire whether they had any involuntary weight loss during the last 6 months. If they had, they were asked how many kilograms (kg) had been lost. Weight loss was grouped as follows: below 5%, between 5 and 10% or above 10% of body weight prior to weight loss.

Based on the BMI and degree of weight loss, each subject was categorized into low, medium or high risk of malnutrition according to the malnutrition universal screening tool ('MUST') (Fig. 1). The 'MUST' tool is one of the nutritional screening instruments recommended by the European Society for Parenteral and Enteral nutrition [11], and it was originally developed by the British Society of Parenteral and Enteral nutrition (www.bapen.org.uk) [12]. It includes an acute disease component with no nutritional intake for >5 days, which normally necessitates hospitalization [12]. As participation in this study required the ability to independently visit a research center, the acute diseases component was set to zero. The weight loss question was slightly modified to state a time span of the "last 6 months", but this encompasses the time span of "the past 3–6 months" in the original 'MUST' tool.

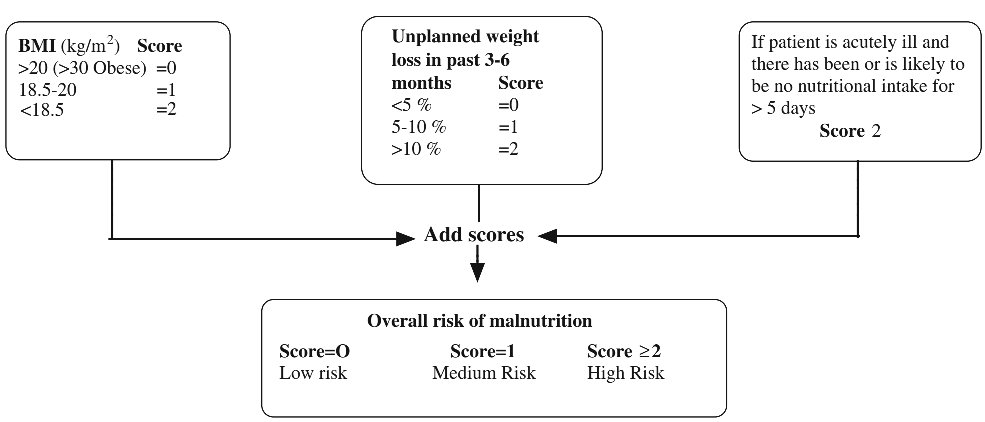

Fig. 1 The malnutrition universal screening tool ('MUST') is composed of a BMI score, a weight loss score and an acute illness component. These are added, and based on the sum score, the risk of malnutrition can be assessed. The "Malnutrition Universal Screening Tool" is reproduced here with the kind permission of BAPEN (British Association for Parenteral and Enteral Nutrition). For further information on 'MUST' and management guidelines, see www.bapen.org.uk

Based on BMI alone, we further categorized the participants into six categories (<20.0, 20.0–22.4, 22.5–24.9, 25.0–27.4, 27.5–29.9 and ≥30 kg/m^2), thereby including the WHO (World Health Organization) definitions of overweight (25.0–29.9 kg/m^2) and obesity (≥30 kg/m^2) [13].

Assessment of HRQoL

HRQoL was measured by the EQ-5D, which is a standardized non-disease specific instrument consisting of two parts: the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS) [10]. The EQ-5D has been utilized in a number of studies, and the instrument is validated in acutely ill, elderly individuals [14] and community-living elderly women receiving medication (clodronate) for osteoporosis [15], but not in large populations of community-living elderly men and women. In a systematic literature review of self-assessed health instruments [16], the EQ-5D was one of the recommended generic health instruments for use in older people.

EQ-5D describes health in generic terms using five specific dimensions, which are important for elderly individuals: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is divided into three levels of severity (no problems, some problems or extreme problems). Due to only a few participants reporting problems at the most severe level (extreme problems), this category was included with the individuals reporting some problems (second level) in the analyses of the various EQ-5D dimensions (Table 2). The EQ-5D instrument is designed for self-completion and was included as part of a self-administrated questionnaire. A single summary EQ-5D index with a maximum score of 1 is obtained by applying a scoring algorithm that assigns weights to each of the possible combinations of health, as described by the three levels within each of the five dimensions. In the current study, we applied the most widely used scoring algorithm, referred to as the UK time-trade-off tariff [17]. Subjects missing values from any of the five dimensions were excluded from the analyses.

In addition to this indirect health index assigned through a descriptive system, a direct method was used asking subjects to rate their health on a visual analogue scale (VAS) with a maximum score of 100. The endpoints were labeled as “worst imaginable health state” and “best imaginable health state.”

The number responding to the EQ VAS scale question (669 men and 637 women) was lower than the number responding to the EQ-5D health state descriptive system. When comparing responders to non-responders on the EQ VAS scale, both groups had a mean EQ-5D health index of 0.82. In the responders, the mean BMI and age were somewhat lower (0.4 kg/m^2 and 0.5 years, respectively). Although minor, these differences were statistically significant (BMI $P = 0.02$ and age $P = 0.005$).

Other variables

Information on socio-demographics and smoking status (Table 1) was also obtained from self-administrated questionnaires.

Data analyses

We stratified the analyses when dealing with risk categories of malnutrition and HRQoL by gender (Tables 2, 3; Figs. 2,

Table 1 Characteristics of the participating elderly men and women, The Tromsø study

	Men	Women	*P*-value[b]
N[a]	1,654	1,632	
Age, years. Mean (SD)	71.4 (5.4)	72.1 (5.6)	<0.001[c]
Single living (%)	24.6	48.2	<0.001[d]
Post-secondary school education (%)	30.0	18.4	<0.001[d]
Household income ≥300,000 NOK[e] (%)	58.4	40.3	<0.001[d]
Smoking (%)			
Never	24.1	47.1	<0.001[d]
Previous	60.3	38.0	
Current	15.6	14.9	
BMI kg/m^2. Mean (SD)	27.0 (3.6)	26.9 (4.6)	0.58[c]
Risk of malnutrition (%)			
Low	94.4	90.6	<0.001[d]
Medium	3.4	6.0	
High	2.1	3.4	
EQ-5D index—mean (95% CI)	0.86 (0.85–0.87)	0.79 (0.78–0.80)	<0.001[c]
EQ VAS score[f]—mean (95% CI)	75.4 (74.3–76.6)	73.0 (71.6–74.4)	0.008[c]

[a] There are minor differences in the number of evaluated subjects due to variations in missing values on the self-administrated questionnaire (concerning education, income and smoking)

[b] *P*-values for the difference between men and women were estimated using the two-sample *t*-test[c], chi-square test[d]

[e] NOK 8 = € 1

[f] 637 women and 669 men reported the EQ VAS score

Table 2 Proportions[a] of the 3,286 elderly men and women reporting problems in the various EQ-5D dimensions, The Tromsø study

EQ-5D dimensions	Sex	All subjects	Subjects by risk of malnutrition			
			Low	Medium	High	*P*-value[b]
Any dimensions	Men	52.9 (864)	52.2 (804)	53.6 (30)	85.7 (30)	<0.001
	Women	69.7 (1,153)	69.0 (1,034)	74.7 (74)	78.9 (45)	0.51
Mobility	Men	14.6 (238)	13.7 (211)	19.6 (11)	45.7 (16)	<0.001
	Women	22.4 (370)	21.9 (328)	29.3 (29)	22.8 (13)	0.31
Self-care	Men	3.3 (54)	2.7 (42)	7.1 (4)	22.9 (8)	<0.001
	Women	4.7 (77)	4.5 (67)	5.1 (5)	8.8 (5)	0.1
Usual activities	Men	12.6 (205)	11.6 (178)	21.4 (12)	42.9 (15)	<0.001
	Women	23.2 (383)	21.8 (326)	35.4 (35)	38.6 (22)	<0.001
Pain/discomfort	Men	45.7 (746)	45.1 (695)	45.4 (26)	71.4 (25)	0.007
	Women	63.9 (1,057)	63.4 (950)	70.7 (70)	64.9 (37)	0.34
Anxiety/depression	Men	12.3 (201)	11.9 (183)	16.1 (9)	25.7 (9)	0.01
	Women	23.3 (385)	22.0 (329)	37.4 (37)	33.3 (19)	0.001

[a] Proportions are given as % (number) reporting problems

[b] *P*-value for linear trend across increasing risk categories of malnutrition

Table 3 Adjusted[a] odds ratios (95% confidence interval) for associations between various EQ-5D dimensions and risk category of malnutrition in 3,286 elderly men and women, The Tromsø study

EQ-5D dimension		Risk category of malnutrition			
		Low	Medium	High	*P*-value[b]
Mobility	Men	1.00	1.43 (0.72–2.84)	4.91 (2.46–9.81)	<0.001
	Women	1.00	1.32 (0.83–2.10)	0.77 (0.40–1.48)	0.95
Self-care	Men	1.00	2.52 (0.86–7.34)	9.56 (4.05–22.57)	<0.001
	Women	1.00	0.98 (0.38–2.52)	1.26 (0.47–3.38)	0.71
Usual activities	Men	1.00	1.94 (0.99–3.78)	5.29 (2.62–10.65)	<0.001
	Women	1.00	1.78 (1.14–2.77)	1.72 (0.97–3.05)	0.005
Pain/discomfort	Men	1.00	1.00 (0.58–1.73)	2.80 (1.37–5.72)	0.011
	Women	1.00	1.35 (0.86–2.11)	1.00 (0.57–1.74)	0.50
Anxiety/depression	Men	1.00	1.43 (0.69–2.96)	2.58 (1.19–5.61)	0.012
	Women	1.00	2.03 (1.32–3.11)	1.59 (0.90–2.81)	0.003

[a] Adjusted for age

[b] *P*-value for linear trend across increasing risk categories of malnutrition

3). However, for the relation between BMI and HRQoL, tests for interaction between BMI and sex were found to be non-significant both for the EQ-5D index ($P = 0.57$) and the EQ VAS score ($P = 0.37$). The combined results for men and women are presented (Figs. 4, 5). Analysis of covariance was used to obtain age-adjusted mean values with corresponding 95% confidence intervals for different risk categories of malnutrition and categories of BMI (Figs. 2, 3, 4, 5). Differences between groups were evaluated by the chi-square test or *t*-test when appropriate (Tables 1, 2). Binary logistic regression with adjustment for age was used to estimate the association between the risk category of malnutrition and the various EQ-5D dimensions (Table 3). The association between increasing risk of malnutrition and the EQ-5D- or EQ VAS score was assessed by linear regression in a multivariate model adjusting for age. We tested for a quadratic relation between BMI categories and HRQoL by also including the BMI categories squared in a multivariate linear regression model (Figs. 4, 5).

The importance of the differences in HRQoL scores between risk groups of malnutrition may be examined by calculating their effect size as the mean difference divided by the standard deviation (SD) of the control group [18]. We evaluated the detected differences against the criteria introduced by Cohen [19] using the SD of the low-risk category of malnutrition. Effect size values of 0.2–<0.5, 0.5–<0.8 and ≥0.8 were characterized as small, medium and large differences, respectively.

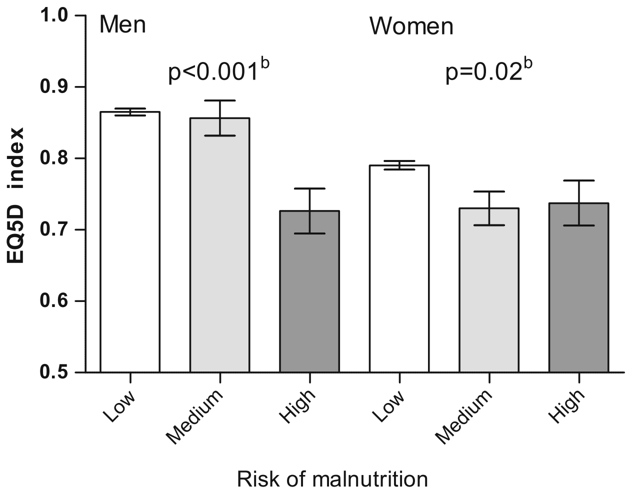

Fig. 2 Mean[a] EQ-5D index by risk of malnutrition in elderly men and women, The Tromsø Study. [a]Adjusted for age. [b]*P*-values for linear trend across the categories. *Vertical lines* indicate 95% CI

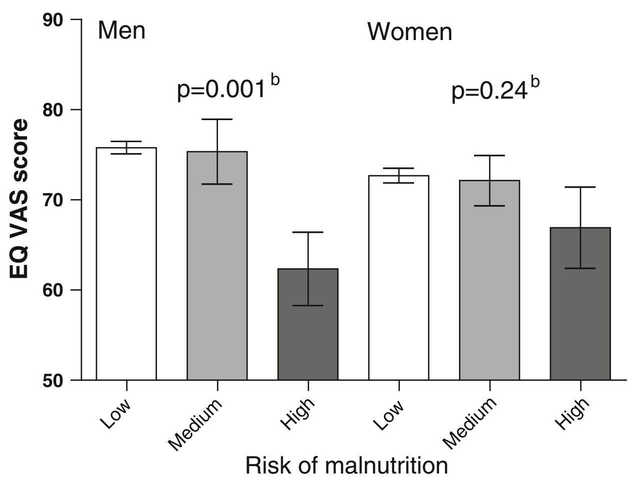

Fig. 3 Mean EQ VAS scores[a] by risk of malnutrition in elderly men and women, The Tromsø Study. [a]Adjusted for age. [b]*P*-values for linear trend across the categories. *Vertical lines* indicate 95% CI

Two-sided *P*-values < 0.05 were considered to be statistically significant. The analyses were performed using SPSS statistical software version 17.0 (SPSS Inc., Chicago, Illinois, USA).

Results

The mean age (SD) was 71.7 (5.5) years, and there was approximately the same number of men (1,632) as women (1,654) included in the analyses (Table 1). Women tended to live alone, have lower education and have lower household income. More women (9.6%) than men (5.6%) were at risk of malnutrition (medium- and high-risk combined). HRQoL was lower in women than in men when

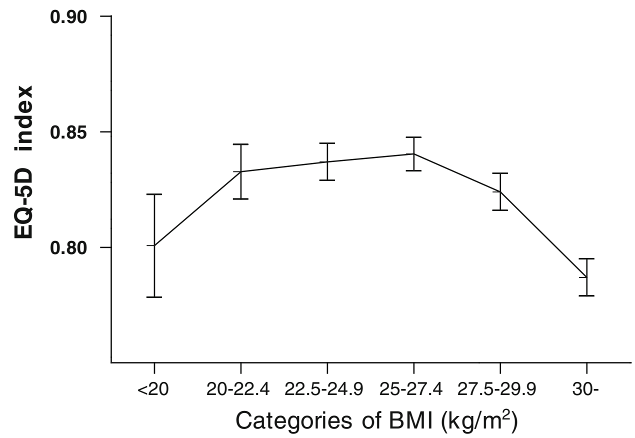

Fig. 4 Mean EQ-5D index[a] by different categories of BMI in elderly men and women, The Tromsø study. [a]Adjusted for age and sex. *Vertical lines* indicate 95% CI

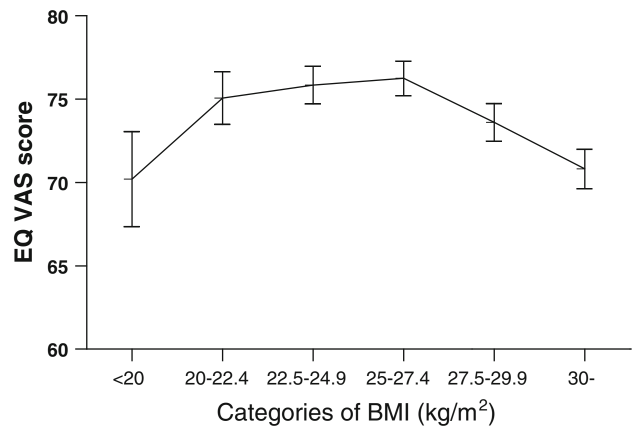

Fig. 5 Mean EQ VAS scores[a] by different categories of BMI in elderly men and women, The Tromsø study. [a]Adjusted for age and sex. *Vertical lines* indicate 95% CI

assessed by the EQ-5D index and the EQ VAS score. For both men and women, the median and mean values of the EQ-5D index were almost identical, whereas the median EQ VAS score was somewhat higher than the mean in both men and women (numbers not shown).

Health dimensions

Table 2 shows the proportions of the participants reporting problems in any of the various EQ-5D dimensions of health. Overall, the majority of both women (70%) and men (53%) reported problems related to at least one of the health dimensions. One in four women reported difficulties in the dimensions of mobility, usual activities and anxiety/depression. The corresponding proportions for men were somewhat lower (12–15%). Pain and discomfort were reported by more than half of the women and by a somewhat lower proportion of the men.

With increasing risk of malnutrition, problems in all five health dimensions were reported more frequently (Table 2). However, the differences between the low- and high-risk categories were substantially larger in men than in women. A test for linear trend across increasing risk categories of malnutrition was statistically significant for two of the dimensions in women and for all five dimensions in men.

The strength of the associations between various risk categories of malnutrition and the different EQ-5D dimensions as outcome variables is further described in Table 3. In men, statistically significant associations were found for all of the five dimensions. For men in the high-risk category of malnutrition, the strongest association was found for self-care (odds ratio (OR) = 9.6). The corresponding OR estimates were 4.9 for mobility and 5.3 for usual activities. In women, the associations were strongest for two dimensions: usual activities (OR = 1.7) and anxiety/depression (OR = 2.0 for the medium-risk category).

Risk of malnutrition and HRQoL

The impact of increasing risk of malnutrition on the EQ-5D summary indices is shown in Fig. 2. The age-adjusted associations between increasing risk of malnutrition and the EQ-5D were significant for both men and women (P-value for men <0.001 and for women 0.02).

For the EQ VAS score (Fig. 3), a similar relationship was significant in men ($P = 0.001$), but not in women ($P = 0.24$).

When comparing the differences in mean score between the low- and high-risk categories of malnutrition, we found that the effect size for the EQ-5D score for men was 0.85 (large) and for women it was 0.26 (small). Corresponding values for the VAS scale were 0.97 (large) for men and 0.31 (small) for women. When comparing the low- and medium-risk categories of malnutrition, we found the effect size for the difference in EQ-5D score in women to be 0.30 (small), and the other estimated effect sizes were minor.

BMI and HRQoL

We found a dome-shaped relationship between BMI categories and both the EQ-5D index and the EQ VAS score, with the highest HRQoL in the BMI category of 25.0–27.5 kg/m^2 (Figs. 4, 5). The P-values for a quadratic term of the BMI categories were <0.01 for both the EQ-5D index and the EQ-5D VAS score (adjusted for age and gender). Separate analyses for men and women revealed the same overall dome-shaped pattern.

Discussion

HRQoL is of increasing interest in epidemiology and health outcomes research. In this population-based study of elderly men and women, we found HRQoL to be significantly reduced in individuals at increased risk of malnutrition. All dimensions in the EQ-5D descriptive system were affected in men, while only two dimensions (usual activities and anxiety/depression) were affected in women. A dome-shaped relationship was seen between BMI and both the EQ-5D index and EQ VAS score.

Risk of malnutrition and HRQoL

To our knowledge, there are no similar, previous large-scale studies of the association between risk of malnutrition and HRQoL in elderly populations utilizing validated instruments. Due to the many different criteria and instruments in use for assessing both HRQoL and nutritional status, it is difficult to compare relevant studies. There are, however, reports from a smaller community-based study [9] and from more selected elderly populations [20–22] that have indicated that an association exists between the risk for malnutrition and reduced HRQoL. One study of hospitalized elderly individuals reports no clear association between malnutrition and HRQoL [23].

There are several possible explanations for the observed associations. Malnutrition and weight loss are important factors in the development of sarcopenia with loss of lean body mass and muscle function [24]. This may in turn be of special importance to EQ5D dimensions like self-care and usual activities, both significantly associated with the risk of malnutrition in the present study. Furthermore, malnutrition may affect the mental health of elderly individuals adversely, thereby reducing HRQoL [25]. Malnutrition may also be associated with diseases and conditions, which in turn decrease HRQoL.

BMI and HRQoL

The relation between BMI and HRQoL has been investigated in previous studies of elderly men and women, finding impaired HRQoL in both obese and underweight individuals [26–28], with the highest HRQoL in individuals of the BMI category 20–24.9 kg/m^2. In the present study, we used narrower BMI categories. The differences in the HRQoL scores between the middle BMI categories were small; however, for the low-weight and obese individuals, we found a reduced HRQoL compared with the summit group consisting of the moderately overweight participants (BMI 25–27.5 kg/m^2). In this respect, our results for HRQoL are in line with studies of mortality, indicating that moderately overweight, elderly men and women have the lowest mortality [29].

HRQoL in obese individuals may be impaired by associated comorbid conditions, especially pain [30]. Possible explanations for the reduced HRQoL among subjects with low BMI will largely correspond to the aspects discussed regarding individuals at increased risk of malnutrition.

The 'MUST' score of malnutrition is recommended for use in a community setting [11] and has acceptable test qualities in hospital populations when compared to more comprehensive instruments [31]. The EQ-5D is a standardized instrument developed to provide a non-disease specific measure of health status and is also suitable for use in studies of population health [10, 32]. The SF-36 questionnaire for HRQoL assessment is more comprehensive and has a larger evidence base [33]. However, in the extensive review of generic, self-assessed health instruments for use in older people by Haywood et al. [16], the EQ-5D was also found to have good reliability, validity and responsiveness. It has been found to have substantial agreement with the SF-36 [15].

One potential limitation of this study is the number of non-attending individuals and participants with missing values. All participants had to visit a research center, and consequently both individuals living in institutions and with physical limitations are underrepresented. Thus, the non-attending individuals were probably frailer, and it is unlikely that the observed associations were weaker in this group than in the participants. The cross-sectional design also limits conclusions about causality, although the most plausible direction originates with risk of malnutrition and moves towards HRQoL.

Gender differences

Women in the present study generally had a lower HRQoL than men, a finding reported in several studies of HRQoL in elderly individuals [34, 35]. This may be caused by a higher prevalence of disability and chronic conditions in women [36]. Other potential explanations for the observed sex difference include a lower socio-economic status, a greater tendency to report health problems or higher expectations of health and function in women when compared to men.

In the male participants, however, the impact of malnutrition on HRQoL was stronger than in women. Gender-specific analyses have not been performed in the previous studies addressing malnutrition and HRQoL. Research on body composition in older people has shown that during weight loss, men loose more lean mass than fat mass, whereas women loose more fat mass than lean mass [37]. It is possible that a relatively higher reduction in lean body mass can partly explain the stronger impact of malnutrition on HRQoL in men than in women.

Are the detected differences important? By using the Cohen criteria for effect sizes, the differences detected between the high- and low-risk categories in men can be regarded as large for both the EQ-5D index and the EQ VAS score. For women, the corresponding differences were low. Effect size estimates are based on the distribution of the data but have often been found to yield values that agree roughly with those estimated from more individually oriented methods [18].

Conclusion

HRQoL was significantly reduced in elderly people at increased risk of malnutrition, and this was more pronounced in men than in women. The highest HRQoL scores were found in moderately overweight individuals.

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Body mass index and mortality in elderly men and women: the Tromsø and HUNT studies

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ABSTRACT

Background The impact of body mass index (BMI; kg/m^2) and waist circumference (WC) on mortality in elderly individuals is controversial and previous research has largely focused on obesity.

Methods With special attention to the lower BMI categories, associations between BMI and both total and cause-specific mortality were explored in 7604 men and 9107 women aged ≥65 years who participated in the Tromsø Study (1994–1995) or the North-Trøndelag Health Study (1995–1997). A Cox proportional hazards model adjusted for age, marital status, education and smoking was used to estimate HRs for mortality in different BMI categories using the BMI range of 25–27.5 as a reference. The impact of each 2.5 kg/m^2 difference in BMI on mortality in individuals with BMI<25.0 and BMI≥25.0 was also explored. Furthermore, the relations between WC and mortality were assessed.

Results We identified 7474 deaths during a mean follow-up of 9.3 years. The lowest mortality was found in the BMI range 25–29.9 and 25–32.4 in men and women, respectively. Mortality was increased in all BMI categories below 25 and was moderately increased in obese individuals. U-shaped relationships were also found between WC and total mortality. About 40% of the excess mortality in the lower BMI range in men was explained by mortality from respiratory diseases.

Conclusions BMI below 25 in elderly men and women was associated with increased mortality. A modest increase in mortality was found with increasing BMI among obese men and women. Overweight individuals (BMI 25–29.9) had the lowest mortality.

INTRODUCTION

The impact of body mass index (BMI; weight (kg)/height (m^2)) and waist circumference (WC) on mortality in the growing elderly population is still controversial. There is concern about the potential increase in mortality related to excess weight,[1] whereas mortality in underweight individuals has received less attention.

As reviewed by Heiat *et al*,[2] Zamboni *et al*,[3] and Janssen and Mark,[4] the recommendations of ideal weight for adults[5] seem to be too restrictive for elderly individuals and being moderately overweight appears to entail limited risk. Previous studies on body weight and mortality in elderly individuals have often focused on obesity and mainly assessed total mortality. Cause-specific mortality beyond cardiovascular diseases (CVDs) has rarely been addressed. Several reports have found increased mortality in underweight individuals, but this association in elderly people has not been fully explained. Thus, there is a need for additional studies with special attention to the lower weight categories.

We explored the associations between BMI, WC and mortality in elderly men and women based on two large population-based Norwegian studies.

METHODS

Study population

The fourth Tromsø Study was carried out in 1994–1995 and the second North-Trøndelag Health Study (HUNT) in 1995–1997. Tromsø is a medium-sized town in northern Norway and North-Trøndelag is a mostly rural county located in central Norway. All inhabitants in the eligible age group were invited to the studies. A total of 19 515 men and women (15 250 from North-Trøndelag and 4265 from Tromsø) aged 65 years and older participated and the overall participation rate was 70.0%. We excluded participants with a follow-up time under 1 year (425 participants) and those missing information about cause-specific mortality (5 participants) or questionnaire data concerning smoking, marital status or level of education (2374 participants). Thus, the final follow-up cohort included 16711 participants. Both surveys have been previously described in detail[6 7] and they used the same core variables and questions.

The regional boards of research ethics approved the surveys and each participating subject provided written informed consent.

BMI, WC and other characteristics

Height and weight were measured with participants wearing light clothes and no shoes. BMI was calculated as weight (kg) divided by height (m) squared. WC was measured horizontally to the nearest centimetre at the height of the umbilicus using a steel tape. Information about educational level, smoking habits, alcohol intake, physical activity and chronic diseases was obtained from self-reported questionnaires. Lower education was defined as primary school only. Alcohol intake was categorised into three levels (<once a month, 1–3 times/month and ≥4 times/month) and physical activity into three levels (low, medium and high). Heart disease and lung disease were defined as myocardial infarction or angina pectoris and asthma or chronic bronchitis, respectively. Data on cancer were obtained from the Norwegian Cancer Registry and data on marital status were obtained from the Population Register of Norway.

In the mortality analysis, we first divided the participants into nine categories based on BMI values (<18.5, 18.5–19.9, 20.0–22.4, 22.5–24.9, 25.0–27.4, 27.5–29.9, 30.0–32.4, 32.5–34.9 and ≥35); thereby including the standard definitions of overweight (BMI 25.0–29.9) and obesity (BMI≥30) (WHO, 2000).[5] In the analyses of cause-specific mortality, we merged all BMI categories below 20 and above 30 due to the limited number of deaths for some of the disease categories. The BMI category with the most participants and the most deaths (25.0–27.4) was chosen as the reference. WC was available for all the HUNT participants and for all Tromsø participants aged 65–74 years as well as for a random sample of participants aged 75–84 years. To compare the impacts of WC and BMI on mortality, we followed a procedure similar to that described by Flegal *et al*[8] and created WC categories that identified similar proportions of participants as each of the nine BMI categories. The cut-off for each WC category was set to the closest shift in WC value; consequently, the numbers of participants in the WC categories were not exactly identical to the numbers of participants in the corresponding BMI categories. The WC category equivalent to the 25.0–27.4 BMI category was used as the reference.

In a separate set of analyses, we modelled BMI as a continuous variable within the <25.0 (lower BMI) and ≥25.0 (higher BMI) ranges yielding HRs for each 2.5 kg/m^2 difference in BMI. For ease of understanding, the HRs for the lower BMI range indicate increased risk with decreasing BMI, whereas the HRs in the higher BMI range indicate increased risk with increasing BMI. Both total and cause-specific mortality were analysed using this model. A similar method of modelling BMI was applied in a recent large study of BMI and mortality.[9]

Follow-up and endpoints

We linked each participant to data from the Norwegian Causes of Death Registry using a personal identification number to identify vital status. Cause of death is in Norway based on the International Classification of Diseases (ICD) system. We used the underlying cause of death. ICD-9 was used for deaths occurring up to 1996 and ICD-10 was used for deaths occurring in 1996 and thereafter. We identified[10] three main categories of causes of death: CVD (ICD-9: 390–459; ICD-10: I00–I99), respiratory disease (ICD-9: 460–519; ICD-10: J00–J98) and cancer (ICD-9: 140–208; ICD-10: C00–C97). All subjects were followed for emigration or mortality from date of study enrolment until 31 December 2007. To reduce the impact of weight loss due to pre-existing serious diseases, we excluded deaths occurring during the first year of follow-up.

Statistical analyses

The differences in baseline characteristics between surviving and non-surviving participants were assessed by the χ^2 test or t-test. HRs for both BMI categories and BMI modelled as a continuous variable were determined using a Cox proportional hazards regression model controlling for potential confounders. We assessed the proportional hazards assumptions by inspecting the log(−log) survival curves for the various BMI categories. Risk relationships in men and women were analysed separately. Adjustments were performed for initial age, smoking, marital status, study site and educational level. In table 1, smoking is categorised into six levels. However, because there was no difference between adjusted models with a six-level and a three-level (never, previous or current) smoking variable, the three-level variable was used for adjustment in the mortality analyses. Analyses were performed using SPSS version 17.0. A two-sided p value <0.05 was considered statistically significant.

RESULTS

During a mean 9.3 years of follow-up, 51.5% of the 7604 men and 39.1% of the 9107 women aged ≥65 years died. There were 7474 deaths in total (643 deaths from respiratory diseases, 3419 deaths from CVD, 1794 deaths from cancer and 1618 deaths from other diseases/conditions). The crude total mortality rates per 1000 person-years were 57.1 and 39.4 in men and women, respectively.

Baseline characteristics by mortality status during follow-up

We compared baseline characteristics of the participants according to whether they died during follow-up (table 1). Men and women who died tended to be older, not to be married and

Table 1 Baseline characteristics of participating elderly men and women according to mortality status during follow-up. Participants from the Tromsø (1994–1995) and HUNT (1995–1997) studies

	Men			Women		
Characteristic	Survivors	Non-survivors	p Value*	Survivors	Non-survivors	p Value*
Number of subjects	3687	3917		5550	3557	
Person-years of follow-up	43233	25457		65267	24993	
Age at inclusion, mean (SD)	70.4 (4.2)	75.1 (6.2)	<0.001†	71.4 (4.8)	76.8 (6.2)	<0.001†
BMI (kg/m^2), mean (SD)	26.6 (3.3)	26.2 (3.7)	<0.001†	27.5 (4.4)	27.2 (4.9)	0.001†
BMI, % (n)						
<20.0	1.3 (49)	3.5 (136)	<0.001‡	2.5 (139)	4.9 (174)	<0.001‡
20.0–24.9	29.8 (1100)	33.9 (1329)		26.5 (1472)	30.2 (1075)	
25.0–29.9	54.5 (2009)	48.1 (1885)		44.9 (2492)	39.1 (1390)	
≥30.0	14.4 (529)	14.4 (567)		26.1 (1447)	25.8 (918)	
Currently married, % (n)	80.2 (2957)	70.0 (2743)	<0.001‡	55.0 (3052)	36.7 (1306)	<0.001‡
Lower education, % (n)	56.3 (2076)	63.6 (2493)	<0.001‡	76.9 (4269)	82.0 (2918)	<0.001‡
Smoking status, % (n)						
Never smoked	21.5 (793)	19.4 (760)	<0.001‡	61.0 (3386)	64.0 (2276)	<0.001‡
Stopped ≥20 years ago	31.6 (1165)	26.2 (1026)		9.1 (507)	6.2 (222)	
Stopped 10–19 years ago	13.4 (494)	14.7 (577)		9.4 (524)	8.3 (296)	
Stopped <10 years ago	10.0 (369)	11.4 (445)		4.6 (258)	4.9 (173)	
Current <10 cigarettes/day	9.0 (332)	10.0 (391)		8.7 (485)	8.5 (304)	
Current ≥10 cigarettes/day	14.5 (534)	18.3 (718)		7.0 (390)	8.0 (286)	

*p Value for differences between groups using the †t test or ‡χ^2 test.
BMI, body mass index; HUNT, the North-Trøndelag Health Study.

have low education. The mean BMI was also slightly lower in individuals who died and the proportion of subjects with BMI below 25.0 was substantially higher among these individuals than among the surviving group.

Total mortality and BMI

In both men and women, individuals in the 25–29.9 BMI category had the lowest mortality (table 2 and figure 1). The same relatively low mortality was observed in moderately obese women. In all BMI categories below 25.0, mortality was increased compared to the reference category. Adjustment for smoking status, educational level and marital status had only a minor impact on the risk estimates.

Table 2 also shows total mortality in the various WC categories. In the lower WC categories, mortality was increased only in the lowest category. In the upper categories, the HRs were statistically significantly increased in the three highest categories in men and the highest category in women.

When modelling BMI as a continuous variable (figure 2), we found a 20% increase in mortality per 2.5 kg/m^2 decrease in BMI in the lower BMI range (<25). In the upper BMI range (≥25), we found a 7–9% increase in mortality per 2.5 kg/m^2 increase in BMI. There were no significant interactions between sex and BMI.

Information about physical activity and alcohol intake was missing for 6353 participants and 1464 participants, respectively. We repeated the analyses of total mortality and cause-specific mortality with adjustment for frequency of alcohol intake and physical activity, respectively, in the subpopulations with information concerning these two variables. However, these additional adjustments had only a minimal impact on the HRs for the relation between BMI and mortality (results not shown).

Approximately 20% of the participants were current smokers, 36% were previous smokers and 43% had never smoked. The interaction between BMI and smoking status in the analysis of total mortality was significant only for women in the higher BMI range (p=0.047); it was non-significant for men in the higher BMI range and for both men and women in the lower BMI range (figure 2).

Cause-specific mortality and BMI

About 1 in 10 deaths was from respiratory diseases and the corresponding mortality was three to four times higher in individuals with a BMI below 20 compared to the reference category (table 3 and figure 3). Mortality was also increased in the 20–24.9 BMI range. When BMI was modelled as a continuous variable (figure 4), a 54–74% increase in mortality from respiratory diseases was observed per 2.5 kg/m^2 lower BMI below 25. In women, no interaction between smoking and BMI was observed. For men in the lower BMI range who had never smoked, there was no relation between BMI and respiratory diseases mortality. However, the corresponding CI was wide due to the small number of deaths.

To further explore mortality from respiratory diseases, we analysed the associations between BMI and respiratory disease mortality in participants without lung disease at baseline. We found similar relationships as displayed in table 3 and figure 4.

The contribution of deaths from respiratory diseases was also explored by analysing total mortality excluding deaths from respiratory diseases. In the lower BMI range, we found that the HR for a 2.5 kg/m^2 decline in BMI below 25 decreased from 1.21 to 1.13 in men. In women, the corresponding reduction in HR was from 1.23 to 1.19. For the categorical analyses (table 2), the overall pattern of the BMI–mortality relationship was retained when deaths from respiratory diseases were excluded. However, the HRs for mortality in the lower BMI categories were somewhat reduced, especially in men.

CVD accounted for almost half of all deaths. Increased CVD mortality was found in the higher BMI range; the effect was most pronounced in men with a BMI ≥30 (table 3; figure 3).

Table 2 Adjusted HRs for total mortality by category of body mass index (BMI) and waist circumference (WC) in elderly men and women. Participants from the Tromsø (1994–1995) and HUNT (1995–1997) studies

BMI (n=16711)				WC (n=15049)			
		HR (95% CI)				HR (95% CI)	
BMI (kg/m^2) categories	Deaths/total (n)	Age-adjusted*	Multivariable adjusted†	WC (cm) categories	Deaths/total (n)	Age-adjusted*	Multivariable adjusted†
Men				**Men**			
<18.5	52/62	2.52 (1.91 to 3.33)	2.32 (1.75 to 3.07)	<73	34/53	1.61 (1.15 to 2.27)	1.49 (1.06 to 2.10)
18.5–19.9	84/123	1.42 (1.13 to 1.77)	1.28 (1.03 to 1.60)	74–77	52/98	1.12 (0.85 to 1.48)	1.03 (0.78 to 1.36)
20.0–22.4	388/667	1.30 (1.15 to 1.45)	1.23 (1.09 to 1.38)	77.5–83.5	255/514	1.19 (1.03 to 1.36)	1.11 (0.97 to 1.28)
22.5–24.9	941/1762	1.14 (1.04 to 1.24)	1.12 (1.02 to 1.22)	84–90.5	750/1637	0.98 (0.89 to 1.08)	0.97 (0.88 to 1.06)
25.0–27.4	1109/2272	1.00 Reference	1.00 Reference	91–97.5	968/2034	1.00 Reference	1.00 Reference
27.5–29.9	776/1622	1.04 (0.95 to 1.14)	1.05 (0.95 to 1.15)	98–104.5	742/1541	1.03 (0.94 to 1.14)	1.04 (0.94 to 1.14)
30.0–32.4	359/709	1.17 (1.04 to 1.32)	1.19 (1.05 to 1.34)	105–111.5	387/729	1.18 (1.05 to 1.33)	1.16 (1.03 to 1.31)
32.5–34.9	136/258	1.30 (1.09 to 1.56)	1.31 (1.09 to 1.56)	112–117.5	133/224	1.39 (1.16 to 1.67)	1.43 (1.20 to 1.72)
≥35.0	72/129	1.55 (1.22 to 1.97)	1.53 (1.21 to 1.95)	≥118.0	92/142	1.63 (1.32 to 2.02)	1.53 (1.24 to 1.90)
Women				**Women**			
<18.5	63/103	1.91 (1.48 to 2.47)	1.78 (1.37 to 2.31)	<65	46/93	1.83 (1.36 to 2.46)	1.68 (1.24 to 2.26)
18.5–19.9	111/210	1.74 (1.42 to 2.12)	1.57 (1.28 to 1.92)	66–68	60/168	1.19 (0.91 to 1.55)	1.13 (0.86 to 1.47)
20.0–22.4	405/862	1.36 (1.20 to 1.54)	1.32 (1.17 to 1.49)	69–74	283/789	1.16 (1.01 to 1.34)	1.12 (0.97 to 1.29)
22.5–24.9	670/1685	1.10 (0.99 to 1.22)	1.10 (0.99 to 1.22)	75–80	488/1508	1.02 (0.91 to 1.15)	1.01 (0.90 to 1.13)
25.0–27.4	733/2094	1.00 Reference	1.00 Reference	81–87	651/1931	1.00 Reference	1.00 Reference
27.5–29.9	657/1788	1.04 (0.93 to 1.15)	1.06 (0.96 to 1.18)	87.5–93	533/1567	1.01 (0.90 to 1.13)	1.01 (0.90 to 1.14)
30.0–32.4	426/1200	0.98 (0.87 to 1.10)	1.00 (0.89 to 1.13)	93.5–99	358/968	1.09 (0.96 to 1.24)	1.11 (0.97 to 1.26)
32.5–34.9	249/618	1.16 (1.00 to 1.34)	1.19 (1.03 to 1.38)	99.5–104.5	212/547	1.15 (0.98 to 1.34)	1.16 (0.99 to 1.35)
≥35.0	243/547	1.39 (1.21 to 1.61)	1.45 (1.25 to 1.67)	≥105	246/506	1.61 (1.39 to 1.86)	1.66 (1.43 to 1.92)

*Adjusted for initial age and study site.
†Adjusted for initial age, study site, smoking, educational level and marital status.

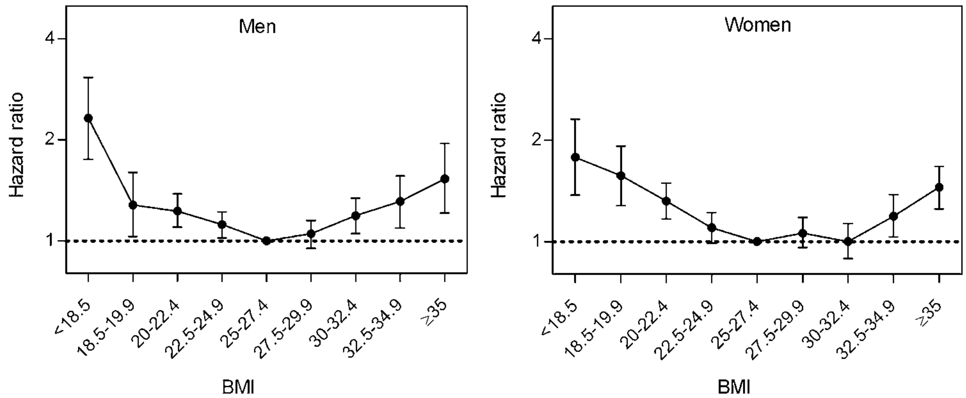

Figure 1 Adjusted HRs (95% CI)* for total mortality rate by body mass index (BMI; kg/m^2) category in elderly men and women. BMI 25–27.4 constitutes the reference category. *Adjusted for smoking status, age, marital status, educational level and study site.

CVD mortality was also increased in women with a BMI <22.5 kg/m^2.

Cancer accounted for one-quarter of all deaths and the relationships between BMI and cancer mortality followed the 'U-shaped' pattern found for total mortality (table 3).

Prior to inclusion in the study, a history of heart disease was reported by 21%, lung disease by 13% and 9% of the participants had a history of cancer. Exclusion of these subjects from the analyses revealed similar relations as described for the main cohort both for total and cause-specific mortality (results not shown).

DISCUSSION

In this population-based study of elderly men and women, we found increased total mortality in elderly individuals with a BMI below 25. No excess mortality was found in overweight individuals (BMI 25–29.9) and only a moderate increase in mortality was observed with increasing BMI in obese individuals (BMI≥30). In the lower BMI range, the strongest impact of BMI on mortality was found for deaths from respiratory diseases. These results were not explained by the presence of cancer or lung disease at baseline.

The crude mortality rates per 1000 person-years (57 in men and 39 in women) observed in the study population were lower than the expected mortality rates (73 in men and 55 in women) if the mortality rates of the entire elderly population of Norway[11] were applied to the study population. This is probably explained by a better general health in the participants than in non-participating elderly individuals.

Lower BMI range

The impact of a decrease in BMI in the lower BMI range was twice the impact of the corresponding increase in BMI in the higher BMI range (figure 2). However, the most striking finding was the relative increase in mortality found in all 'normal weight' individuals in the BMI categories below 25.

Mortality from respiratory diseases explained about 40% of the increased total mortality found in men in the lower BMI range. For women, the corresponding figure was 17%. Previous studies of elderly individuals have demonstrated increased mortality from respiratory diseases in selected groups with a BMI below 20–22.7.[12 13] We also found substantially increased mortality from respiratory diseases in the 20–22.4 and 22.5–24.9 BMI categories, which are generally regarded as healthy weight.

Asthma and chronic bronchitis are prevalent conditions associated with the lower BMI categories in elderly men and women.[14] When we analysed subjects without these conditions, the impact of BMI on mortality in the lower range persisted.

Smoking is a major risk factor for both premature death[15] and malnutrition[16] in elderly individuals, and we adjusted all analyses for smoking status. Our results suggest that the impact of BMI ≥25 on mortality was greater in current smoking women than in women who had never smoked.

A number of studies have reported increased mortality among individuals in the lowest BMI categories.[2–4 9 17] Mortality tends to increase when BMI falls below the range of 19–23. Very few studies of elderly men and women, with information about smoking habits included, have been able to demonstrate a significant increase in mortality in the normal BMI range of 22.5–24.9 compared to moderately overweight subjects. For some of the studies, this may be explained by a focus on obesity, the use of wide reference categories (BMI 18.5–25) or a limited number of participants.

Why is mortality higher in the lower BMI range?

Being underweight is associated with loss of both peripheral and respiratory muscles,[18] and this association may partly explain the increases in both total mortality and mortality from

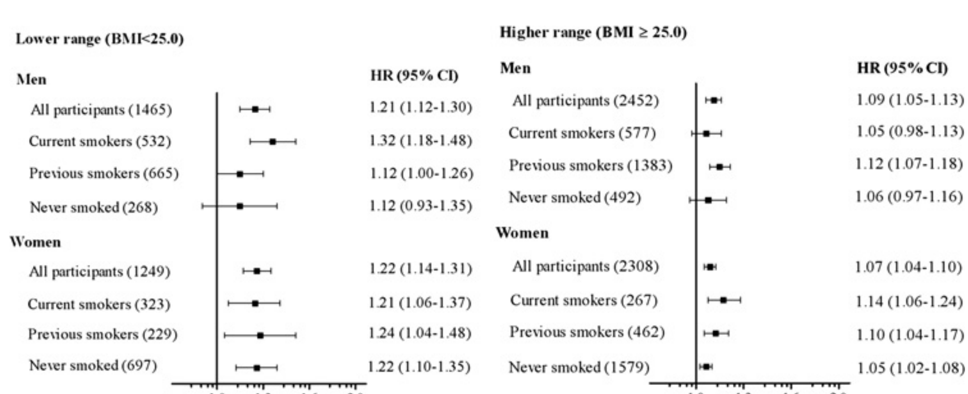

Figure 2 Adjusted HRs* for total mortality for every 2.5 kg/m^2 difference in body mass index (BMI) in elderly men and women. In the lower range, HR indicates risk of mortality with decreasing BMI, whereas in the higher range, HR indicates risk of mortality with increasing BMI. The numbers in parentheses indicate the number of deaths in each category. Bars represent 95% CIs. *Adjusted for smoking status (all participants only), age, marital status, educational level and study site.

Table 3 Adjusted HRs* for cause-specific mortality by body mass index (BMI) category in elderly men and women. Participants from the Tromsø (1994−1995) and HUNT (1995−1997) studies

	Respiratory diseases		Cardiovascular diseases		Cancer		Other causes	
BMI	Deaths	HR (95% CI)	Deaths	HR (95% CI)	Deaths	HR (95% CI)	Deaths	HR (95% CI)
Men								
<20.0	31	4.35 (2.87 to 6.60)	46	1.14 (0.84 to 1.54)	32	1.43 (0.99 to 2.07)	27	1.51 (1.01 to 2.26)
20−22.4	62	2.45 (1.76 to 3.40)	141	0.98 (0.82 to 1.19)	103	1.22 (0.98 to 1.54)	82	1.28 (0.99 to 1.65)
22.5−24.9	103	1.58 (1.19 to 2.10)	410	1.07 (0.94 to 1.22)	255	1.17 (0.99 to 1.39)	173	0.97 (0.80 to 1.18)
25.0−27.4	87	1.00 Reference	504	1.00 Reference	285	1.00 Reference	233	1.00 Reference
27.5−29.9	47	0.81 (0.57 to 1.16)	379	1.12 (0.98 to 1.28)	216	1.12 (0.94 to 1.34)	134	0.87 (0.70 to 1.07)
≥30.0	40	1.18 (0.81 to 1.71)	274	1.33 (1.14 to 1.54)	141	1.16 (0.95 to 1.42)	112	1.23 (0.98 to 1.55)
Women								
<20.0	28	3.30 (2.07 to 5.27)	64	1.28 (0.98 to 1.67)	36	1.49 (1.03 to 2.15)	46	2.03 (1.46 to 2.82)
20−22.4	42	1.83 (1.21 to 2.75)	178	1.21 (1.01 to 1.44)	77	1.16 (0.89 to 1.53)	108	1.56 (1.23 to 1.99)
22.5−24.9	59	1.32 (0.91 to 1.91)	298	1.01 (0.87 to 1.18)	145	1.12 (0.89 to 1.40)	168	1.20 (0.96 to 1.48)
25.0−27.4	52	1.00 Reference	355	1.00 Reference	158	1.00 Reference	168	1.00 Reference
27.5−29.9	35	0.84 (0.54 to 1.28)	343	1.14 (0.98 to 1.32)	128	0.99 (0.78 to 1.25)	151	1.05 (0.84 to 1.31)
≥30.0	57	1.06 (0.73 to 1.55)	427	1.09 (0.95 to 1.26)	218	1.28 (1.04 to 1.57)	216	1.16 (0.94 to 1.41)

*Adjusted for smoking status, age, marital status, educational level and study site.

respiratory diseases observed in this study among underweight participants. Furthermore, a low BMI may increase vulnerability to acute diseases. An elevated in-hospital case-fatality rate among underweight patients has been found for several conditions.[19] It has been shown that the immune response is decreased in elderly malnourished individuals,[20] which may increase the relative mortality rate among underweight elderly subjects during intercurrent diseases.

Reverse causation—that is, the possibility that pre-existing illnesses or conditions associated with increased mortality lead to loss of body weight—is a concern in studies of lower BMI and mortality.[21 22] To overcome this problem in our analyses, we used several methods. First, we excluded deaths occurring during the first year of follow-up. Second, we repeated the analyses of mortality excluding participants with a history of cancer at baseline as these patients might have reduced weight because of the disease. However, the relation between low BMI and mortality was not influenced by this exclusion. Finally, to explore the effect of underweight-associated pulmonary disease, we analysed both total mortality and mortality from respiratory diseases in individuals not reporting asthma/chronic bronchitis at baseline. Neither of these two BMI-mortality relations were significantly influenced by this exclusion.

In addition, we stratified the analyses for smoking habits (figure 2) and found that the increased total mortality in subjects with low BMI was not due to smoking. Nevertheless, some unknown bias from pre-existing diseases or conditions might have influenced the BMI−mortality relations.

Higher BMI range

The prevalence of obesity is rising in elderly individuals and the proportion of obese individuals in the present study (20.7%) was almost at the level found in US populations in the same period.[23] We found moderately increased mortality in obese individuals—more so in men than in women. Most previous studies have found increased mortality in obese elderly individuals, but the increase was somewhat less pronounced than in middle-aged adults.[4]

Using BMI alone for assessment of obesity may be a limitation because it provides only an indirect estimate of abdominal adiposity. In the present study, WC as a measure of abdominal obesity was also recorded in a subset of the participants. However, overall, WC was not a stronger risk factor for total mortality than BMI in the higher weight categories. This finding is in line with the results of a recent study by Flegal *et al*.[8] In the lower weight categories, BMI was a stronger risk factor than WC.

Several explanations have been proposed for the limited impact of overweight or obesity on mortality in this age group.[3] Possible explanations include a healthy survival effect in obese

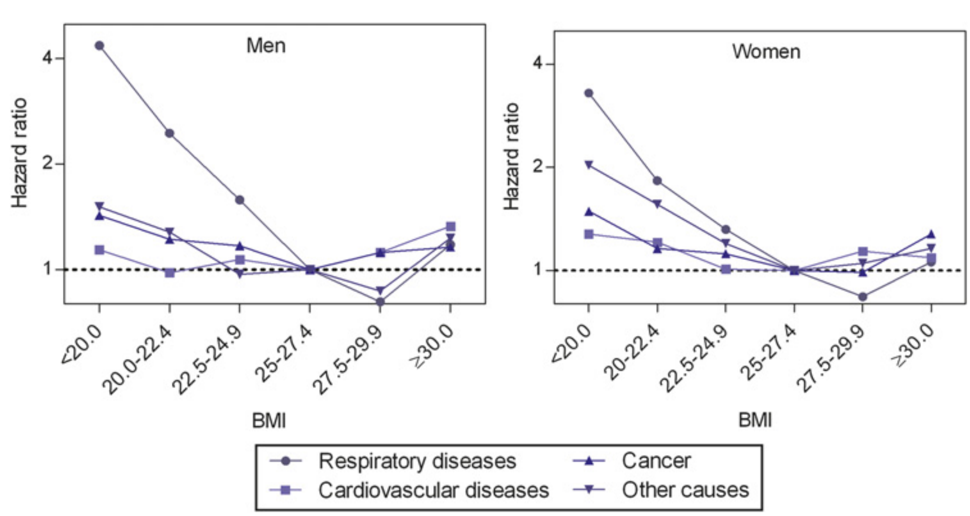

Figure 3 Adjusted HRs* for cause-specific mortality by body mass index (BMI; kg/m^2) category in elderly men and women. BMI 25−27.4 constitutes the reference category. *Adjusted for smoking status, age, marital status, educational level and study site.

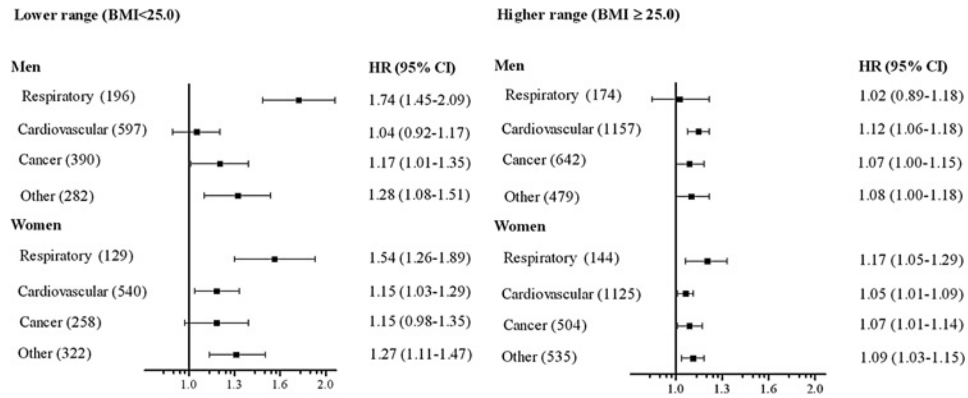

Figure 4 Adjusted HRs* for cause-specific mortality for every 2.5 kg/m^2 difference in body mass index (BMI) in elderly men and women. In the lower range, HR indicates risk of mortality with decreasing BMI, whereas in the higher range, HR indicates risk of mortality with increasing BMI. Bars represent 95% CIs. The numbers in parentheses indicate the number of deaths in each disease category. *Adjusted for smoking status, age, marital status, educational level and study site.

individuals meaning that those most vulnerable to the effects of obesity have already died before reaching older age. Furthermore, elderly people have a shorter life expectancy. Obesity-related consequences develop slowly and before these consequences appear, individuals who become obese later in life may die from other diseases.[24]

Optimal body weight

We found the optimal weight with the lowest mortality to be in the overweight categories (BMI 25–29.9), whereas moderately obese individuals had only a modest increase in mortality. This finding is in line with several previous studies of elderly individuals[25] and has been described as the 'obesity paradox'.[24] It has also been observed that moderate overweight hospitalised elderly patients have reduced mortality.[26] These findings are important because almost half of the elderly population are overweight (BMI 25–29.9) and it is frequently assumed that these individuals have increased mortality.[24]

One strength of the present study is the strictly population-based design with inclusion of individuals from both urban and rural areas. Some previous studies in this field have used cohorts based on particular professional affiliations or health insurance membership, introducing the possibility of bias.[13] Furthermore, in the present study, height, weight and WC were measured rather than self-reported. The participation rate was relatively high (70%), but participation required the ability to independently visit a research centre. It is probable that the non-participating individuals were frailer and had more co-morbidities; any potential bias would probably be in the direction of more conservative estimates.

What is already known on this subject

- The body mass index (BMI)–mortality relationship is U-shaped in both adult and elderly individuals and shifted to the right in the older age categories. Results from previous studies in elderly individuals are conflicting about the upper and especially the lower BMI cut-off points for optimal weight with regard to mortality.
- There is a lack of data concerning the relationship between BMI and mortality, particularly cause-specific mortality, in the elderly and the impact of mortality from respiratory diseases on the BMI–mortality relationship.

What this study adds

- In the present large study of elderly individuals from Norway, mortality was significantly increased in all body mass index (BMI) categories below 25, including the 'normal weight' BMI categories. The impact of decreases in BMI in the lower BMI range was twice the impact of the corresponding increases in BMI in the higher BMI range. In men, this finding could be explained to some extent by increased mortality from respiratory disease.
- Waist circumference and BMI performed approximately equally in identifying individuals in the higher weight categories with increased mortality.
- More attention should be given to elderly individuals in the lower BMI categories and moderately increased BMI (25–29.9) should not be a concern with regard to mortality in this age group.

CONCLUSION

Our results show that in elderly men and women, a BMI below 25 was associated with increased total mortality. In men, this finding could be explained to some extent by an increased risk of death from respiratory diseases. A modest increase in mortality was found with increasing BMI for obese elderly men and women. Overweight individuals, including moderately obese women, had the lowest mortality.

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Competing interests None.

Ethics approval This study was conducted with the approval of the Regional Committees for Ethics in Medical Research, Tromsø and Trondheim, Norway, and by the Norwegian Data Inspectorate.

Contributors J-MK, BKJ, JH and JF were responsible for the initial design of the study. J-MK did the analysis and wrote the first draft of the paper. BKJ contributed to the analysis, interpretation of the results and the review of the drafts. TW contributed particularly to the statistical analysis and interpretation. JH and KM contributed to the analysis and interpretation of the data and review of the drafts. All authors contributed to the critically revision of the article and approved the final published version to be published.

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