Nutritional status among older people
Risk factors and consequences of malnutrition

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List of Papers

This thesis is based on the following original papers referred to in the text by their Roman numerals.


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Abstract

Despite the high frequency and serious consequences of protein–energy malnutrition, prevention and treatment of malnutrition do not currently receive appropriate attention. Increased awareness of the importance of nutritional screening among older people is needed. The overall aim of this thesis was to extend our current knowledge about malnutrition and the consequences of a poor nutritional status in relation to preterm death, and to identify possible risk factors for developing malnutrition among older people. The aim of Paper I was to estimate the prevalence of malnutrition and to examine the associations between mealtime habits, meal provision, and malnutrition among older people admitted to a Swedish hospital. The aim of Paper II was to examine whether nutritional status, defined according to the three categories in the full Mini Nutritional Assessment (MNA) instrument, is an independent predictor of preterm death in older people.

The baseline survey was a cross-sectional study of 1771 patients aged ≥65 years who were admitted to hospital. Nutritional status was assessed using the MNA instrument, and possible risk factors associated with malnutrition were recorded during the hospital stay (Paper I). Overall survival was followed up after 35–50 months in a cohort study of 1767 participants (Paper II).

Of the 1771 participants, 35.5% were well-nourished, 55.1% were at risk of malnutrition, and 9.4% were malnourished at baseline. An overnight fast >11 hours was associated with risk of malnutrition (odds ratio (OR) 1.46; 95% confidence interval (CI) 1.14–1.87) and being malnourished (OR 1.67; 95% CI 1.04–2.69). Fewer than four eating episodes a day was associated with both risk of malnutrition (OR 1.88, 95% CI 1.52–2.32) and being malnourished (OR 3.10; 95% CI 2.14–4.49). Not cooking independently was also associated with both risk of malnutrition (OR 1.9; 95% CI 1.30–2.93) and being malnourished (OR 5.04; 95% CI 2.95–8.61). At the 50-month follow-up, the survival rates were 75.2% for well-nourished participants, 60.0% for those at risk of malnutrition, and 33.7% for malnourished participants. After adjusting for confounders, the hazard ratios (95% CI) for all-cause mortality were 1.56 (1.18–2.07) in the group at risk of malnutrition and 3.71 (2.28–6.04) in the malnourished group. Nutritional status defined according to the three categories in the full MNA independently predicted preterm death in people aged 65 years and older.

This thesis provides additional knowledge of the current nutritional situation among older people admitted to hospital. The high prevalence and serious consequences of malnutrition demonstrated in this thesis underline the importance of screening and taking actions to counteract malnutrition among older people. The data showing that the length of overnight fasting and number of eating episodes per day are possible risk factors for malnutrition are consistent with the current nutritional recommendations. This knowledge may stimulate care providers to decrease the length of overnight fasting and increase the number of eating episodes per day among older people at risk of malnutrition.
### Abbreviations

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<th>Description</th>
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<tr>
<td>ESPEN</td>
<td>European Society of Clinical Nutrition and Metabolism</td>
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<td>PEM</td>
<td>Protein–energy malnutrition</td>
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<td>MNA</td>
<td>Mini Nutritional Assessment</td>
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<tr>
<td>BMI</td>
<td>Body mass index</td>
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<td>SD</td>
<td>Standard deviation</td>
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<td>ANOVA</td>
<td>Analysis of Variance</td>
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<tr>
<td>OR</td>
<td>Odds ratio</td>
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<tr>
<td>CI</td>
<td>Confidence interval</td>
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<td>HR</td>
<td>Hazard ratio</td>
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Introduction

Initiatives to promote nutritional care
Public awareness of malnutrition has increased in recent years, and improvement in nutritional care for older people is on the agenda both internationally and nationally. In 2003, the Council of Europe published a resolution on food and nutritional care in hospitals that was signed by 18 European countries, including Sweden. The resolution states that the nutritional risk of all patients should be routinely assessed at admission to hospital and that those who are malnourished or at risk of malnutrition should have a treatment plan that includes dietary goals, monitoring of food intake and body weight, and adjustment of the treatment plan. However, in clinical practice, nutritional risk screening is not routine in Swedish hospitals.

On a national level, the Swedish government has recognized the seriousness of malnutrition. Beginning in 2007, the municipalities and county councils in Sweden have been given national incentive grants to improve the care of older people (≥65 years old) with multimorbidity, including nutritional care. In 2010 and forward, performance-based government funding has been given to the municipalities and county councils to implement a quality register, Senior Alert, in hospitals, primary health care and municipality elderly care. At present, 284 municipalities (98%) and 21 county councils (100%) report data to the quality register. The aim is to increase the quality of care for people 65 years and older by recording risk assessments and actions taken to prevent and treat malnutrition, pressure sores, falls, and problems with oral health. The introduction of the quality register is a step forward in the processes of attaining the Council of Europe’s nutritional goals.

Senior Alert comprises four evidence-based instruments covering the four risk areas. However in Sweden, there is a lack of up-to-date data on the prevalence of malnutrition among older people admitted to hospital before the quality register was introduced. Also, there remains a need for studies evaluating the independent effect of nutritional status on survival, after controlling for competing risks, if no targeted interventions against malnutrition are provided.

Demographic changes and definition of malnutrition
In Western countries, there is a demographic transition towards a progressively increasing percentage of older people. About 1.8 million of the 9.5 million inhabitants in Sweden (19%) are 65 years and older, and this percentage is expected to increase to 25% within the next 50 years. In addition, life expectancy is predicted to rise from 84 to 89 years for women and from 80 to 87 years for men from 2011 to 2060. The risk of developing malnutrition increases with advancing age. Therefore, it can be anticipated that the proportion of malnourished people will increase in the future.
The European Society of Clinical Nutrition and Metabolism (ESPEN) defines malnutrition as “a state of nutrition in which a deficiency or excess (or imbalance) of energy, protein, and other nutrients causes measurable adverse effects on tissue/body form (body shape, size and composition) and function, and clinical outcome” p.182. The most frequent state of malnutrition in older people is protein–energy malnutrition (PEM), which is characterized by a deficiency in protein and energy. In this thesis, malnutrition refers to PEM.

**Nutritional status**

Because of the lack of a standard diagnostic criterion (gold standard) to define malnutrition, various screening and assessment tools have been developed to evaluate nutritional status. Most tools include questions about body mass index (BMI), recent weight loss, and decreased food intake.

To promote routine nutritional screening, the ESPEN has published guidelines on nutritional screening for different settings. The Mini Nutritional Assessment (MNA) instrument is recommended for people aged 65 years and older independent of their setting. The original full MNA is an 18-item questionnaire developed in the 1990s by practising geriatricians in the USA and Europe to provide a simple, reliable way to assess nutritional status. The development and validation studies were performed on older people, both frail and healthy, in France and the USA. The MNA was validated against a clinical evaluation of nutritional status as assessed by two physicians, which was considered the gold standard. The clinical evaluation was based on a comprehensive nutritional assessment including anthropometry, biochemical markers, dietary intake, and functional geriatric assessment. In the validation studies of the MNA, the sensitivity was found to be 96% and the specificity 98%. However, because there is no gold standard to determine nutritional status, the sensitivity and specificity of the MNA vary depending on which reference is used.

**Prevalence of malnutrition**

The exact prevalence of malnutrition is unknown. This is partly because of the lack of a gold standard for the definition of malnutrition. However, the prevalence of malnutrition defined according to the MNA also varies depending on the setting. An international pooled dataset including more than 4500 people aged 65 years and older (mean age 82 years) in different settings reported a 23% overall prevalence of malnutrition and that 46% were at risk of malnutrition. The percentage of people with malnutrition was highest in geriatric rehabilitation units (51%) followed by hospitals (39%), nursing homes (14%), and the community (6%). In a large Belgian cross-sectional multicentre study (n = 2329) of people aged 75 years and older (mean age 83 years) in hospital elderly wards, the prevalence of malnutrition was 33%, and almost 43% were at risk of malnutrition.
In Sweden, several studies have aimed to estimate the prevalence of malnutrition in different settings. \(^{14-19}\) Two multicentre studies were performed in hospital settings. \(^{16,19}\) However, both these studies estimated the prevalence of malnutrition in people \(\geq 18\) years of age and thus did not use the MNA instrument. \(^{16,19}\) Consequently, in Sweden, no large-scale study has assessed the nutritional status using the MNA solely in older people in a hospital setting.

**Risk factors for malnutrition**

Malnutrition is a condition with multifactorial causes, \(^{20}\) and the cause of malnutrition at the individual level is not always clear. The question is whether the aging process by itself leads to malnutrition or whether malnutrition in older people indicates other underlying disease(s). \(^{21}\) Factors associated with malnutrition, such as impaired functional ability, \(^{5,22}\) can be both a cause and effect of malnutrition. In this thesis, factors associated with malnutrition are hereafter referred to as risk factors for malnutrition.

Age is the most important risk factor for malnutrition. \(^{5-7}\) With increasing age, the natural drive to eat and drink decreases, resulting in the so-called anorexia of aging. This is partly because of the decline in smell and taste sensations that accompanies aging. \(^{20}\) The decline in food intake compensates for the decline in energy utilization that occurs with aging. \(^{23}\) These age-related changes are regarded as an adaption to the natural decrease in energy requirement but also predispose older people to malnutrition by increasing the risk of an extreme reduction in food intake. If additional risk factors such as disease develop, dietary intake is often no longer sufficient to meet the requirements. \(^{20,23}\) Therefore, it is crucial to identify modifiable risk factors that can prevent an excessive decline in food intake in older people.

With age, the risk of developing various diseases and conditions increases. Diseases such as dementia, \(^{7,22}\) symptoms of depression, \(^{7,22}\) and the presence of infections \(^{24,25}\) are often associated with malnutrition. Drug therapy can also negatively affect nutritional status through the side effects often caused by polypharmacy \(^{26}\) such as decreased appetite, nausea, alterations in taste and smell, dry mouth, constipation, diarrhoea, and confusion. \(^{27}\)

Mealtime habits such as overnight fasting and the number of eating episodes and meal provision such as receiving meals on wheels are modifiable factors thought to be related to malnutrition. \(^{28-30}\) European \(^1\) and more specific Nordic recommendations \(^{31}\) state that the overnight fast should not exceed 11 hours in older people and that the number of eating episodes should be at least four each day in adults. \(^{31}\) On a national level, the Swedish National Board of Health and Welfare performs an annual national survey, called “Open Comparisons”, which compares the quality of health care in Swedish municipalities. In this survey, the length of the overnight fast and number of eating episodes are included in the quality indicator “good meal pattern”. To fulfil this quality indicator, meals should be offered at least six times a day on given time intervals according to expert recommendations, so that the overnight fast does not exceed 11 hours. \(^{32}\) Actions to prevent malnutrition are also suggested in the national quality register (Senior Alert).
One of these actions is to decrease the length of overnight fasting to <11 hours. Despite these recommendations, no clinical study has been undertaken to clarify whether there is an association between malnutrition and the length of overnight fasting or the number of eating episodes per day.

**Consequences of malnutrition**

It is important to identify older people with poor nutritional status because malnutrition is related to negative consequences, such as increased morbidity, poor quality of life, and increased health care costs. Even more critically, a systematic review in 2012 that evaluated different nutrition screening tools concluded that there is some evidence that malnutrition is associated with increased mortality. However, it is uncertain whether this association is independent of confounders.

When examining the relationship between malnutrition and mortality, most studies analyse the total MNA score or use varying methods of subcategorization. Fewer studies have investigated the three nutritional status groups used in clinical practice (well-nourished, at risk of malnutrition, or malnourished) separately. Finally, considerable covariation may exist between nutritional status and possible confounders. Therefore, it is important to determine whether nutritional status predicts a preterm death after adjusting for possible confounders.
Rationale of this thesis

The planning for the present project started in 2007, when the municipalities and county councils received national incentive grants from the Swedish government to improve nutritional care for older people with multimorbidity. The overall aims were to extend our current knowledge about malnutrition and the consequences of a poor nutritional status in relation to preterm death, and to identify possible risk factors for developing malnutrition among older people.

No large-scale Swedish study has evaluated nutritional status exclusively in older people admitted to hospital. Therefore, up-to-date data are needed to increase our awareness of malnutrition and the consequences of poor nutritional status if no nutritional interventions are given. There is some evidence that malnutrition is associated with increased mortality. However, it is uncertain whether this association is independent of confounders. There is also a lack of evidence behind the nutritional recommendations about the length of the overnight fast and number of eating episodes per day. Thus, there is a need for studies to confirm that the length of the overnight fast and the number of eating episodes are associated with malnutrition.
Overall and specific aims

The overall aim of this thesis was to extend our current knowledge about malnutrition and the consequences of a poor nutritional status in relation to preterm death, and to identify possible risk factors for developing malnutrition among older people.

The specific aims were as follows.
Paper I: To estimate the prevalence of malnutrition and to examine the associations between mealtime habits, meal provision, and malnutrition among older people admitted to a medium-sized Swedish hospital.

Paper II: To examine whether nutritional status defined according to the three categories in the full MNA instrument is an independent predictor of preterm death in older people.
Methods

This thesis is based on data collected from participants ≥65 years of age admitted to hospital whose nutritional status was assessed during their hospital stay. Nutritional status was assessed by the original 18-item MNA instrument, hereafter referred to as the full MNA. An overview of the methods used in the licentiate thesis is presented in Table 1.

Table 1. Overview of the methods used in the thesis.

<table>
<thead>
<tr>
<th>Design</th>
<th>Paper I</th>
<th>Paper II</th>
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<tbody>
<tr>
<td>Participants</td>
<td>1771 participants ≥65 years of age admitted to hospital during a 15-month period (2008–2009).</td>
<td>1767 participants ≥65 years of age admitted to hospital and who had their nutritional status assessed by the full MNA at baseline in 2008–2009.</td>
</tr>
<tr>
<td>Data collection</td>
<td>Nutritional status assessed with the full MNA during a hospital stay.</td>
<td>Data on overall survival retrieved from the Swedish population register 35 to 50 months after the nutritional assessment at the hospital.</td>
</tr>
<tr>
<td>Statistical analysis</td>
<td>Factors associated with malnutrition analysed with multinomial logistic regression models.</td>
<td>Survival data analysed with Kaplan–Meier survival curves, log-rank test, and Cox proportional hazard regression models.</td>
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Design (Papers I and II)

The cross-sectional study (Paper I) was conducted over 15 months (from 3 March 2008 to 29 May 2009) at a medium-sized county hospital in central Sweden. This baseline survey was performed to estimate the prevalence of malnutrition among patients ≥65 years of age admitted to hospital. Nutritional assessment was performed with the MNA instrument during the hospital stay, and factors potentially associated with malnutrition were recorded. The participants were followed up in a cohort study (Paper II) 35 to 50 months after the nutritional assessment at baseline to analyse the relationship between nutritional status and overall survival.
Participants (Papers I and II)
In the cross-sectional study, a total of 2517 individuals were assessed for eligibility. The included sample comprised 1771 participants in two internal medicine wards ($n = 706$), two surgical wards ($n = 681$), and one orthopaedic ward ($n = 384$) at baseline. The final sample for the cohort study comprised 1767 participants. A flow chart describing the recruitment, reasons for exclusion and loss to follow-up are presented in Figure 1.

**Figure 1.** Flow chart describing participant recruitment.
Data collection (Papers I and II)
Baseline data on nutritional status and clinical characteristics were collected consecutively during the hospital stay. Nutritional status was assessed with the MNA given by registered dietitians, nurses, or assistant nurses (18 personnel). Before the study, the health care professionals received training on interpreting the questions in the MNA and performing the measurements.

The participants were followed up in the cohort study through the Swedish population register until 23 May 2012, which was 35 to 50 months after the nutritional assessment at baseline.

Nutritional status (Papers I and II)
In the present study, nutritional status was assessed in all participants with the full MNA. The questions in the MNA cover the preceding three months and comprise four areas. These include anthropometric measurements (arm and calf circumference, recent weight loss, and BMI); a global assessment (lifestyle, medication, mobility, presence of acute stress, and cognitive impairment or depression); dietary questions (changes in appetite, meals per day, daily intake of protein, fruit, vegetables, fluid, and autonomy of feeding); and a subjective assessment (self-perception of health and nutrition). The 18 questions are weighted, and the threshold values of the instrument categorize patients into three nutritional status groups: well-nourished (MNA score 24–30), at risk of malnutrition (MNA score 17–23.5), or malnourished (MNA score <17).

BMI was calculated with the standard formula of (weight in kg)/(height in m²). Weight was measured with a calibrated chair or mobile lift scale (n = 21) to the nearest kg after emptying the bladder and with the patient wearing a light hospital robe. Height was measured to the nearest centimetre with a stadiometer. Participants unable to stand upright were measured with a sliding calliper (n = 345) or, as a last resort, by calculating their height from half the arm span (demi-span) (n = 18) using the formula (1.40 × demi-span [cm]) + 57.8 for men and (1.35 × demi-span [cm]) + 60.1 for women.

Risk factors for malnutrition (Paper I)
Data on clinical characteristics were collected at baseline to examine possible risk factors for malnutrition including age, sex, BMI, smoking status, medication use, diagnoses, length of overnight fast, number of eating episodes per day, meal provision, and living situation. Age was retrieved from the personal identification number. Smoking status was defined as current or non-smoker. Medication use before admission and the patient’s diagnoses at discharge were retrieved from the patient’s medical records. The diagnoses were defined according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). The length of the overnight fast was defined as the period between the last eating episode in the evening and the first eating episode the following morning.
The number of eating episodes per day was recorded as how often the patient usually ate breakfast, lunch, dinner, and between-meal and evening snacks. Meal provision was recorded as cooking independently and/or with help from a spouse (cooks independently), meals on wheels, or meals in a nursing home or restaurant. Living situation was defined as living alone, cohabiting, or living in a nursing home. Country of birth was obtained from the Swedish population register.

Preterm death (Paper II)
The main focus of the cohort study was to examine the association between nutritional status as measured with the MNA and overall survival during the follow-up period. Survival was calculated from the date of the MNA assessment to the date of death. Date of emigration and end of follow-up were used as censoring dates. The participants’ characteristics registered at baseline were considered as potential confounders for the association between nutritional status and overall survival.

Sample size calculation
As a basis for a sample size calculation, studies evaluating malnutrition and mortality in older people in hospital were used. In these studies, the percentage of well-nourished older people was 17% to 59%, and the percentage of malnourished older people was 16% to 49%. Thus, the smallest percentages of well-nourished and malnourished people one would expect, in an extreme case, would be 17% well-nourished and 16% malnourished older people. Based on the aforementioned studies, the expected mortality during the three years of follow-up was 24% among well-nourished people and 35% among the malnourished. To obtain a power (1–β) of 80% at a two-sided significance level of α = 0.05 with a Z-test for difference in percentage with an expected difference in mortality of 11 percentage points, a total study population of 1682 participants would be needed. To take into account expected dropouts, non-response, and missing values, the aim was to recruit a total of 2080 participants. Because the dropout rate was lower than expected, a decision was made to end recruitment when the nutritional status of 1795 participants had been assessed in the study.

Statistical analysis
For descriptive statistics, categorical data are presented as frequencies and percentages n (%), ordinal data are presented as median and interquartile range (q1–q3), and discrete and continuous data are given as mean and standard deviation (SD). Univariate tests of differences between the three nutritional assessment status groups were performed using Pearson’s χ²-test for categorical data, the Kruskal–Wallis test for ordinal and discrete data, ANOVA for continuous data, and log-ranks tests for survival data. Kaplan–Meier curves were calculated for survival data.
For multivariate analyses, Paper I used multinomial logistic regression models with nutritional assessment status as the dependent variable. The analyses were performed in two steps. In the first step, a base model was constructed by including as independent variables all significant variables in the univariate analysis, except for those that contributed directly or indirectly to the MNA score, together with interaction effects. In the second step, a final model was constructed using a backward stepwise selection procedure with an entry probability of 0.05 and removal probabilities of 0.2 for the main effects and 0.05 for the interaction effects. In a subgroup analysis of the 1685 participants living at home, the variable meal provision was also included.

Paper II used Cox proportional hazards regression models for multivariate analyses, with nutritional status as the main variable of interest. The latter was entered as a three-level (well-nourished, at risk of malnutrition, malnourished) categorical variable, with well-nourished used as the reference category. The participants’ characteristics at baseline were considered as potential confounders. The analyses were performed in four steps. In the first step, nutritional status and potential confounders were entered into separate Cox regression models. In the second step, variables that were significant in the first step were entered into a multivariate Cox regression model (base model). In the third step, non-significant variables were removed from the base model through a backward selection procedure until the model included only significant variables (reduced model). In the fourth step, all confounding variables included in the reduced model were tested for interaction effects with nutritional status, and significant effects were then added to the reduced model. Finally, non-significant variables were removed through a backward selection procedure until the model included only significant variables (final model). All regression models were hierarchical.

For all statistical tests, a two-sided p-value < 0.05 was considered significant. All analyses were performed in IBM SPSS Statistics 18/20.

**Ethical considerations**

The study was approved by the Uppsala Ethical Review Board (approval number: 2007-323). All participants provided their written informed consent before entering the study. If a participant was unable to communicate, a relative was asked if he/she objected to the patient’s participation in the study.
Results

Nutritional status (Paper I)
The mean age ± SD of the included patients was 78.1 ± 7.8 years at baseline, which was significantly lower than that of those excluded (mean age 82.0 ± 8.2 years; \(p < 0.001\)). Women were predominant among both the included (56.0%) and excluded (53.3%) patients. The sex distribution did not differ between those excluded and those included (\(p = 0.266\)). Most of the participants lived at home (\(n = 1685; 95.1\%\)) before their admission to hospital, and the others lived in a nursing home (\(n = 86; 4.9\%\)). According to the MNA, 35.5% (\(n = 629\)) of the participants were well-nourished, 55.1% (\(n = 976\)) were at risk of malnutrition, and 9.4% (\(n = 166\)) were malnourished. The participants from medical, surgical and orthopaedic clinics did not differ significantly regarding nutritional status (\(p = 0.382\)).

Risk factors for malnutrition (Paper I)
In the multinomial logistic regression analysis, an overnight fast >11 hours was associated with risk of malnutrition (odds ratio (OR) 1.46, 95% confidence interval (CI) 1.14–1.87) and being malnourished (OR 1.67; 95% CI 1.04–2.69). Fewer than four eating episodes a day was associated with both risk of malnutrition (OR 1.88; 95% CI 1.52–2.32) and being malnourished (OR 3.10; 95% CI 2.14–4.49). In a subgroup analysis (\(n = 1685\)) that excluded those living in a nursing home, not cooking independently was associated with both risk of malnutrition (OR 1.95; 95% CI 1.30–2.93) and being malnourished (OR 5.04; 95% CI 2.95–8.61). The association between overnight fast >11 hours and malnutrition was no longer significant in the malnourished group not living in a nursing home.

Preterm death (Paper II)
A total of 1767 participants were followed up in the cohort study. The follow-up period was between 35 and 50 months (median 3.5 years). During this period, 37% (\(n = 655\)) died. The survival curves for the three nutritional status groups are shown in Figure 2. At the 50-month follow-up, survival was 75.2% (\(n = 472\)) for the well-nourished group, 60.0% (\(n = 584\)) for those at risk of malnutrition, and 33.7% (\(n = 56\)) for the malnourished (\(p < 0.001\)).
Figure 2. Kaplan–Meier survival curves according to Mini Nutritional Assessment categories (well-nourished, at risk of malnutrition, or malnourished). There were significant differences in survival among the three nutritional status groups (log-rank test \( p < 0.001 \)).

In univariate Cox regression, the hazard ratio (HR) (95% CI) for all-cause mortality was 1.79 (1.49–2.15) for the group at risk of malnutrition \( (p < 0.001) \) and 4.00 (3.13–5.11) for the malnourished group \( (p < 0.001) \), compared with the well-nourished group. After adjusting for confounding variables in the final multivariate Cox regression model, the mortality risks were still substantially higher in the group at risk of malnutrition (HR 1.56; 95% CI 1.18–2.07) and the malnourished group (HR 3.71; 95% CI 2.28–6.04) compared with the well-nourished.

Excluding the 33 participants with dementia from the final Cox regression model decreased the HR to 1.54 (1.16–2.05) for the group at risk of malnutrition and increased the HR to 3.86 (2.36–6.31) for the malnourished group.
Discussion

Nutritional status (Paper I)
In the cross-sectional study, more than half of the study population was at risk for malnutrition and almost one out of 10 were malnourished. The prevalence of malnutrition was lower than expected; previous studies using the MNA in Sweden have estimated the prevalence among older people in hospitals to 26 %,\textsuperscript{41} and internationally the prevalence of malnutrition in hospitals using the MNA varies between 23 and 38.7 %.\textsuperscript{7,12,13} One possible explanation for this difference is that the most frequent reason for not participating in the cross-sectional study was “unable to communicate and no relative could answer the questions” (n = 356). The excluded patients were also significantly older than the included patients. Thus, it is reasonable to assume that those with multimorbidity were excluded from the study and that this can partly explain the relatively low prevalence of malnutrition. Another possible reason is that almost all participants (95.1%) were living at home before hospital admission and the remaining (4.9%) came from nursing homes. According to previous Swedish studies, the prevalence of malnutrition in older people living at home is low (0–1%),\textsuperscript{14,15} compared with those living in nursing homes (30%).\textsuperscript{18} The malnutrition prevalence in the present study is consistent with that of a previous Swedish study of older people receiving support at home, which reported an 8% prevalence of being malnourished and 41% prevalence of being at risk of malnutrition.\textsuperscript{28}

Risk factors for malnutrition (Paper I)
The mealtime habits, length of overnight fast, and number of eating episodes per day were associated with both risk of malnutrition and being malnourished. These findings support the nutritional recommendations for the Nordic countries, which state that the overnight fast should not exceed 11 hours in older people and that adults should have at least four eating episodes per day.\textsuperscript{31} The findings also support the recommendations from the National Board of Health and Welfare in Sweden, which includes an overnight fast of <11 hours in the quality indicator “good meal pattern”, for comparing the quality of health care in the Swedish municipalities.\textsuperscript{32} In the subgroup analysis of participants living at home, the association between malnutrition and overnight fasting was no longer significant (p = 0.158). One explanation for this may be a decisive loss of statistical power when those living in nursing homes were excluded from the analysis, since this group included 15.7% (n = 26) of the malnourished participants.

Not cooking independently was associated with both risk of malnutrition and being malnourished. One explanation may be that older people at risk of malnutrition use meals on wheels more frequently and have a reduced function in daily life activities compared with the well-nourished.\textsuperscript{28}
This association may be bidirectional; that is, the decline in function, which increases the need for help (e.g., in the form of meals on wheels), can both be a cause and an effect of malnutrition. Regardless of the underlying reason, older people who do not have the strength or ability to cook independently should be recognized as individuals at risk of malnutrition.

Preterm death (Paper II)
In this prospective cohort study of 1767 participants ≥65 years of age, nutritional status defined according to the three categories of the full MNA was independently associated with preterm death. Findings from other studies support a relationship between nutritional status and mortality. A literature review from 2012 that analysed 28 papers evaluating different nutritional screening tools (NSTs) and their relationship with mortality reported an association between poor score on the NSTs and mortality. However, this review did not specifically focus on whether there is a relationship between nutritional status according to the MNA and mortality in older people in hospital. Further, most studies have either analysed the importance of the total MNA score or use varying methods of subcategorization. Fewer studies have investigated the three nutritional status groups separately.

A large study from Taiwan (n = 2802), which included independently living older people residing in the community, reported a HR of 2.4 for risk of malnutrition and 6.5 for being malnourished at the four-year follow-up. However, this study did not adjust for covariates such as concomitant diseases, but only for sex and age, and it remains uncertain whether malnutrition is an independent risk factor for mortality. By contrast, a small Swedish study (n = 68) of older people receiving support at home found an OR of 3.3 (95% CI 1.1–9.8) for death at the three-year follow-up for the combined group of malnourished people and those at risk of malnutrition after adjusting for age and cardiovascular disorders.

Our results are consistent with those of previous studies that used the full MNA to examine the association between nutritional status and mortality in older people in a hospital setting. Most of these studies did not conduct any regression analysis, which is a limitation when analysing the predictive value of the MNA in an observational study. Only a few studies measured mortality after discharge from hospital. One Australian study (n = 476) used the Cox regression model to analyse long-term mortality and adjusted the analyses for major disease classifications at admission. The study was based on retrospective nutritional assessment data of older people who had already been assessed with the MNA at two rehabilitation hospitals before the study started. At the 18-month follow-up, the HR was 3.4 (95% CI 1.07–10.87) in the malnourished group. However, the survival analysis only included those who had survived 12 months. This introduces bias and hampers a direct comparison with our cohort, which exhibited substantial mortality in the first year of follow-up. By contrast, one prospective Scandinavian study (n = 101) adjusted the regression analysis for age, sex, and Charlton comorbidity index, but did not find an association between malnutrition assessed with the MNA and mortality at the one-year follow-up.
The prospective design of our cohort study, the large sample size, and the adjustment for several important confounders including comorbidities, contribute to clarifying the independent relationship between nutritional status defined by the MNA and mortality.

**Methodological considerations**

The major strengths of the two studies were the sample size, the use of a widely utilized instrument to assess nutritional status, and the training given to the health care professionals for interpreting the questions in the MNA and performing the measurements.

The strength in the cohort study was the limited number lost to follow up (n = 4) and the length of the follow-up. Study II is so far the largest study examining the relationship between mortality and the three nutritional status groups, as defined by the MNA (well-nourished, at risk of malnutrition, or malnourished) among older people admitted to hospital. From the clinical point of view, it is more relevant to examine the three nutritional status groups rather than to examine the overall MNA score (0–30) because these categories are used to screen patients for malnutrition in the municipalities and county councils in Sweden through the Senior Alert quality register.

The prospective study design in the cohort study allowed us to control for a number of comorbidities and several other patient characteristics recorded at baseline. This is essential when examining the independent relationship between nutritional status and mortality in an observational study. Other unrecognized potentially confounding factors may exist and these could affect the HRs. However, the large risk estimates did not change noticeably in the four-step regression model, making it unlikely that the results occurred by chance.

The major limitation of the cross-sectional study is the characteristics of the excluded patients. An analysis of the exclusion criteria showed that the most common reason for being excluded from the study was “unable to communicate and no relative could answer the questions”. The excluded patients were significantly older than those included. Consequently, the participants in the current study might have been healthier than the average population of older people found in hospitals, and the true prevalence of malnutrition may have been underestimated in the present population. Further, because study I was a cross-sectional study, no causal relationships could be identified. Factors identified as associated with malnutrition in the cross-sectional study could be risk factors for malnutrition but could also be a result of malnutrition. Regardless of the underlying reason, older people who have a long overnight fast, few eating episodes and do not have the strength or ability to cook independently should be recognized as individuals at risk of malnutrition.

A limitation in both studies is that the results cannot be generalized to institutionalized older people. The findings from this study relate to those who were living at home before admission to hospital, as only a minority (4.9%) came from nursing homes.
General discussion

Despite the high frequency and serious consequences of malnutrition, as demonstrated in the present and in previous studies, the prevention and treatment of malnutrition do not currently receive appropriate attention. Increased awareness of the importance of nutritional screening is needed. There have been recent initiatives to promote nutritional care both in Europe and on a national level. According to the recommendations for food and nutritional care in European hospitals, all patients admitted to hospital should be screened regarding their nutritional status. Further, the national quality register (Senior Alert) introduced in the municipalities and county councils in Sweden incorporate the MNA screening instrument. This represents good progress in the process of improving nutritional care and implementing the resolution from the Council of Europe in the Swedish health and social care system.

The two studies in this thesis provide additional knowledge about the current nutritional situation among older people admitted to hospital. Several different international studies have used the MNA instrument for nutritional assessment of older people admitted to hospital. However, on a national level, no large Swedish study has estimated the prevalence of malnutrition exclusively in older people admitted to hospital. The cross-sectional study provides up-to-date data of the prevalence of malnutrition, as defined by the MNA, in older people admitted to hospital before the national quality register was implemented. Paper I is also the first study to report an association between malnutrition and the length of overnight fasting and number of eating episodes per day. These parameters are included in the quality indicator "good meal pattern" in Swedish municipality elderly care and in the national quality register Senior Alert. Hence, the current study supports the importance of care givers taking action to decrease the length of the overnight fast and to increase the number of daily eating episodes in older people at risk of malnutrition. The cohort study demonstrates the independent role of nutritional status as a predictor of preterm death and confirms previous data on the consequences of malnutrition. There was a profound effect on survival in this study involving routine intervention that was not directed specifically against malnutrition.

Screening for malnutrition is an important first step towards increased awareness. The screening process is a prerequisite for detecting nutritional problems and risk factors for malnutrition as early as possible and for promoting nutritional interventions. Nutritional supplementation and dietary advice results in a modest weight gain or weight maintenance. More research is needed to identify which interventions are most effective in terms of patient-centred outcomes and who would and would not benefit from such options. The high prevalence and serious consequences of malnutrition as demonstrated in the two studies in this thesis emphasize the urgent need to answer these questions.
Conclusions

- Two-thirds of older people admitted to hospital were malnourished or at risk of malnutrition, as defined by the full MNA.
- An overnight fast exceeding 11 hours, fewer than four eating episodes a day, and not cooking independently were associated with malnutrition and with risk of malnutrition.
- Nutritional status defined according to the three categories in the full MNA independently predicts preterm death in people 65 years and older.

Clinical implications

The evidence that the length of overnight fasting and number of eating episodes per day are possible risk factors for malnutrition is consistent with the current nutritional recommendations. This knowledge might stimulate caregivers to taking actions towards decreasing the length of the overnight fast and increasing the number of eating episodes per day in older people at risk of malnutrition.

The independent association between nutritional status assessed with the MNA and preterm death emphasizes the usefulness of the MNA for screening nutritional status. The finding that two-thirds of older people admitted to hospital were malnourished or at risk of malnutrition, and thus had an increased risk of death, underline the importance of screening for nutritional status in older people and taking appropriate actions to counteract malnutrition. It is unknown which interventions are most effective and to whom these interventions should be targeted however, the present study supports the actions of policymakers in continuing to establish effective interventions against malnutrition in older people admitted to hospital. Large-scale prospective studies are needed to evaluate the effect of nutritional interventions in terms of quality of life, functional status, and survival.
Sammanfattning, Summary in Swedish

Trots den höga förekomsten och de allvarliga konsekvenserna av protein-energi malnutrition (häröfter kallat undernäring) är prevention och behandling av undernäring inte tillräckligt uppmärksammat. Ökad medvetenhet om vikten av nutritionsscreening bland äldre personer är nödvändigt. Det övergripande syftet med denna avhandling var att öka vår nuvarande kunskap om undernäring och konsekvenserna av ett försämrat nutritionsstatus med avseende på en för tidig död, samt att identifiera möjliga riskfaktorer för att utveckla undernäring bland äldre personer. Syftet med delarbete I var att uppskatta prevalensen av undernäring samt att undersöka sambandet mellan måltidsvanor, måltidsförsörjning och undernäring bland äldre personer som skrivs in på ett svenskt sjukhus. Syftet med delarbete II var att undersöka om nutritionsstatus definierat enligt de tre kategorierna i hela MNA instrumentet är en oberoende prediktor för en för tidig död hos äldre personer.


Utav 1771 undersökta deltagare var 35,5 % välnärda, 55,1 % hade risk för undernäring och 9,4 % var undernärda vid baslinjen. En nattfasta > 11 timmar var associerad med risk för undernäring (odds ratio (OR) 1,46; 95 % konfidensintervall (CI) (1,14–1,87) och undernäring (OR 1,67; 95 % CI 1,04–2,69). Dessutom, färre än fyra ättillfällen per dag var associerad med risk för undernäring (OR 1,88; 95 % CI 1,52–2,32) och undernäring (OR 3,10; 95 % CI 2,14–4,49). Slutligen, att inte laga mat själv var också associerat med risk för undernäring (OR 1,95; 95 % CI 1,30–2,93) och undernäring (OR 5,04; 95 % CI 2,95–8,61).

Vid uppföljning efter 50 månader var överlevnaden 75,2 % för välnärda deltagare, 60,0 % för dem med risk för undernäring och 33,7 % för undernärda. Efter justering för störningsfaktorer (confounders), var hazard ratio (95 % CI) för total mortalitet 1,56 (1,18–2,07) hos dem med risk för undernäring och 3,71 (2,28–6,04) för de undernärda. Nutritionsstatus definierat enligt de tre kategorierna i hela MNA var en oberoende prediktor för en för tidig död hos personer 65 år och äldre.

Denna avhandling ger ytterligare kunskap om den aktuella näringsmässiga situationen bland äldre personer som skrivs in på sjukhus. Den höga förekomsten och de allvarliga konsekvenserna av undernäring som framkommit i denna avhandling, understryker vikten av screening och att vidta åtgärder för att motverka undernäring. Uppgifterna om nattfastans längd och antalet ättillfällen per dag som möjliga riskfaktorer för undernäring är föreligna med de nuvarande näringsrekommendationerna. Denna kunskap kan stimulera vård- och omsorgspersonal till att minska nattfastans längd och öka antalet ättillfällen bland äldre personer som har risk för undernäring.
Forthcoming research

Paper III

The association between nutritional status in older people admitted to hospital and energy and nutrient intake 10 years earlier.

**Aim:** To analyse the associations between current nutritional status in older people admitted to hospital and their previous dietary intake.

**Design:** A prospective cohort study.

**Participants:** The study population comprises 728 participants whose nutritional status was assessed in a cross-sectional study ($n = 1771$) performed in 2008–2009 and who also participated in two cohort studies of eating habits in 1997.

**Data collection:** The personal identification number of the participants in the cross-sectional study was matched with the personal identification number from two cohort studies—the Swedish Mammography Cohort (SMC) and the Cohort of Swedish Men (COSM)—to identify participants in both studies. The participants answered a food frequency questionnaire (FFQ) in 1997, and the results of the FFQ will be used to analyse the associations between previous dietary intake and malnutrition 10 years later.

**Progress:** Data have been collected and will be analysed in autumn 2013.

Paper IV

The association between nutritional status in older people admitted to hospital and health care consumption during the subsequent two years.

**Aim:** To analyse the association between nutritional status and health care consumption during the subsequent two years after assessment of nutritional status at hospital.

**Design:** A prospective nested case–control study.

**Participants:** All malnourished participants from a cross-sectional study performed in 2008–2009 will comprise the cases ($n = 166$) and will be matched against an equal number of well-nourished controls from the same study ($n = 166$). The controls will be matched for sex and family practitioner.

**Data collection:** The participant’s health care consumption will be followed up two years after the nutritional assessment in 2008–2009. Data on health care consumption will be collected through the hospital inpatient care, hospital outpatient care, primary health care, and the health care system in the municipalities. Drug prescription data will be collected through the Swedish Drug Register.

**Progress:** Data will be collected during autumn 2013 and spring 2014, and the analyses are planned to take place in autumn 2014 and spring 2015.
References


