# Unravelling decline of physical functioning in acutely hospitalized older patients

## From risk factors to targeted intervention

Jesse J. Aarden

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Thesis University of Amsterdam, the Netherlands

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# Unravelling decline of physical functioning in acutely hospitalized older patients

**From risk factors to targeted intervention**

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# General introduction

# General introduction

The number of older people around the world is rapidly increasing and will continue to increase in the coming decades. Ensuring that healthcare and social systems adjust to this demographic shift is a major global challenge. Between 2015 and 2050, the proportion of the world's population over 60 years of age is estimated to almost double from 12% to 22%.[1] This will increase the number of older adults with chronic diseases and consequent disabilities. A cross-sectional study from a database of 1.8 million older adults from Scotland reported that 42% of the respondents had one or more morbidities and that 23% had multiple morbidities.[2] In addition, over 46% of adults aged 60 years and over have disabilities, which means they cannot independently perform all basic activities of daily life.[3]

The ability to perform basic activities in daily life (ADLs) depends on multiple factors, which are classified in the International Classification of Functioning, Disability and Health (ICF) framework. The ICF framework is the standard, holistic view on functioning in daily life.[4] It describes different domains of functioning and their impact on daily life. Physical functioning is defined by body functions, activities, and participation while disability is defined by impairments, limitations, and restrictions. These domains are influenced by personal and environmental factors (Figure 1), which can facilitate participation but also can serve as barrier for physical functioning. The ICF framework classifies functioning and disability associated with health while the International Classification of Diseases (ICD) classifies the diagnosis of diseases. The ICD and ICF are complementary, and users are encouraged to use them together.[4]

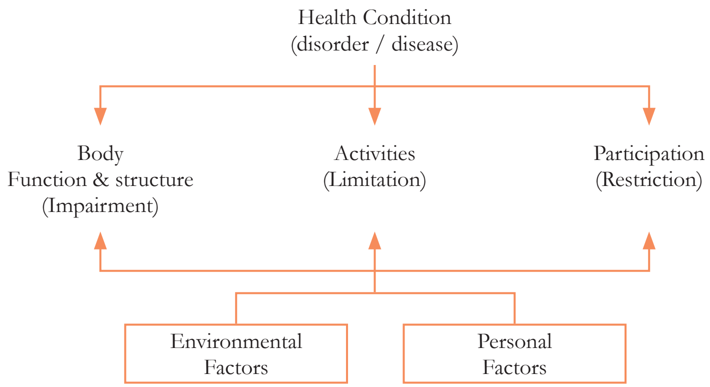


**Figure 1.** International Classification of Functioning, Disability and Health of the World Health Organization

The increase in older adults with chronic conditions and disabilities has increased healthcare utilization as these individuals are regularly hospitalized because of their disabilities.[5] Acute hospitalization of older patients has been associated with comorbidities, multimorbidities, polypharmacy and other physical and psychosocial problems. Older adults are frequently admitted to hospital with acute illness or injuries.[6] These acute illnesses are responsible for 50% of all new-onset disabilities in general older populations;[7] 30–60% of these individuals experience hospital-associated disability (HAD), even when the illness is successfully managed.[8-10] The loss of ADLs after hospitalization reduces self-care, independent living and participation in society and increases the dependency on care and/or caregivers. This negative spiral increases the demand for long-term healthcare services and costs for society.[11,12]

## Hospital-associated disability

HAD is defined as the development of new disabilities and reduced ADLs after acute medical illness with hospitalization.[9] Older adults with HAD have an increased chance of readmission, institutionalization, and mortality and a reduced quality of life. Identifying the risk factors that contribute to the decline in daily activities and independency is crucial to preventing functional decline after hospitalization.[13] Covinsky et al.[9] have described risk factors for HAD in older patients (Figure 2).

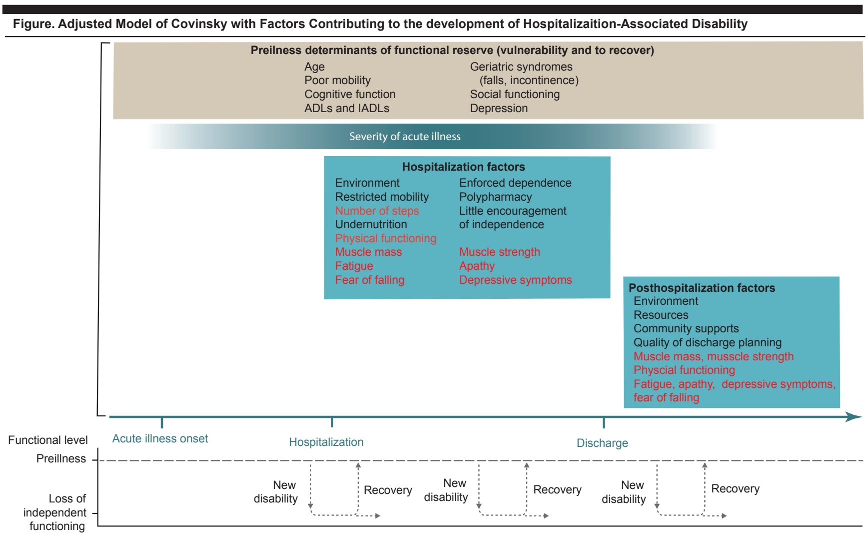


**Figure 2.** Factors contributing to Hospitalization-Associated Disability according to Covinsky et al. 2011 (printed with permission)

In the upper part of the Covinsky model, risk factors for HAD are described, including pre-illness determinants of functional reserve (vulnerability and capacity to recover), the severity of acute illness, hospitalization factors, and post-hospitalization factors.[9] Between acute onset of illness with hospitalization and hospital discharge, multiple risk factors can lead to a new disability with reduced physical functioning and recovery. This model shows that HAD is multifactorial and cannot be effectively treated by focusing on one aspect. Readmission and mortality were reduced by a systematic comprehensive geriatric assessment, followed by a transitional care programme that considered the risk factors described by Covinsky et al.[9] However, this approach did not improve self-reported ADL functioning in acutely hospitalized older patients.[14]

After discharge from hospital, exercise interventions may improve physical functioning in older individuals. However, whether exercise interventions improve physical functioning during hospitalization remains uncertain.[15-18] The success of exercise interventions during hospitalization may be hindered by several factors, including a short hospital stay, uncertainty about the minimal level of physical activity needed to improve physical functioning,[18] inappropriate selection of outcome measures and lack of focus on geriatric conditions that hinder physical activity. A recent study showed that a simple and safe inpatient exercise programme can reduce HAD in older patients during hospitalization.[19] However, whether exercise interventions can reduce HAD in acute hospitalized older patients with complex care needs after they are discharged from hospital remains unclear.

The following gaps in our knowledge of physical functioning in acutely hospitalized older patients have been identified:

1. Risk factors regarding physical functioning in acutely hospitalized older patients have been identified, but we do not know how these factors interact.
2. The level of physical functioning is rarely reported in published studies.
3. Longitudinal data on physical functioning after acute hospitalization are scarce.
4. Physical activity after discharge from hospital is not frequently reported.
5. Healthcare professionals have insufficient information to offer tailored interventions after discharge from hospital.

These gaps contribute to the development of HAD and are discussed in the following paragraphs.

## Risk factors for development of disability

**Pre-illness determinants of functional reserve**

Risk factors for HAD and physical functioning include numerous pre-illness determinants of functional reserve such as old age,[20] poor mobility,[21] decreased cognitive functioning,[22] geriatric syndromes,[23,24] and poor social functioning.[25]

In general, pre-illness determinants and self-reported activity levels before hospitalization are determined by a comprehensive geriatric assessment at admission, but longitudinal follow ups are frequently lacking. The level of physical functioning is also increasingly being assessed by performance tests to determine a patient's actual physical ability.[26,27] In the last decade, researchers and clinicians have become interested in assessing muscle mass, muscle strength and physical functioning in older patients, as these are preconditions for performing daily activities. For example, sarcopenia (low muscle mass and strength)[26] and frailty (weight loss, low muscle strength, exhaustion, slowness, and low physical activity level)[28] have been identified as predictors of decreased physical functioning in older patients and are associated with HAD.[26,29-32] Being able to objectively assess sarcopenia and frailty could improve our understanding of HAD and promote the development of effective interventions.

**Severity of acute illness and hospitalization factors**

An acute medical illness with inflammation, comorbidities, inactivity[33,34] and poor nutritional intake[35] leads to a catabolic state in which proteolysis is higher than protein synthesis.[36,37] This loss of protein can reduce muscle mass, muscle strength and physical functioning and can indicate that the underlying illness is severe and may lead to further deconditioning.[38] Some studies have shown that the medical condition was improved, that muscle mass and muscle strength not significantly altered in older adults during acute hospitalization and that physical functioning did not completely recover after discharge from hospital.[39,40] This discordance between the recovering from a medical illness and losing physical functioning is a common sequela of acute hospitalization in older adults.[41] Although longitudinal studies are lacking, it has been hypothesized that physical functioning and muscle mass and muscle strength do not recover completely in older patients after acute hospitalization. Additional factors such as inadequate environment, restricted mobility, undernutrition, enforced dependence, polypharmacy, and little encouragement to be independent can increase the risk of HAD.[10,21] Limited physical activity during hospitalization may also play a role.[21,42] One study showed that taking less than 900 steps per day during hospitalization was associated with HAD at discharge;[43] taking 2000–9000 steps per day has been recommended for healthy individuals.[44] In this thesis, we will gain insight into activity levels during and after hospitalization and how these activity levels associate with HAD.

**Post-hospitalization factors**

As described by Covinsky et al.,[9] several risk factors after discharge from hospital have been associated with HAD, such as inadequate environment, limited resources, minimal community support and poor discharge planning.[9] These factors align with the environmental factors in the ICF model. Other post-hospitalization factors can also impair recovery from HAD. Psychosocial factors such as apathy, fear of falling and fatigue are highly prevalent among older patients and have been reported as barriers to the recovery of muscle mass, muscle strength and physical functioning after hospitalization.[24] Muscle mass, muscle strength and physical functioning are not objectively assessed in the current mode of Covinsky et al.[9] However, knowing how these factors change over time in relation to psychosocial factors after hospitalization is crucial to determine the causes of HAD. This is currently undefined in the literature.

## Hospital-ADL study

We addressed this knowledge gap in our observational longitudinal hospital-associated disability and impact on daily life (Hospital-ADL) study, which was designed by an interprofessional team of clinicians and researchers (physical therapists, psychologists, nurses, geriatricians).[45] The aim of the Hospital-ADL study was to investigate changes in physical functioning, muscle mass and muscle strength in acutely admitted older patients and to determine how these changes interacted with psychosocial factors and affected health outcomes during and after discharge from hospital. Data collection started in October 2015 at the Amsterdam University Medical Centers (UMC) location Academic Medical Center (AMC) and was completed in February 2018. Patients were recruited from six hospitals in the Netherlands and data was collected at hospital admission, hospital discharge and at home visits one- and three months after hospital discharge. The Hospital-ADL study revealed underlying mechanisms behind HAD in the three months after hospitalization. These underlying mechanism with (an interaction of) demographic, psychosocial and physical factors can be used to develop interventions that prevent HAD and enhance recovery.

## Towards tailored interventions

To develop effective interventions for acutely hospitalized older patients with complex care needs, it is crucial to thoroughly understand how all ICF factors affect physical functioning. Muscle mass and strength are important for restoring physical functioning. Starting exercises in hospital and immediately after discharge from hospital can help to rebuild muscle mass and muscle strength. Although much is known about how exercise increases muscle mass, muscle strength and physical functioning,[46-50] an exercise programme for older adults after acute hospitalization is still lacking. Findings from the Hospital-ADL study can be used by healthcare professionals to develop an exercise intervention that is tailored to acutely hospitalized older patients. In the absence of randomized clinical trials focusing on the recovery of older patients after discharge from hospital, information from experts in the field is essential and can provide starting points for developing such an intervention. To this end, this thesis includes a Delphi consensus study, which collected expert opinions on a resistance exercise training (RET) intervention for this population.

## Aims and outline of this thesis

The overall aim of this thesis is to unravel the mechanisms of HAD by determining changes in muscle mass, muscle strength and physical functioning during and after hospitalization and how these changes associate with psychosocial functioning in acutely hospitalized older patients. The specific aims of this thesis are to:

1. Examine changes in physical functioning. muscle mass and muscle strength after acute hospitalization.
2. Identify physical risk factors for poor health outcomes.
3. Provide evidence to develop an exercise intervention that is tailored to acute hospitalized older patients to prevent HAD and improve independent living.

In **Chapter 2**, the impact of hospitalization on physical functioning and recovery over time in older patients who underwent hip fracture surgery is described. **Chapter 3** presents the Hospital-ADL study and summarizes the study design and assessments that were performed to unravel the mechanism of Hospital Associated Disability. **Chapter 4** describes the longitudinal association between muscle strength and mobility in acutely hospitalized older patients. **Chapter 5** focuses on changes in muscle mass, muscle strength and physical functioning in older patients during hospitalization and after discharge. **Chapter 6** determines how the number of steps taken during hospitalization and in the first week post-discharge affect functional decline after discharge from hospital. **Chapter 7** presents a Delphi consensus study, where an international panel of experts discussed a core outcome set of assessment tools and an exercise intervention for older patients after discharge from hospital. Finally, in **Chapter 8**, we summarize the results of the different chapters and discuss the methodological considerations and the clinical, educational, and scientific implications of our findings on future research.

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2

# Hip fractures in older patients: trajectories of disability after surgery

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## Abstract

**Background:** Hip fracture in older patients often lead to permanent disabilities and can result in mortality.

**Objective:** To identify distinct disability trajectories from admission to one-year post-discharge in acutely hospitalized older patients after hip fracture.

**Design:** Prospective cohort study, with assessments at admission, three-months, and one-year post-discharge.

**Setting and participants:** Patients ≥ 65 years admitted to a 1024-bed tertiary teaching hospital in the Netherlands.

**Methods:** Disability was the primary outcome and measured with the modified Katz ADL-index score. A secondary outcome was mortality. Latent class growth analysis was performed to detect distinct disability trajectories from admission and Cox regression was used to analyze the effect of the deceased patients to one-year after discharge.

**Results:** The mean (SD) age of the 267 patients was 84.0 (6.9) years. We identified 3 disability trajectories based on the Katz ADL-index score from admission to one-year post-discharge: 'mild'- (n=54 (20.2%)), 'moderate'- (n=110 (41.2%)) and 'severe' disability (n=103 (38.6%)). Patients in all three trajectories showed an increase of disabilities at three months in relation to baseline and 80% did not return to baseline one-year post-discharge. Seventy-three patients (27.3%) deceased within one-year post-discharge, particularly in the 'moderate'- (n=22 (8.2%)) and 'severe' disability trajectory (n=47 (17.6%)).

**Conclusions:** Three disability trajectories were identified from hospital admission until one-year follow-up in acutely hospitalized older patients after hip fracture. Most patients had substantial functional decline and 27% of the patient's deceased one-year post-discharge, mainly patients in the 'moderate'- 'and severe' disability trajectories.

## Background

Hip fracture is often a fatal event in older people; approximately 30% die within twelve months post-discharge[1,2] and of those who survive, many patients experience permanent disabilities.[3] The incidence of hip fractures increases substantially with age. Incidence rates of 22 and 24 per 100.000 people for male and female at 50 years towards 630 and 1289 per 100.000 people for male and female at 80 years of age have been reported.[4] One year after hip surgery, 29-50% of older patients do not reach pre-operative levels of physical functioning.[3,5]

Well-known risk factors for permanent disability after hip fracture are premorbid functional status, higher levels of physical disability at the time of admission to the hospital, presence of dementia, delirium, co- and multimorbidity, type of surgery and older age. Not only the hip fracture itself, but also prolonged hospitalization after surgery contribute to disability.[5-9] These risk factors also influence the rehabilitation strategies and the improvement and adaption in daily activities. However, not all older patients after hip surgery show a similar development of physical disability over time and study populations are heterogeneous.[9]

Some studies detected distinct disability trajectories in older patients after hip fracture[3,10,11] although the number of included patients with hip fracture was limited or the primary focus of these studies was on fall incidents. Identification of different disability trajectories in hospitalized older patients after a hip fracture might provide specific starting points of personalized rehabilitation as well as palliative care at post-hospital discharge.

Therefore, the aim of the study was to identify distinct disability trajectories from admission to one-year post-discharge in acutely hospitalized older patients (≥ 65 years of age) after a hip fracture, whereas the second aim was to study mortality in relation to disability trajectories.

## Methods

### Design and setting

A prospective study was performed, including older patients with a hip fracture who were admitted from 2004-2009 to the Academic Medical Center (AMC) Amsterdam, the Netherlands, a 1024-bed tertiary university teaching hospital. The Medical Ethics Committee of the AMC approved the study, and the patients or proxies provided written informed consent before inclusion.

### Subjects

Patients were eligible to participate if they were ≥ 65 years of age and were acutely admitted with a hip fracture to the orthopedic or traumatology wards. Patients were excluded if 1) no informed consent was given 2) the physician indicated that the patient was too ill to participate, 3) transfer to the intensive care unit or coronary care was indicated or 4) inability to speak or understand the Dutch language.

**Data collection**
Trained research nurses were part of the geriatric consultation team (consisting of at least one clinical nurse specialist and one geriatrician) and visited all patients with a hip fracture on the first day after hospital admission. After the patient, or the proxy in case of cognitive impairment (Mini Mental State Examination score of 20 or lower), provided informed consent, the nurse performed a comprehensive geriatric assessment. Clinical characteristics were collected at hospital admission (T0), three months (T1) and twelve months (T2) post-discharge. At hospital admission this was a personal interview, at three- and twelve-months post-discharge a telephone assessment was performed. First, we checked in the electronic medical record if the patient was deceased. If so, the date of death was denoted. Patients who were alive were interviewed by phone. The scores of the tests were administered as well as the living situation.

**Primary and secondary outcome**
Disability in activity daily living (ADL) was our primary outcome of interest and was measured with the modified Katz ADL index score at hospital admission, three- and twelve-months post-discharge. At admission the patient or proxy was asked about the situation two weeks prior to hospital admission to assess premorbid ADL functioning. The modified Katz ADL index score measures limitations of patients in the domains of physical activities of daily living (ADL) and instrumental activities of daily living (IADL). The modified Katz consists of fifteen items.[13] The first six items of the modified Katz are equal to the items of the Katz-ADL index and assess the ability of an individual to independently bath, dress, use a toilet, transfer to and from a chair, the use of incontinence products and the ability to eat without help. The other items address whether a person needs help to use a telephone, to go shopping, to prepare food, to perform household tasks, to travel, to take medication, to handle own finances, brushing and combining hair or shaving and whether one needs help walking about. Each item was scored as independent (0) or dependent (1). The maximum score of dependency is fifteen. In this study disability was defined as a loss of at least one point on the Katz ADL index score. The modified Katz questionnaire has shown to be valid and reliable.[14,15]

**Covariates**
*Cognition:* Patients were screened on global cognitive impairment, measured with the 11-item Mini Mental State Examination (MMSE). Based on the number of correct responses, the MMSE provides a total score ranging from 0 to 30. A score less than 24 denote cognitive impairment[16] and patients were categorized in two groups (cognitive impairment yes/no). Patients with a score of 21 points or higher were interviewed themselves. When the score was between 16-20 points, indicating moderate global cognitive impairment, the score was crosschecked with their primary proxy. In case of disagreement, the response of the proxy was scored. Below or equal to 15 points, data were obtained from the proxy.

*Comorbidity:* The Charlson Comorbidity Index (CCI) was used at baseline and assesses the number and severity of comorbidities. The score on the CCI has an index range from 0-31, with a higher score indicating a higher number of comorbidities and more severe co-morbidities. The method of classifying comorbidity provides a simple, applicable, and valid method of estimating risk of death from comorbid disease for use in longitudinal studies.[17]

In addition, mean age, marital status, living arrangement, length of stay in hospital (LOS) body mass index (BMI) were assessed.

**Statistical methods**

To identify homogeneous subgroups of patients with distinct disability as measured by the Katz, latent class growth analysis (LCGA) was used. LCGA estimates each participant's probabilities for membership in a specific subgroup, with assignment to a specific trajectory based on the highest probability for membership. We used PROCTRAJ in SAS software.[18] The Bayesian information criterion (BIC) was used whether each trajectory was best fit by intercept only or by linear, quadratic, or cubic terms. The final model was evaluated by using average posterior probabilities of class membership; an average value of 0.9 or higher within each trajectory was considered as an excellent fit, and less than 0.7 was considered poor.[19] A sensitivity analysis was performed to evaluate the effect of missing data on the estimations for the missing data. In this analysis all missing data were excluded and the remaining data were used to identify trajectories.

After performing the LCGA analysis, subgroups were identified and the relevant descriptive statistics were generated on age, gender, marital status, living arrangement, years of education, comorbidity, Katz score, cognition, LOS and BMI. The differences between the subgroups and the differences within the groups for baseline, three months and twelve months were calculated by ANOVA. LCGA were performed using SAS software. Cox regression analysis was performed to investigate the effect of disability upon dying after one-year post-discharge, adjusted for age, gender and cognition. All analysis were performed in SPSS version 22. The Cox regression model was adjusted for age, gender, and cognition. Also, other analyses were done with SPSS. P-values $< 0.05$ were considered statistically significant.

## Results

**Study population**

A total of 267 patients were included in the study with a mean age (standard deviation (SD)) of 84.0 (6.9) years, 21% was male and 56% lived independently. Baseline characteristics are presented for the distinct subgroups and consisted of 54 patients (20%) in the 'mild' disability group, 110 (41%) in the 'moderate' disability group and 103 (39%) patients in the 'severe' disability group respectively

(Table 1). At baseline the subgroups were significantly different with regard to marital status, living arrangements, deceased within one-year post-discharge, length of stay (LOS), ADL disability and cognition.

**Table 1.** Baseline clinical characteristics of study population

| Variable | Total (n=267) | Mild disability (n=54) | Moderate disability (n=110) | Severe disability (n=103) | P-value |
|---|---|---|---|---|---|
| Age in years (mean (SD)) | 84.0 (6.9) | 78.7 (6.2) | 84.3 (5.9) | 86.5 (6.3) | NS |
| Gender n= (% male) | 65 (24.3) | 17 (31.5) | 24 (21.8) | 24 (23.3) | NS |
| Living alone n= (%) | 197 (73.8) | 34 (12.7) | 85 (31.9) | 78 (29.2) | P < 005 |
| Independent living n= (%) | 186 (70.0) | 53 (19.8) | 87 (32.6) | 46 (17.2) | P < 0.05 |
| Years of education (after 6th year) | 9.5 (3.6) | 10.8 (4.1) | 9.1 (3.1) | 8.7 (3.6) | NS |
| Charlson comorbidity 16index[a] | 6.2 (2.1) | 6.1 (13.8) | 6.1 (3.2) | 6.4 (2.0) | NS |
| Impairments in ADL and IADL[b] | 6.1 (3.9) | 1.5 (1.4) | 5.0 (2.1) | 9.7 (3.0) | P < 0.05 |
| Cognitive impairment[c] | 20.7 (7.5) | 26.3 (2.9) | 23.2 (5.0) | 14.0 (7.4) | P < 0.05 |
| Body Mass Index[d] | 24.5 (4.1) | 24.7 (4.2) | 24.9 (4.2) | 23.6 (4.0) | NS |

Abbreviations: SD, Standard Deviation; NS, Not Significant; P-value, probability value; ADL = Activity Daily Living; IADL = Instrumental Activities Daily Living.

[a] Charlson comorbidity index range 0-31

[b] Katz ADL range 0-15

[c] Mini Mental State Examination (MMSE) range 0-30

[d] Body Mass Index = square of the body height in kg/m2

**Disability trajectories**

Three disability trajectories were identified from admission to one-year post-discharge, classified as 'mild'-, 'moderate'- and 'severe' disability. The three disability trajectories differed already at baseline and this difference continued in the course over time (Table 2). Patients in the 'mild' disability group had a mean (standard deviation (SD)) admission score of 1.5 (1.4) on the modified Katz). The score of 1.5 increased at three months post-discharge to 3.7 (2.5) and improved at twelve-months post discharge to 2.4 (1.9) (p-value < 0.05). Trajectory 2 was classified as 'moderate' disability (mean (SD) score of 5.0 (2.1) at admission, with a significant increase towards 8.0 (2.4) at three months and 7.8 (2.3) one-year post-discharge (p-value < 0.05). Finally, trajectory 3 was identified as 'severe' disability (mean (SD) score 9.7 (3.0) at admission with a significant increase towards 13.2 (1.6) at three months and 12.9 (2.2) at one-year post-discharge (p-value < 0.05).

**Table 2.** Impairment in ADL measured with Katz in three subgroups

| | Baseline* (T0) | 3 months (T1) | 12 months (T2) | P-value |
|---|---|---|---|---|
| Mild disability trajectory (n=54) | 1.5 (1.4) | 3.7 (2.5) | 2.4 (1.9) | P < 0.05 |
| Moderate disability trajectory (n=110) | 5.0 (2.1) | 7.9 (2.4) | 7.8 (2.3) | P < 0.05 |
| Severe disability trajectory (n=103) | 9.7 (3.0) | 13.1 (1.6) | 12.9 (2.2) | P < 0.05 |
| Total group (n=267) | 6.1 (3.9) | 8.9 (4.2) | 7.8 (4.5) | P < 0.05 |

Abbreviations: ADL, Activity Daily Living; P-value: Probability value.
*Katz was measured at baseline 2 weeks prior to hospital admission

At admission patients in the 'mild' disability trajectory compared to the 'moderate'- and 'severe' disability trajectories lived significantly more often independently together with a wife or husband, less often had cognitive impairment and had a shorter length of stay (respectively for the 'mild'- 'moderate'- and 'severe' disability trajectories with a mean (SD) of 10.3 (6.3), 15.0 (11.1) and 19.7 (25.6)) days in hospital after surgery, whereas the amount of comorbidities, age, gender, years of education and BMI was not found to be significantly different between the trajectories (Table 1).

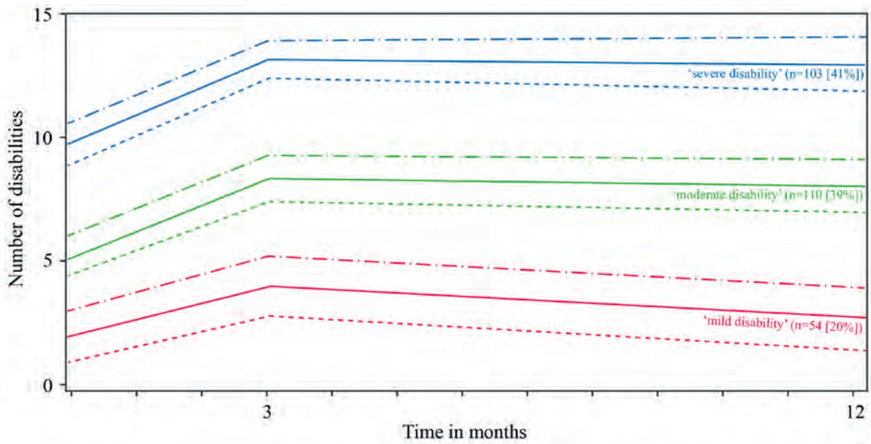


**Figure 1.** Trajectories of disability (mean and 95% confidence interval) measured by the modified Katz score in older hospitalized patients after hip fracture. Higher scores indicate worse outcome. Subgroup 1: 'mild' disability, subgroup 2: 'moderate' disability and subgroup 3: 'severe' disability. Measurements were at admission (baseline), at three months and twelve months after discharge from the hospital.

**Sensitivity analysis**

At baseline, data of all patients were available. At three- and twelve-months data of 98 patients were missing. The majority of the missing data was due to the fact that 73 (27.3%) patients were deceased within one-year post-discharge. In order to evaluate the robustness of the trajectories sensitivity analysis was performed on the remaining 169 patients, without the patients with one or more missing data. The results of the sensitivity analysis showed the same disability trajectories with the initial analysis.

**Mortality**

In total 73 (27.3%) patients were deceased within one-year post-discharge. In the 'severe' disability trajectory the number (percentage) of patients was 47 (17.6%), in the 'moderate' disability trajectory 22 (8.2%), and in trajectory 'mild' disability 4 (1.5%), respectively. At baseline the Katz-ADL score for deceased patients differed significantly of the non-deceased patients (mean score (SD): 8.3 (3.5) and 5.3 (3.8), respectively) (Table 3).

**Table 3.** Baseline clinical characteristics of the deceased versus non-deceased

| Variable | Total (n=267) | Non deceased (n=194) | Deceased (n=73) | P-value |
|---|---|---|---|---|
| Age in years (mean (SD)) | 84.0 (6.9) | 83.3 (6.5) | 85.8 (7.4) | NS |
| Gender n= (% male) | 65 (24.3) | 43 (22.2) | 22 (30.1) | NS |
| Impairments in ADL and IADL[a] | 6.1 (3.9) | 5.3 (3.8) | 8.3 (3.5) | $P < 0.05$ |
| Cognitive impairment[b] | 20.7 (7.5) | 22.2 (6.3) | 16.1 (8.8) | NS |

Abbreviations: SD, Standard Deviation; NS, Not Significant; P-value, probability value; ADL = Activity Daily Living; IADL = Instrumental Activities Daily Living.

[a] Katz ADL range 0-15

[b] Mini Mental State Examination (MMSE) range 0-30

Compared to patients in the 'mild' disability group, patients in the 'moderate'- and 'severe' disability group had a three and respectively eight times higher risk of mortality at one-year post-discharge (Hazard Ratio (HR) 2.98; 95% CI, 1.03-8.66 and HR, 7.96; 95% CI, 2.87-22.09, respectively). Cognition affected the HR of the 'moderate' disability group (2.42; CI: 0.83-7.10) in the 'severe' disability group (2.96; CI, 0,92-9.53). Age and gender did not change the HR of the Hazard proportional model.

## Discussion

The current study aimed to identify distinct disability trajectories from admission to one-year post-discharge in acutely hospitalized older patients (> 65 years of age) after hip fracture. We found three distinct disability trajectories ('mild', 'moderate', 'severe') from hospital admission to one-year post-discharge based on the modified Katz-ADL score in acutely hospitalized older patients after a hip fracture. Patients in the 'mild' disability trajectory almost completely returned to baseline functioning after one year, whereas patients in the 'moderate'- and 'severe' disability trajectories increased in disability until one-year post-discharge. The increase in disability in these trajectories was already achieved at three months and remained constant towards one-year post-discharge.

In total 73 patients (27.3%) died within one-year post-discharge, which is in line with the high overall mortality rates observed in other studies.[1,2] We found that patients in the 'moderate'- and 'severe' disability group had a three- and eight-times higher risk respectively of mortality at one-year post-discharge. Risk of dying was affected by cognition, with the strongest influence in the 'severe' disability group. This finding is in line with the review of Smith et al.[20] and may be related to additional factors such as a poorer general health. The manner in which cognition influences the risk of dying in the disability subgroups during hospitalization is unclear. In future studies the important role of cognition should be explored more into depth with emphasizes on the relation to severity of disability.

Studies on disability trajectories in older patients after hip surgery are scarce.[3,10] In the study of Gill et al.[10] four distinct recovery trajectories in older patients after fall incidents (no, little, gradual and rapid recovery) were identified. Patients were measured on a monthly basis before and after hospitalization. The study of Gill reported that the number of disabilities decreased in the first months after serious falls. Post-fall trajectories were consistently worse for hip fractures than for other serious injuries (such as rib- or pelvis fractures). In contrast, our study showed that the number of disabilities increased in the first three months and stabilized until one-year post-discharge. The difference in the first three months might be influenced by interviewing patients or proxy about their abilities two weeks prior to hospital admission. The number of disabilities in our study at baseline might be an underestimation at hospital admission, which could affect the course of disability in the first months.

Within patients with a hip fracture, identification of disability trajectories may have implications for clinical practice. It can be suggested that the three disability trajectories may lead to a more personalized approach. In patients in the 'mild'- and 'moderate' disability trajectories an interdisciplinary rehabilitation (including exercise) management might be indicated to prevent deterioration and to improve their functional performances. In patients within the 'severe' disability trajectory, due to the high number of deceased patients, palliative care might be indicated. Tseng et al[3] concluded in their study that distinct trajectories of functional recovery could serve as useful outcome measures in clinical research and practice.

De Morton et al[21] concluded that an interdisciplinary intervention including exercises might increase the proportion of patients discharged to home and reduce length and cost of hospital stay of acutely hospitalized older patients. Exercise goal setting and discharge planning in combination with patient contact time during hospitalization might improve effectiveness of the interventions. However, only few trials with a focus on exercises for this specific group were available in the literature review of the Morton et al..[21] Based on our results and the results of Gill et al and Morton et al., it can be hypothesized that highest effects of exercise interventions are to be expected in the first three months after surgical intervention.

Our study has some limitations that need to be considered when interpreting the results. First, in this prospective cohort study in older patients, data were missing on a substantial group of patients. These missing data were due to high mortality rates and loss of data due to various other reasons such as loss of forms at the wards. The missing data might have an effect on the outcome of three disability trajectories, and therefore we performed a sensitivity analysis. No differences were found when patients with missing data were excluded from analysis. Secondly this study was able to detect subgroups and trajectories based on functional ability in daily life but the number of patients in each group was limited. However, the three disability trajectories showed robustness, which means that the groups were homogeneous, and had the same course of disability. Thirdly, the study was only performed in a tertiary university teaching hospital where the rate of patients with complex needs is rather high. This might have had an effect on the number of patients in the 'moderate' and 'severe' disability trajectories. This limits generalizability. Finally, data in present study were collected in a time where medical interventions were different from the current interventions and this might have affected the results, although osteosynthesis in surgery is still used in the same way as before.

**Conclusion**

In conclusion older patients with hip fracture exhibit different degrees of functional recovery from hospital admission towards one-year follow-up: three disability trajectories from hospital admission towards one-year follow-up in acutely hospitalized older patients after a hip fracture were identified. Most patients had substantial decline and 27% of the patient's deceased one-year post-discharge. Future studies on rehabilitation management of older patients within the three disability trajectories are indicated. Patients in the 'moderate'- and 'severe' disability group had a three to eight times higher risk of mortality at one-year post-discharge.

**Acknowledgements**
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**Conflicts of interest**
All authors declare no conflict of interest.

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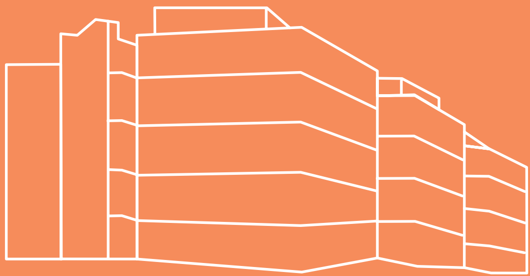
# Unravelling the potential mechanisms behind hospitalization-associated disability in older patients; the Hospital-Associated Disability and impact on daily Life (Hospital-ADL) cohort study protocol



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## Abstract

**Background:** Over 30 % of older patients experience hospitalization-associated disability (HAD) (i.e., loss of independence in Activities of Daily Living (ADLs)) after an acute hospitalization. Despite its high prevalence, the mechanisms that underlie HAD remain elusive. This paper describes the protocol for the Hospital-Associated Disability and impact on daily Life (Hospital-ADL) study, which aims to unravel the potential mechanisms behind HAD from admission to three months post-discharge.

**Methods/design:** The Hospital-ADL study is a multicenter, observational, prospective cohort study aiming to recruit 400 patients aged ≥70 years that are acutely hospitalized at departments of Internal Medicine, Cardiology or Geriatrics, involving six hospitals in the Netherlands. Eligible are patients hospitalized for at least 48 h, without major cognitive impairment (Mini Mental State Examination score ≥15), who have a life expectancy of more than three months, and without disablement in all six ADLs. The study will assess possible cognitive, behavioral, psychosocial, physical, and biological factors of HAD. Data will be collected through 1] medical and demographical data; 2] personal interviews, which includes assessment of cognitive impairment, behavioral and psychosocial functioning, physical functioning, and health care utilization; 3] physical performance tests, which includes gait speed, hand grip strength, balance, bioelectrical impedance analysis (BIA), and an activity tracker (Fitbit Flex®), and; 4] analyses of blood samples to assess inflammatory and metabolic markers. The primary endpoint is additional disabilities in ADLs three months post-hospital discharge compared to ADL function two weeks prior to hospital admission. Secondary outcomes are health care utilization, health-related quality of life (HRQoL), physical performance tests, and mortality. There will be at least five data collection points; within 48 h after admission (H1), at discharge (H3), and at one (P1; home visit), two (P2; by telephone) and three months (P3; home visit) post-discharge. If the patient is admitted for more than five days, additional measurements will be planned during hospitalization on Monday, Wednesday, and Friday (H2).

**Discussion:** The Hospital-ADL study will provide information on cognitive, behavioral, psychosocial, physical, and biological factors associated with HAD and will be collected during and following hospitalization. These data may inform new interventions to prevent or restore hospitalization-associated disability.

## Background

Studies have observed that at least 30 % of older patients hospitalized with an acute medical illness show a persistent decline in their ability to maintain Activities of Daily Living (ADLs).[1-5] Such activities are prerequisites to self-care and independent living and include bathing, dressing, transferring out of bed, eating, toileting, and being mobile in and around the house.[1,3-7] This decline has been denoted hospitalization-associated disability (HAD) and is defined as the loss of ability to perform one or more of the basic ADLs.[6]

HAD is an important problem; it is the leading cause of loss of independence at older age[4] and it is a complex and highly dynamic process with possible recurrent dis- ability episodes in older patients.[6,8] Research shows that older persons who have been hospitalized have a 60- fold increased risk to develop permanent disabilities.[9] The first month after hospital discharge has been identified as a critical period for recovery, after which disabilities have a high risk of becoming permanent.[3] Moreover, patients with new disabilities are at high risk for other adverse outcomes within three months post discharge: 20 % have readmissions,[10] and post-discharge mortality is 25 %.[1,3,11,12] In light of the high prevalence in older patients, and the rapid aging of western societies with a concomitant rise in hospitalizations, a better understanding of HAD is urgently needed.

Previous research has been able to identify a number of generic risk factors for hospitalization-associated disability such as older age,[5] the severity of acute illness, geriatric conditions, cognitive impairment and delirium.[1,6,13,14] However, a more fine-grained analyses and characterization of potentially modifiable risk factors is virtually absent from the literature. Little is known, for example, about: 1] the course of loss of muscle mass and strength, and the amount of physical activity older patients perform; 2] the association of cognitive, (psycho-) somatic, behavioral, and psychological restrictive symptoms with the onset and recovery from HAD within the critical period of three months post-discharge such as cognitive impairment, fatigue, pain, sleep quality, shortness of breath, dizziness, fear of falling, diminished self-efficacy, apathy, depression, and anxiety and; 3] the association of the inflammatory activity and related sickness behaviors with the onset and recovery from HAD. Moreover, most previous studies have utilized relatively long follow-up intervals (e.g., from admission to three months or more).[1-3,15] Thus information is lacking on events and processes that take place during the weeks after discharge, which are thought to be critical to recovery.

The current study – Hospital-Associated Disability and impact on daily Life (Hospital-ADL study) – aims to investigate cognitive, behavioral, psychosocial, physical, and bio- logical factors that may be associated with HAD in acutely hospitalized older adults, performing frequent assessments to capture their dynamic development from hospital admission to three months post-discharge.

This overall aim can be separated into the following five sub-ordinate aims:

1. To study the temporal profile of HAD (i.e., loss of ADL) from hospitalization to three months post-discharge.
2. To investigate the course of physical functions that are essential to support ADL, such as muscle mass, muscle strength, and physical performance and spontaneous activity, and test its predictive value for the onset and recovery from HAD, health care utilization, and health-related quality of life (HRQoL) at three months post-discharge.
3. To study the prevalence, incidence, and course of cognitive, (psycho-) somatic, behavioral, and psychological problems older patients experience from hospitalization up to three months post-discharge that might be restrictive in recovery from HAD post-discharge such as cognitive impairment, fatigue, pain, sleep quality, shortness of breath, dizziness, fear of falling, diminished self-efficacy, apathy, depression, and anxiety.
4. To study the association of aforementioned symptoms with HAD, health care utilization, and HRQoL.
5. To study the association of metabolic and proinflammatory factors, and physical and behavioral concomitants (e.g., sickness behaviors, loss of muscle mass) with the onset of and recovery from HAD, health care utilization, and HRQoL.

## Methods/Design

**Study design and setting**

The Hospital-ADL study is a multicenter, observational, prospective cohort study designed by an interdisciplinary team of researchers in the field of geriatrics, nursing, psychology, physical therapy, and rehabilitation. Six hospitals will participate: 1] the Academic Medical Center in Amsterdam (AMC), a 1002-bed university teaching hospital; 2] the Isala in Zwolle, a 994-bed regional teaching hospital; 3] the Tergooi in Blaricum, a regional teaching hospital (633-bed spread over two sites: Hilversum and Blaricum); 4] the Slotervaart Hospital in Amsterdam, a 310-bed regional teaching hospital; 5] the BovenIJ Hospital in Amsterdam, a 313-bed regional teaching hospital, and; 6] the Meander Medical Center in Amersfoort, a 543-bed regional teaching hospital. The study has started October 1, 2015 and will end after the last patient has been followed up for three months post-discharge. We expect the recruitment phase to be completed late 2016.

**Patients**

We aim to recruit 400 non-fully disabled adults aged ≥70 years. The following inclusion criteria apply: 1] acutely admitted at departments of Internal Medicine, Cardiology or Geriatrics for 48 h or more in one of the above-mentioned hospitals;

2] 70 years and older; 3] have approval from the attending Medical Doctor for inclusion; 4] score of 15 or higher on the Mini-Mental State Examination[16] 5] Dutch language proficiency sufficient to complete questionnaires. Patients will be excluded if they: 1] have a life expectancy of three months or less as assessed by the attending Medical Doctor, or 2] are disabled in all six basic ADL as determined by the Katz-ADL index.[17]

**Procedures**

Eligible patients will be contacted, and the patient will be informed about the objectives of this study and the study procedures, upon which written informed consent is obtained. Furthermore, a legal representative of the patient will be contacted if the patient has a MMSE score between 15 and 20. Two mobile geriatric assessment teams will visit all six hospitals and will be present on Monday, Wednesday, and Friday for consenting and to perform assessments. The mobile geriatric assessment teams consist of a psychologist, physical therapist, and/ or a health scientist. The teams are trained in the study procedures of obtaining informed consent, to perform assessments and physical performance tests with ad- equate inter- and intra-rater reliability (>0.8) and completing the electronic case report form (eCRF).

Table 1 provides an overview of the location, content of assessment and duration of data collection per time point. There will be at least five data collection points; within 48 h after admission (H1), at discharge (H3), and at one (P1; home visit), two (P2; by telephone) and three months (P3; home visit) post-discharge. If the patient is admitted for more than five days, additional measurements will be planned during hospitalization on Monday, Wednesday, and Friday (i.e., the days that the mobile geriatric assessment team is present) (H2).

Data will be collected through: 1] medical and demo- graphical data (e.g., socio-demographic characteristics, severity of acute illness, and geriatric-, and chronic conditions); 2] personal interviews (including cognitive, behavioral, psychosocial, and physical parameters, and health care utilization, see description of information collected below); 3] physical performance tests (e.g., gait speed, muscle strength, muscle mass, mobility and physical functioning, see below) and; 4] blood samples (e.g., to assess markers of inflammation).

The personal interviews will take place during hospitalization (H1, H2, and H3), at the participant's home or residence (P1 and P3; one- and three-months post-discharge), and by telephone (P2; two months post- discharge). Physical performance data will be collected within 48 h after admission (H1), during hospitalization on Monday, Wednesday, and Friday (H2), at discharge (H3), and at one- and three-months post-discharge (P1 and P3).

**Primary outcome**

The primary outcome is the level of ADL functioning three months post-discharge compared to premorbid functioning, which are measured with the 6-item Katz-ADL index score of the modified Katz-ADL index.[18] The Katz-ADL index score assesses the degree of independence in bathing, dressing, toileting, use of incontinence materials, transfer from bed-chair and eating.[17]

**Secondary outcomes**

Secondary outcomes include:

1. Health care utilization (extension of the Minimal Dataset (MDS)[19] and Comprehensive Geriatric Assessment of the Transitional Care Bridge (TCB),[20] see below).
2. Quality of life as measured with the EuroQol-5D[20] and the three items of the MDS[19] (see description below).
3. Physical performance tests (see below for description of included tests).
4. Mortality.

**Table 1.** Time, location, content of assessment and duration of the Hospital-ADL study

| Time | Location | Content of assessment | Duration (minutes) |
|---|---|---|---|
| H1 (Within 48 h after admission) | Hospital | Medical & demographical data<br>Socio-demographic characteristics<br>Geriatric conditions<br>Severity of acute illness (medical record)<br>Personal interview/self-report data<br>Cognitive functioning ADL/ physical functioning<br>Behavioral & psychosocial functioning<br>Health care utilization (medical record)<br>Physical performance tests<br>Blood parameters | 60 |
| H2 (During hospital stay on Monday-Wednesday-Friday) | Hospital | Medical & demographical data<br>Severity of acute illness (medical record)<br>Short personal interview/self-report data<br>Physical performance tests<br>Blood parameters | 20-30 |
| H3 (At hospital discharge) | Hospital | Personal interview/self-report data<br>Cognitive functioning<br>ADL/physical functioning<br>Physical performance tests<br>Blood parameters | 40 |

**Table 1.** *Continued*

| Time | Location | Content of assessment | Duration (minutes) |
|---|---|---|---|
| P1 (One month post-discharge) | Home visit | Medical & demographical data<br>Socio-demographic characteristics<br>Geriatric conditions<br>Personal interview/self-report data<br>Cognitive functioning<br>ADL/physical functioning<br>Behavioral & psychosocial functioning<br>Health care utilization (medical record)<br>Physical performance tests | |
| P2 (Two months post-discharge) | By telephone | Personal interview/self-report data<br>ADL/physical functioning<br>Behavioral & psychosocial functioning<br>Health care utilization (medical record) | 20 |
| P3 (Three months post-discharge) | Home visit | Medical & demographical data<br>Socio-demographic characteristics<br>Geriatric conditions<br>Personal interview/self-report data<br>Cognitive functioning<br>ADL/physical functioning<br>Behavioral & psychosocial functioning<br>Health care utilization (medical record)<br>Physical performance tests<br>Mortality (medical record) | 60 |

### Scales and assessments

Table 2 gives a detailed overview of the primary and secondary outcomes at each time point.

(1) Medical and demographical data

*Socio-demographic characteristics*. Socio-demographic data include age, gender, date and time of admission, highest level of education, ethnicity, marital status and living arrangement.

*Geriatric conditions*. A comprehensive geriatric assessment (CGA) will be collected, which will provide insight in the pre-illness determinants such as polypharmacy, substance use, incontinence, and vision- and hearing impairments.

*Chronic conditions*. The number and severity of comorbidities will be scored with the Charlson Comorbidity Index.[22] Depending on the risk of mortality, each condition is assigned a score of 1, 2, 3, or 6. Higher scores indicate a greater risk of mortality.

**Table 2.** Summary of outcome measures and time points of assessment in Hospital-ADL study

| | **Question or instrument** | **H1** | **H2** | **H3** | **P1** | **P2** | **P3** |
|---|---|---|---|---|---|---|---|
| 1. Medical & demographical data | | | | | | | |
| Age | Date of birth | ×* | | | | | |
| Gender | | × | | | | | |
| Postal code | | × | | | | | |
| Date and time of admission | | ×* | | | | | |
| Education | (In accordance with Verhage, 1966[57]) | × | | | | | |
| Ethnicity | Country of birth patient and parents | × | | | | | |
| Marital status[18] | | × | | | | | |
| Living arrangement[18, 19] | | × | | | × | | × |
| Medical comorbidity | CCI[21] | ×* | | | | | |
| Severity of acute illness | MEWS[22] | ×* | ×* | ×* | | | |
| Admission diagnosis | | ×* | | | | | |
| 2. Personal interviews/self-report data | | | | | | | |
| 2.1 Cognitive functioning | | | | | | | |
| Cognitive impairment | MMSE[23] | × | | × | × | | × |
| Delirium | CAM[24, 58] | × | | | | | |
| | Assessing whether: 1] the patient needs help with self-care; 2] the patient has previously undergone a delirium and; 3] the patient has a cognitive impairment[25] | ×* | | | | | |
| 2.2 Behavioral & psychosocial functioning | | | | | | | |
| Fear of falling | NRS fear of falling | × | × | × | × | × | × |
| Anxiety | STAI-6[31] | × | | × | × | × | × |
| Apathy | GDS-15[29] | × | | × | × | × | × |
| General self-efficacy | ALCOS-12[34] | | | × | × | × | |
| Quality of life | 1] In general, how is your quality of life?; 2] How would you grade your life at this moment, with a range between 0 and 10? and; 3] Compared to one year ago, how would you rate your health in general now?[18] | × | | × | × | × | × |

**Table 2.** *Continued*

| | Question or instrument | H1 | H2 | H3 | P1 | P2 | P3 |
|---|---|---|---|---|---|---|---|
| | EQ-5D[20] | × | | × | × | × | × |
| 2.3 ADL/Physical functioning | | | | | | | |
| Disability in ADLs | Modified Katz Index Scale[16, 17] | × | | × | × | × | × |
| Independency in walking | FAC[42] | × | × | × | × | × | × |
| Mobility | Could you walk outside for 5 minutes two weeks before admission/ currently? And how often did/do you do physical activity two weeks before admission/currently?[19] | × | | × | × | × | × |
| Falls | Have you fallen once or more in the past (six) month(s)? If yes, how many times?[25] | × | | × | × | × | × |
| Pain | NRS pain[35] | × | × | × | × | × | × |
| Fatigue | NRS fatigue[37] | × | × | × | × | × | × |
| Impact of fatigue | MFIS-5[38] | | | | × | × | × |
| Sleep quality | PSQI[39] | × | | × | × | × | × |
| Sleep medication | PSQI[39] | × | | × | × | × | × |
| Daytime sleepiness | Do you currently suffer from daytime sleepiness? If yes, does this affect your daily living? | × | × | × | × | × | × |
| Polynocturia | Do you currently suffer from polynocturia? If yes, does this affect your daily living? | × | × | × | × | × | × |
| Dizziness | Do you currently suffer from dizziness? If yes, does this affect your daily living? | × | × | × | × | × | × |
| Shortness of breath | Do you currently suffer from shortness of breath? If yes, does this affect your daily living? | × | × | × | × | × | × |
| Hearing impairment | Do you experience difficulties with hearing, despite the use of a hearing aid? | × | | | × | | × |
| Vision impairment | Do you experience difficulties with your vision, despite the use of glasses? | × | | | × | | × |
| Nutrition | SNAQ[25, 41] | × | | × | × | × | × |

**Table 2.** *Continued*

| | Question or instrument | H1 | H2 | H3 | P1 | P2 | P3 |
|---|---|---|---|---|---|---|---|
| Dependency | Do you smoke? Do you use alcohol?[19] | × | | | × | | × |
| Polypharmacy | Do you use five or more different medications?[19] | × | | | × | | × |
| 2.4 Health care utilization | | | | | | | |
| Readmission | Have you been hospitalized in the last (six) month(s)? If yes, for how many days?[18] | ×* | | | × | × | × |
| Nursing home admission | Have you had a nursing home admission in the last month? If yes, for how many weeks totally?[18] | | | | × | × | × |
| Consult physiotherapist and/or occupational therapist | Have you had a consultation with your physiotherapist and/or occupational therapist in the last month? If yes, how many times? | | | | × | × | × |
| Consult general practitioner | Have you had a consultation with your general practitioner in the last month? If yes, in the evening, night or weekend and how many times totally?[19] | | | | × | × | × |
| Home care | Do you use home care? If yes, care assistance and/or domestic help and how many hours per week[19] | | | | × | × | × |
| 3. Physical performance tests | | | | | | | |
| Handgrip strength | JAMAR®[59–61] | × | × | × | × | | × |
| Mobility | DEMMI[45] | × | × | × | × | | × |
| Agility | CSR[47] | × | × | × | × | | × |
| Balance, strength, and gait | SPPB[46] | × | × | × | × | | × |
| Walking distance | 2MWT[49] | × | × | × | × | | × |
| Body composition | BIA (Bodystat Quadscan 4000)[50] | × | × | × | × | | × |
| Activity tracker | Fitbit Flex[51] | × | × | × | × | | × |
| 4. Blood parameters | | | | | | | |
| Inflammation markers | CRP[52] | × | × | | | | |
| | WBC diff | × | × | | | | |
| | TNF-α[53–55] | × | × | | | | |
| | IL-6[53–55] | × | × | | | | |

Table 2. *Continued*

| | Question or instrument | H1 | H2 | H3 | P1 | P2 | P3 |
|---|---|---|---|---|---|---|---|
| | IL-8[55] | × | × | | | | |
| Mortality | Date of death | | | | | ×* | |

Note: H1 = within 48 h after admission; H2 = during hospitalization on Monday, Wednesday, and/or Friday; H3 = at discharge; P1 = one-month post-discharge (home visit); P2 = two months post-discharge (by telephone); P3 = three months post-discharge (home visit);
×* = Data will be obtained from medical record.
CCI Charlson Comorbidity Index, MEWS Modified Early Warning Score, MMSE Mini Mental State Examination, CAM Confusion Assessment Method, NRS Numeric Rating Scale, STAI-6 State Trait Anxiety Inventory-6, GDS-15 Geriatric Depression Scale-15, ALCOS-12 Algemene Competentie Schaal-12 (General Self-Efficacy Scale), EQ-5D EuroQol-5D, FAC Functional Ambulation Categories, MFIS-5 Modified Fatigue Impact Scale-5, PSQI Pittsburgh Sleep Quality Index, SNAQ Short Nutritional Assessment, DEMMI De Morton Mobility Index, CSR Chair Sit and Reach test, SPPB Short Physical Performance Battery, 2MWT 2 Minute Walking Test, BIA Bioelectrical Impedance Analysis, CRP C-Reactive Protein, WBC diff White Blood Cell Differential, TNF-α Tumor Necrosis Factor-α, IL-6 Interleukin-6, IL-8 Interleukin-8

*Severity of acute illness*. The severity of the acute illness will be measured with the Modified Early Warning Score (MEWS). The MEWS is based on 1] respiratory rate; 2] heart rate; 3] systolic and diastolic blood pressure; 4] level of consciousness; 5] temperature, and; 6] oxygen saturation.[23]

**Personal interviews/self-report data**

(2.1) Cognitive functioning

*Cognitive impairments*. The most commonly used Mini Mental State Examination (MMSE) will be applied to classify the severity of a cognitive impairment. It is a validated 23-item screening of cognitive impairment. The MMSE consists of a series of questions and tests, which assess different mental abilities, including memory, attention, language, and planning. Cognitive impairment is defined as a score of 23 or less on the MMSE.[16]

*Delirium*. The Confusion Assessment Method (CAM) will be used to identify the presence of delirium. The CAM consists of four features: 1] acute onset and fluctuating course; 2] inattention; 3] disorganized thinking, and 4] altered level of consciousness. The diagnosis of delirium requires the presence of both features 1 and 2, and the presence of either feature 3 or 4.[24] Furthermore, we want to assess the risk for developing delirium with the following statements of the Dutch Safety Management Programme (Veiligheidsmanagementsysteem (VMS)): 1] the patient needs help with self-care, 2] the patient has previously undergone a delirium, and 3] the patient has a cognitive impairment such as dementia.[25,26]

(2.2) Behavioral and psychosocial functioning

*Fear of falling*. A Numeric Rating Scale (NRS) will be applied to measure fear of falling, in which a participant selects a whole number (0–10 integers). Zero represents no fear of falling and ten the worst possible fear of falling.

*Depression.* The Geriatric Depression Scale-15 (GDS-15) will be used to measure symptoms of depression (Cronbach's α = 0.75.[27] The GDS-15 is a self-report scale of 15 items on a binary (yes/no) scale and assesses symptoms over the preceding week. The total score is the sum of the 15 items (range 0–15 points, higher scores indicating more depression). The following categories of the GDS-15 will be used: a score of 0 to 4 will be considered 'normal', a score of 5 to 8 a 'mild depression,' 9 to 11 a 'moderate depression,' and 12 to 15 a 'severe depression'.[28]

*Apathy.* Three items of the GDS-15 will be used to measure apathy (sensitivity of 69 % and specificity of 85 %.[29] The three apathy items include the following questions: 1] "Do you prefer to stay at home, rather than going out and doing new things?"; 2] "Have you dropped many of your activities and interests?" and 3] "Do you feel full of energy? Higher scores indicate more apathy. A score of ≥2 points is indicative for apathy.[29]

*Anxiety.* The State-Trait Anxiety Inventory-6 (STAI-6) will be used to measure anxiety symptoms (Cronbach's α = 0.79-0.81.[30] The STAI-6 is a short-form of the 20-item state scale of the Spielberger State-Trait Anxiety Inventory (STAI)[31], that maintains results that are comparable with this full-form.[30] It consists of six items on a 4-point Likert scale (1] not at all/almost never; 2] somewhat/sometimes; 3] moderately so/often, and 4] very much so/almost always). Furthermore, it remains sensitive to different levels of anxiety.

*Perceived self-efficacy.* The General Self Efficacy Scale (In Dutch: Algemene Competentie Schaal (ALCOS-12)) will be used to measure general perceived self-efficacy (Cronbach's α = 0.78.[32]). It is based on the Self-Efficacy Scale[33] and is a Dutch translated self-report rating scale of 12 items on a 5-point Likert scale (1] strongly disagree; 2] disagree; 3] no disagreement/agreement; 4] agree and 5] strongly agree). The ALCOS-12 includes three subscales: competence (Cronbach's α = 0.72), perseverance in adversity (Cronbach's α = 0.67), and taking initiative (Cronbach's α = 0.74).[32] The total score is the sum of the 12 items (range 12–60), whereby the following categories of the ALCOS-12 will be used: a score of 12 to 38 will be defined as a 'low competence level', a score of 39 to 54 as 'average' and 55 to 60 as 'high'.[34]

*Health-Related Quality of life.* The EuroQol-5D (EQ-5D), a widely used preference based generic health-related quality of life (HRQoL) instrument with well-established psychometric properties will be administered.[20] The EQ-5D consists of five dimensions: 1] mobility; 2] self-care; 3] usual activities; 4] pain/discomfort and 5] anxiety/ depression. These dimensions have three response choices (no problems; some problems or severe problems). Moreover, the following questions will be used to measure quality of life: 1] "In general, how is your quality of life (participants answer the item with one of five possible responses: excellent; very good; good; moderate or; bad)?"; 2] "How would you grade your life at this moment, with a range between 0 and 10?" and; 3] "Compared to one year ago, how would you rate your health in general now (five response choices: much better; slightly better; much the same; slightly worse or; much worse)?".[19]

(2.3) Physical functioning

*Dizziness, polynocturia and shortness of breath*. Symptoms of dizziness and shortness of breath will be assessed by asking: "Do you suffer from polynocturia/dizziness/shortness of breath at this moment? If yes, does this affect your daily functioning?"

*Pain*. A gold standard of pain intensity measurements, the Numeric Rating Scale (NRS), will be applied to measure pain. The NRS for pain is a validated continuous scale with a score range between 0 and 10 (0 represents no pain and 10 the worst possible pain).[35, 36]

*Fatigue*. The Numeric Rating Scale (NRS) will be used to measure fatigue. The NRS for fatigue is a continuous scale with a score range between zero and ten (zero represents no pain and ten the worst possible fatigue).[37]

*Impact of fatigue*. The abbreviated version of the 21-item Modified Fatigue Impact Scale (MFIS) will be used to quantify the impact of fatigue. The short version consists of five items that are divided into three subscales: physical- (2 items), cognitive- (2 items), and psychosocial functioning (1 item) subscale. An example of a MFIS-5 statement is: "Because of my fatigue during the past four week, I have been less alert." The total score of the MFIS-5 is the sum of the raw scores on a 5-point Likert scale (0] never; 1] rarely; 2] sometimes; 3] often, and 4] almost always). Higher scores indicate greater fatigue.[38]

*Sleep*. The Pittsburgh Sleep Quality Index (PSQI) will be utilized to measure two components of sleep: sleep quality and sleep medication. Sleep quality will be quantified by asking: "During the past month, how would you rate your sleep quality overall?" Sleep medication will be measured by asking: "During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?" The score of sleep quality and sleep medication have a range of 0 (better) to 3 (worse).[39] In addition, we measure daily sleepiness on a binary scale (yes/no) with the following question: "Do you currently suffer from daytime sleepiness? If yes, does this affect your daily living?"

*Nutrition*. The widely used Short Nutritional Assessment Questionnaire (SNAQ) will be applied to identify malnourished hospital patients (Cronbach's alpha = 0.58[40]).[25,26] The total score of the SNAQ is the sum of the raw scores, whereby the following categories of the SNAQ will be used: a score of 0 to 1 will be defined as 'no malnutrition', a score of 2 as 'moderate malnutrition' and a score of 3 as 'severe malnutrition'.[41]

*ADL functioning*. The 15 items modified Katz-ADL index will be used to measure physical functioning.[17,18] The modified Katz-ADL index consists of statements of their independency in performing basic Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) (formulated in two versions on a binary (yes/no) scale: two weeks before admission or currently).

*Mobility*. The Functional Ambulation Categories (FAC) will be used to classify mobility, using six categories: a category of 1 will be defined as 'independent unlimited,' a category of 2 as 'independent limited' and categories 3 to 5 as 'dependent'. Allocation to these last categories is based on levels of assistance and supervision needed.[42] Furthermore, we will measure mobility with two questions in according to the Comprehensive Geriatric Assessment (CGA) of the Dutch Society of Clinical Geriatrics (NVKG, 2012): 1] "Were you able to walk outside the house for five minutes (formulated in two versions: two weeks before admission or currently)?", and 2] "How often did/do you perform physical activity two weeks before admission/currently?".[20]

*Falls*. To measure the number of falls in the past (six) month(s) the following question of the VMS will be used: "Have you fallen once or more in the past (six) month(s)? If yes, how many times?"[25, 26]

(2.4) Health care utilization

*(Re)admission(s)*. Any (re)admission(s) to the hospital will be measured. We will search the medical record for (re)admission(s) in the same hospital six months before hospitalization and during three months post-discharge, and we will also retrieve this information by self-report at P1-P3 with the following self-report question: "Have you been hospitalized in the last month? If yes, for how many days?"[19] Data that will be collected out of the hospital system are date of admission and discharge for any readmission, whether the admission was planned or unplanned and the reason for the readmission.

*Nursing home admission(s)*. The amount of nursing home admission or whether they were admitted to the nursing home and the length of stay will be measured with the subsequent question: "Have you had a nursing home admission in the last month? If yes, for how many weeks totally?"[18]

*Consult of physical therapist and/or occupational therapist*. The amount of consults of a physiotherapist and/or occupational therapist will be measured by asking: "Have you had a consultation with your physical therapist and/or occupational therapist in the last month? If yes, how many times?"

*Consult general practitioner*. The amount of consults of a general practitioner will be measured by asking: "Have you had a consultation with your general practitioner in the last month? If yes, in the evening, night or weekend and how many times in total?"[19]

*Home care*. The use of home care will be measured with the subsequent question: "Do you use home care? If yes, care assistance and/or domestic help and how many hours per week?"[20] A distinction will be made between household help from a nursing aid and help from a registered nurse.

(3) Physical performance tests

*Handgrip strength*. The hand grip strength will be measured with the widely used Jamar® grip strength dynamometer (Lafayette Instrument Company, USA). The handgrip strength test is used to provide an objective index of general upper body strength. Handgrip strength is a reliable instrument (good to excellent test-retest reproducibility and excellent inter-rater reliability) to indicate skeletal muscle mass.[43] Participants will perform the task thrice with each hand. The highest score from either hand will be used and registered in the eCRF. Normative values of adults are described in a study of Mathiowetz.[44]

*Mobility*. To measure the mobility, we will use the 15-item Morton Mobility Index (DEMMI). Subjects will be asked to perform several mobility tasks, in the order of bed, chair, stand, and walking activities to maximize patient safety, which will result in an ordinal raw score (range: 0–19). The ordinal raw score will be converted into a total interval DEMMI score (range: 0 to 100 points). Moreover, the DEMMI has a hierarchical structure, and thus each assessed participant can be evaluated. Higher scores indicate a better mobility performance.[45] Balance, strength, and gait speed. The Short Physical Performance Battery (SPPB) will be applied to measure the balance, strength, and gait speed. Participants will be asked to stand with their feet in various balance positions, walk a distance of four meter and to rise from a chair and return to the seated position five times as quickly as possible. Higher scores indicate a better performance.[46]

*Back and hamstring flexibility*. The Chair Sit and Reach (CSR) test will be used as a measure of flexibility. Participant will be asked to extend one leg as straight as possible, hands-on top of each other, and then to reach to his/her foot as far as possible. Lower distances between the tip of his/her toes and their extended fingers indicating a higher back and hamstring flexibility.[47, 48]

*Walking distance*. The 2 Minute Walking West (2MWT) will be applied to measure the maximal walking distance in meters. Participants will be asked to walk back and forth along a premeasured corridor of 15 meter in two minutes. Longer walking distances indicating a better walking capacity.[49]

*Body composition*. The Bioelectrical Impedance Analysis (BIA) (Bodystat Quadscan 4000) will be used as method for estimating body composition, in particular fat-free mass (FFM) and high fat mass (FM). Electrodes will be attached to the ankle and wrist. A small electric signal will circulate, which measures the resistance and reactance of this electrical signal in the human body.[50]

*Activity level*. The Fitbit Flex® will be applied to monitor the sleep quality, measure motion patterns, determine the calories burned, distance traveled, and steps taken.[51] Participants will be asked to wear the Fitbit Flex® from hospital admission up to one and a half weeks post-discharge.

(4) Blood parameters

*Inflammation markers*. Inflammation markers, such as C-Reactive Protein (CRP),[52] Tumor Necrosis Factor-α (TNF-α), the interleukins IL-6[53–55] and IL-8),[55] and White Blood Cell Differential (WBC diff), will be determined from blood plasma and serum. Blood will be collected during the customary laboratory rounds during hospitalization. Venous blood will be collected in 4.5 ml EDTA and serum vacutainers. Samples will be centrifuged and stored at −80 C° until analysis. Sample handling and analyses will be performed according to ISO standards.

**Planned statistical analyses**

Data will be analyzed in accordance with the research questions outlined in the introduction, applying appropriate General Linear Models (e.g., linear regression,

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repeated measures ANOVA/ANCOVA) as well as log- linear models (e.g., logistic regression in case of binary outcomes). Mortality, a (censored) numerical outcome, will be tested using survival analysis. The global $\alpha$ level will be set at 0.05 with hypothesis-wise adjustment for multiple testing. All analyses will be performed using SPSS version 22.0.[56] Castor Electronic Data Capture (EDC) will be used to build electronic Case Report Forms (eCRFs) for save and valid data collection.

Primary endpoint in the study will be HAD as measured with the Katz-ADL index score. For multivariable analyses (General Linear models and log-linear models) a custom 10:1 case-to-outcome ratio is utilized as a maximum. Utilizing a repeated measures design, power calculations imputing a conservative $\alpha$ level of 0.01 yielded a power of 95 % for associations of a small effect-size (Cohen's f = 0.069), whereas a power of 80 % was established for associations with an effect-size of 0.058 (Cohen's f).

## Discussion

More than 30 % of the older patients experience hospitalization-associated disability (HAD) after acute hospitalization,[1, 3, 4] which implies the loss of ability to perform one or more of the basic ADLs.[6] HAD is the leading cause of functional decline at older age.[4] With a higher number of older persons and an increasing life expectancy, there is an urgent need to unravel the potential mechanisms behind HAD as well as how the mechanisms can be influenced. To our knowledge, the Hospital-ADL study is the first study that investigates cognitive, behavioral, psychosocial, physical, and biological factors simultaneously. The current study will provide novel information regarding possible underlying mechanisms behind HAD within the critical period of three months post hospitalization, which is expected to lead to the development of interventions that can prevent or restore HAD.

**Ethics approval and consent to participate**

The study is approved by the Institutional Review board of the Academic Medical Center (AMC) in The Netherlands (Protocol ID: AMC2015_150). Written informed consent is obtained from all participants before inclusion. The research is performed according to the Dutch Medical Research Involving Human Subjects Act and principles of the Declaration of Helsinki (1964).

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# Muscle strength is longitudinally associated with mobility among older adults after acute hospitalization: The Hospital-ADL study

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## Abstract

**Background:** 30 to 60% of the acute hospitalized older adults experience functional decline after hospitalization. The first signs of functional decline after discharge can often be observed in the inability to perform mobility tasks, such as raising from a chair or walking. Information how mobility develops over time is scarce. Insight in the course of mobility is needed to prevent and decrease mobility limitations.

**Objectives:** The objectives of this study were to determine (i) the course of mobility of acute hospitalized older adults and (ii) the association between muscle strength and the course of mobility over time controlled for influencing factors.

**Methods:** In a multicenter, prospective, observational cohort study, measurements were taken at admission, discharge, one- and three months post-discharge. Mobility was assessed by the De Morton Mobility Index (DEMMI) and muscle strength by the JAMAR. The longitudinal association between muscle strength and mobility was analysed with a Linear Mixed Model and controlled for potential confounders.

**Results:** 391 older adults were included in the analytic sample with a mean (SD) age of 79.6 (6.7) years. Mobility improved significantly from admission up to three months post-discharge but did not reach normative levels. Muscle strength was associated with the course of mobility (beta=0.64; $p<0.01$), even after controlling for factors as age, cognitive impairment, fear of falling and depressive symptoms (beta=0.35; $p<0.01$).

**Conclusion:** Muscle strength is longitudinally associated with mobility. Interventions to improve mobility including muscle strength are warranted, in acute hospitalized older adults.

## Introduction

After acute hospitalization, 30 to 60% of older adults $^{3}$65 years of age experience functional decline, resulting in limitations of activities of daily life, unplanned readmissions to hospital or even death.[1-5] The first signs of functional decline can often be observed in the inability to perform mobility tasks, such as raising from a chair or walking.[6]

Recent studies[7,8] showed that mobility is impaired in most older adults at the time of acute hospital admission. Despite an improvement during and after hospitalization, mobility levels remain below reference levels up to one-month post-discharge.[7-9] While it has been suggested that after hospitalization, three months might be needed to regain mobility to the level before hospitalization,[3] no information is available on the course of mobility over a longer time period as well as influencing factors, that might affect the course.

Muscle strength is considered as an essential prerequisite for mobility and muscle weakness and is associated with reduced mobility and functional decline.[10,11] The role of muscle strength in the development of mobility limitations is best explained through the concept of functional reserve capacity: individuals with relative higher muscle strength are relatively less affected in their mobility than older adults with low muscle strength.[12] Hence, it is conceivable that muscle strength plays an important role in reduced mobility and recovery, over the post-discharge course.[13-15]

Besides muscle strength, factors such as age, cognitive impairment, depressive symptoms, fear of falling, fatigue and nutrition have been associated with reduced mobility and functional decline after acute hospitalization.[16-20] These factors may be barriers to regain mobility and may interact with muscle strength. A better understanding of the longitudinal association between muscle strength and the course of mobility over a longer time-period post-discharge and the influence of demographic- and psychosocial factors will help to understand the mechanisms of reduced mobility. This insight could help to develop tailored interventions to improve the level of mobility and daily functioning in acute hospitalized older adults.

Therefore, the aims of this longitudinal study were to determine: (i) the course of mobility from admission up to three months post-discharge, (ii) the association between muscle strength and the course of mobility and (iii) the role of demographic and psychosocial factors in this association up to three months post-discharge, in acute hospitalized older adults.

## Methods

### Design and Setting

The Hospital-Associated Disability and impact on daily Life (Hospital-ADL) study, a multicenter observational prospective cohort study, was conducted by a multidisciplinary geriatric team. Participants were recruited from those who were admitted to the wards of Internal Medicine, Cardiology or Geriatrics at six participating hospitals in the Netherlands. The study was approved by the Institutional Review board of the Amsterdam UMC, Academic Medical Center (AMC) in The Netherlands (Protocol ID: AMC2015_150) and performed according to the Dutch Medical Research Involving Human Subjects Act and principles of the Declaration of Helsinki (1964). Local approval was additionally provided by all participating hospitals.

**Participants**

Older adults aged ≥70 years who were acutely admitted for at least 48 hours were approached for participation. In addition, further inclusion criteria were applied: 1] approval of the attending Medical doctor; 2] Mini-Mental State Examination (MMSE) score ≥ 15; 3] sufficient Dutch language proficiency to complete questionnaires. Older adults were excluded if they 1] had a life expectancy of less than three months, as assessed by the attending Medical Doctor; 2] were disabled in all six basic ADL's as determined by the Katz-ADL index.

**Data collection**

LR and RS visited the participating wards and contacted all eligible patients within 48 hours after hospital admission. After informed consent was obtained, older adults were enrolled in the study. The geriatric team completed interviews and executed performance tests with participants at baseline (T0) (within 48 hours after admission), discharge (T1) and at one- (T2) and three months (T3) post-discharge (at participants home or residence). The researchers were trained to administer the study protocol in order to reduce variability. Data was collected between October 1, 2015 and June 1, 2017.

**Mobility**

Mobility was assessed with the De Morton Mobility Index (DEMMI). The DEMMI is a unidimensional mobility measure for older adults making the transition from hospital to the community and based on Rasch analysis. The DEMMI consists of 15 items and a raw ordinal score is converted to an interval-level score out of 100. Higher scores indicate a better mobility performance. Older adults are considered as independent for daily living with a score of 74. Previous studies showed good reliability and validity in studies with older adults during and after hospitalization. The reported minimal clinical important difference was 10 points.[9,21] The DEMMI consists of the following items: perform a bridge, roll onto side, lie to sit, sit unsupported in chair, sit to stand from chair, sit to stand without using arms, stand unsupported, stand feet together, stand on toes, tandem stand, walking distance, walking assistance, pick up pen from floor, walk backwards, and jump. Participants were asked to perform these tasks and were scored according to the standardized protocol.

### Muscle strength

Muscle strength was measured using a Jamar® handgrip strength dynamometer (Lafayette Instrument Company, USA). The handgrip strength was measured to provide an objective index of general upper body strength. Handgrip strength showed good to excellent test-retest reliability and interrater reliability and good validity among hospitalized older adults.[22] Normative values of older adults are available from Dodds et al.[12] for gender related age groups We considered muscle strength lower than one standard deviation of the mean score as decreased muscle strength. Participants were measured in supine or sitting position and encouraged to show maximal isometric handgrip strength and performed the task thrice bilaterally. The highest score (in kilogram) of both hands was used for the analysis.

### Other variables

Confounding variables, possibly affecting the association of muscle strength with course of mobility, were assessed. Participants were assessed on 1) cognitive impairment with the Mini Mental State Examination (MMSE);[23] 2) depressive symptoms with the Geriatric Depression Scale-15 (GDS-15),[24] 3) fatigue and fear of falling (FOF) using a 10-point numeric rating scale; 4) number and severity of comorbidities with the Charlson Comorbidity Index (CCI),[25] 5) malnourishment with the Short Nutritional Assessment Questionnaire (SNAQ).[26] In addition, mean age, length of stay, highest level of education, marital status, living arrangement, length of stay in hospital (LOS) and Body Mass Index (BMI) were collected.[27]

### Statistical analysis

Baseline characteristics were calculated using descriptive statistics. Data was checked on normality by plotting histograms of the residuals. A Linear Mixed Model (LMM) was performed to analyse the course of mobility and the association between the course of mobility and muscle strength. In this procedure it is not essential to use multiple imputation of missing data before performing the LMM.[28] To evaluate the effect of potential confounders (gender, age, cognitive impairment, depressive symptoms, fear of falling and fatigue) on this association, variables were stepwise added to the model. For every potential confounder it was determined if the beta (β) in the association between muscle strength and mobility changed with more than 10%. A 10% change of the regression coefficient of the determinant in the crude model after adjustment for one factor was indicative for relevant confounding. Finally, confounding on the association of muscle strength with the course of mobility, was determined, based on a 10% change of the regression coefficient again. Prior to these analyses, interaction effects between muscle strength and time, gender and age in the association with the course of mobility were calculated to analyse whether stratification was needed.

To analyse if the associations between muscle strength and mobility was similar for older adults with decreased muscle strength, a sensitivity analysis was performed. All parameter estimates were expressed with a 95% confidence interval (95%CI), and results were considered significant if $p<0.05$. Analyses were conducted with the SPSS Statistics® (version 24.0).

## Results

### Characteristics of the study sample

1024 acute hospitalized older adults were admitted to the participating hospital wards ≥48 hours. Of these unplanned admissions, 519 (50.7%) participants met the inclusion criteria and were approached, of whom 401 (77.3%) participants agreed to participate. Participants were excluded because they were not approachable (163 (15.9%)), a score ≤14 on the MMSE (144 (14.1%)), were delirious (67 (6.5%)), did not speak or understand Dutch (40 (3.9%)), were too ill to participate (39 (3.8%)), had a life expectancy of ≤3 months (39 (3.8%)) or other reasons (13 (1.3%)) (e.g. deaf, disabled in all six basic ADLs). Ten participants (2.5%) had no data for the DEMMI at any of the time points and were excluded from the sample. Finally, 391 older adults were included in the statistical analysis (Fig 1).

Data of the DEMMI was available at baseline for 356/391 (91.1%), at discharge for 321/391 (82.1%), at one-month post-discharge for 278/391 (71.1%) and at three months post-discharge for 226/391 (57.8%) participants. At three months post-discharge 37 (9.0%) participants were deceased and 189 participants (48.3%) were lost to follow up.

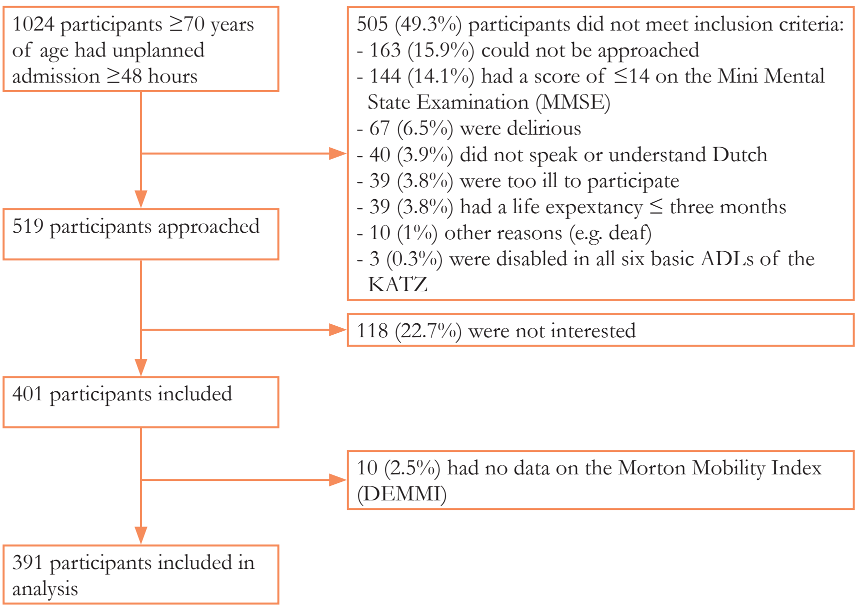


**Figure 1.** Inclusion of participants in the study (N=391)

For the 391 participants (men: n=201; 51.4%, women: n=190; 48.6%) the mean (sd) age was 79.7 (6.7) years. The median (IQR) length of stay was 5.7 (3.9-8.9) days. At baseline, DEMMI (mean (sd)) score was 55.8 (23.0) points for all participants with a significant difference between men and women (mean (SD) men 58.2 (23.2) points, women 53.3 (22.3) points; p=0.04) (Table 1).

**Table 1.** Baseline Characteristics of the Study Population

| | **All participants (n=391)** | **Men (n=201)** | **Women (n=190)** |
|---|---|---|---|
| Age (years), mean (SD) | 79.6 (6.7) | 79.2 (6.4) | 80.1 (6.9) |
| Living arrangements before admission N (%) | | | |
| Independent | 332 (84.9) | 181 (90.0) | 201 (79.5) |
| Nursing home | 8 (2.0) | 2 (1.0) | 6 (3.2) |
| Senior residence/Assisted living | 51 (13.0) | 18 (9.0) | 33 (17.4) |
| Marital status N (%) | | | |
| Married or living together | 205 (52.4) | 142 (70.6) | 63 (33.2) |
| Single or divorced | 60 (15.3) | 22 (10.9) | 38 (20.0) |
| Widow/widower | 126 (32.2) | 37 (18.4) | 89 (46.8) |
| Primary admission diagnosis, N (%) | | | |
| Cardiovascular disease | 121 (30.9) | 66 (32.8) | 55 (28.9) |
| Gastrointestinal disease | 43 (11.0) | 21 (10.4) | 22 (11.6) |
| Pulmonary disease | 71 (18.2) | 34 (16.9) | 37 (19.5) |
| Infection | 56 (14.3) | 30 (14.9) | 26 (13.7) |
| Other | 100 (25. 6) | 50 (24.9) | 50 (26.3) |
| Education N (%) | | | |
| Primary school | 99 (25.3) | 42 (20.9) | 57 (30.0) |
| Elementary technical/domestic science school | 86 (22.0) | 46 (22.9) | 40 (21.1) |
| Secondary vocational education | 116 (29.7) | 55 (27.4) | 61 (32.1) |
| Higher level high school/third level education | 90 (23.0) | 58 (28.9) | 32 (16.8) |
| Body Mass Index (kg/m2), mean (SD) | 25.2 (5.1) | 25.0 (4.9) | 25.5 (5.2) |
| Length of stay (days), median (IQR) | 5.7 (3.9-8.9) | 5.8 (3.8-8.1) | 5.7 (3.9-10.1) |
| Charlson comorbidity index (CCI), mean (SD) | 2.2 (2.0) | 2.3 (2.0) | 2.1 (1.9) |
| Nutrition (SNAQ), mean (SD) | 1.6 (1.8) | 1.5 (1.8) | 1.7 (1.8) |
| Mobility (DEMMI) (n=356), mean (SD) | 55.8 (23.0) | 58.2 (23.8) | 53.3 (22.3) * |
| Mobility (DEMMI) (n=356), median (IQR) | 57 (41-74) | 62 (41-74) | 57 (40-67) |
| Grip strength (JAMAR in kg) (n=368), mean (SD) | 27.3 (10.8) | 33.9 (10.1) | 20.2 (5.9) * |

**Table 1.** *Continued*

| | All participants (n=391) | Men (n=201) | Women (n=190) |
|---|---|---|---|
| MMSE cognitive impairment, mean (SD) | 25.9 (3.2) | 26.2 (3.2) | 25.6 (3.3) |
| Depressive symptoms (GDS), mean (SD) | 4.0 (2.9) | 3.5 (2.7) | 4.4 (3.0) * |
| Fatigue (NRS), mean (SD) | 5.4 (2.9) | 4.9 (2.9) | 5.9 (2.7) * |
| Fear of Falling (NRS), mean (SD) | 3.0 (3.3) | 2.2 (3.1) | 3.7 (3.4) * |
| KATZ 6 ADL, median (IQR) | 1 (0-3) | 0.5 (0-2) | 1 (0-3) * |

Abbreviations: SD = Standard Deviation; IQR=Interquartile range; Body Mass Index (BMI) = weight / square of the body height in kg/m2; CCI = Charlson comorbidity index range 0-31 with a higher score indicating more comorbidity; SNAQ = Short Nutritional Assessment Questionnaire range 0-5; DEMMI = De Morton Mobility Index range 0-100 with a higher score indicating better mobility; MMSE = Mini Mental State Examination range 0-30 with a higher score indicating less cognitive impairment; GDS = Geriatric Depression Scale range 0-15 with A higher score indicating more depressive symptoms; Fatigue NRS = Numeric Rating Scale range 0-10. Fear of Falling NRS = Numeric Rating Scale range 0-10 with higher score on the NRS indicating more fatigue or fear of falling. KATZ 6 ADL = Activities of Daily Living range 0-6 with a higher score indicating more disabilities.
* p-value<0.05; Independent T-test and Mann-Whitney U test were used for continues and categorical variables.

**Course of mobility**

Linear Mixed Model showed a significant improvement in the course of mobility after hospital admission up to three months post-discharge; with a progression in DEMMI score of 57 to 62 points from admission to discharge, towards a score of 67 points at one-month and 68 points at three months post-discharge (Fig 2). At three months post-discharge, 74 out of 226 (40.1%) participants scored lower than 74 points on the DEMMI, indicating a mobility level below the normative level for independent living.[21]

**Association between muscle strength and mobility**

Table 2 shows that in the crude model, a longitudinal association between muscle strength and course of mobility up to three months post-discharge was found (beta=0.64; p<0.01). This means that a difference of one-kilogram in muscle strength is associated with a difference of 0.64 points on the DEMMI. There were no significant differences of the beta in the association between muscle strength and mobility at different time-points.

Gender was determined as effect modifier (muscle strength*Gender, beta=0.73; p<0.01) and therefore, the analysis for men and women are presented separately. The crude model of the association showed different associations for men (beta=0.55; p<0.01) and women (beta=1.19; p<0.01) respectively. Age and cognitive impairment were identified as confounders for both men and women. For women only, also depressive symptoms, fear of falling and fatigue were identified as confounders. Marital status, living arrangement, educational level, body mass index, comorbidity, nutrition and length of stay did not influence the beta in the association of muscle strength and mobility.

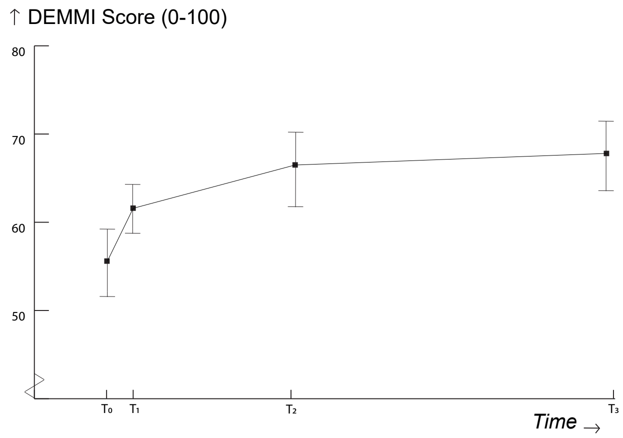


**Figure 2.** Course of mobility from admission to hospital up to three months post-discharge from hospital
DEMMI = the Morton Mobility Index score reange 0-100; the error bar represents 95% confidence interval (95% CI).
T0 = admission to the hospital, T1 = discharge from hospital, T2 = one-month post-discharge from hospital, T3 = three-months post-discharge from hospital

**Sensitivity analysis**
At baseline, 52 out of 391 (13.3%) participants had decreased grip strength. For participants with low muscle strength at baseline, the association between muscle strength and course of mobility did not change substantially.

## Discussion

This multicentre cohort study yielded three clinical important findings. First, the level of mobility improved significantly in acute hospitalized older adults from admission up to three months post-discharge. Second, muscle strength was longitudinally associated with the course of mobility up to three months post-discharge. Third, the association between muscle strength and the course of mobility was different in men and women, confounded by age and cognitive impairment for both women and men whereas for women, also, fear of falling and depressive symptoms confounded the association. These findings highlight that multiple factors play a role in regaining mobility after acute hospitalization.

During hospitalization, the observed improvement of the level of mobility, was in line with two other studies.[6,8] After hospitalization, however, the course of mobility differed. In contrast with our study, Bodilsen et al.[6] found that mobility stabilized up to one-month post-discharge. An explanation for the difference

**Table 2.** Longitudinal association of muscle strength with course of mobility

| | | All participants (n=391) | Men (n=201) | Women (n=190) |
|---|---|---|---|---|
| **Model 1: crude model** | **Parameter** | **beta* (95% CI)** | **beta* (95% CI)** | **beta* (95% CI)** |
| | Grip strength | 0.64 (0.50-0.79) | 0.55 (0.35-0.76) | 1.19 (0.85-1.53) |
| **Model 2 (adjusted): influence per factor on grip strength** | Age | 0.51** (0.36-0.66) | 0.37** (0.15-0.58) | 1.02** (0.67-1.37) |
| | Marital Status | 0.59 (0.44-0.74) | 0.55 (0.35-0.75) | 1.14 (0.80-1.49) |
| | Living Arrangement | 0.60 (0.50-0.79) | 0.53 (0.33-0.74) | 1.13 (0.79-1.48) |
| | Educational level | 0.63 (0.48-0.78) | 0.55 (0.35-0.75) | 1.17 (0.83-1.52) |
| | Body Mass Index | 0.69 (0.54-0.85) | 0.57 (0.36-0.78) | 1.27 (0.91-1.63) |
| | Comorbidity | 0.63 (0.48-0.78) | 0.53 (0.32-0.73) | 1.15 (0.81-1.49) |
| | Cognitive impairment | 0.53** (0.39-0.68) | 0.45** (0.25-0.66) | 0.98** (0.64-1.32) |
| | Depressive symptoms | 0.56** (0.42-0.71) | 0.51 (0.31-0.72) | 0.97** (0.63-1.30) |
| | Fear of Falling | 0.55** (0.41-0.70) | 0.50 (0.30-0.70) | 1.08** (0.75-1.42) |
| | Fatigue | 0.60 (0.45-0.74) | 0.56 (0.37-0.76) | 1.05** (0.71-1.38) |
| | Nutrition | 0.62 (0.48-0.77) | 0.56 (0.35-0.76) | 1.13 (0.78-1.48) |
| | Length of Stay | 0.62 (0.46-0.56) | 0.52 (0.30-0.74) | 1.18 (0.84-1.52) |
| **Model 3: final model with confounders** | Grip strength | 0.35** (0.20-0.49) (age, cognitive impairment, depressive symptoms, fear of falling) | 0.32** (0.10-0.54) (age, cognitive impairment) | 0.68** (0.35-1.01) (age, cognitive impairment, depressive symptoms, fear fear of falling, fatigue) |

CI=Confidence interval. * P-value below <0.01. ** Beta more than 10% different from beta in crude model could be that they used the Timed Up and Go test as measurement tool, which focuses on standing up from a chair and walking instead of a broader spectrum of mobility such as transfers out of bed, balance tests and walking for a longer time. Moen et al.[8] reported mobility only at two time-points: baseline and three weeks post-hospital. Although several studies reported regaining pre-admission mobility can take up to three months, there is currently no study reporting in detail on the course of mobility up to three months post-discharge.[3] Our study provides novel information that the largest improvement occurs during hospitalization and in the first month post-discharge and stabilises up to three months post-discharge.

Muscle strength was found to be associated with the course of mobility up to three months. This finding is in accordance with a previous study where muscle strength is considered as 'vital sign' of poor performance and is associated with reduced mobility.[9] Our study adds to this that the association between muscle strength and course of mobility is consistent during the first three months post-discharge and substantially influenced by several factors. It was reported previously[4] that several factors may affect the mobility after hospitalization but the interaction between the factors was not described until now.

Our study is consistent with the hypothesis[6,29] that muscle strength is an important target for interventions. It has been shown that interventions that focus on increasing muscle strength, particularly progressive resistance training may be beneficial to restore mobility, even in vulnerable older adults.[29] However, our study showed that besides muscle strength, factors such as age, cognition, depressive symptoms, fear of falling and fatigue should be taken into account in the development and application of exercise intervention. Depressive symptoms, fear of falling and fatigue may be barriers to start exercises and regain mobility after hospitalization.

**Strengths and limitations of the study**

The key strength of this study is the multicenter longitudinal design, with multiple measurements up to three months post-discharge. It needs to be acknowledged that the study has several limitations. Firstly, information was lacking regarding mobility prior to admission, hence it was not possible to compare mobility post-discharge with pre-admission levels. Secondly, data was not available for all older adults at all time points. This is a well-known challenge in research in geriatric population and is difficult to avoid.[30] Data was missing because of death, refusal or deterioration in health and could have influenced our results. However, application of advanced statistical analysis has the advantage of its ability to deal with missing data and provides unbiased results. Thirdly, our selection criteria may have an effect on the generalizability of the study. Participants with a score of 15 or lower on the MMSE scale were excluded. As a consequence, the most vulnerable older adults may have been excluded. Fourthly, no data was available after three months post-discharge so it is unknown if the association continues over a longer time.

**Conclusion**

Muscle strength is longitudinally associated with the course of mobility even after controlling for factors as cognitive impairment, depressive symptoms, fatigue and fear of falling. Interventions to improve mobility including muscle strength are warranted, in acute hospitalized older adults.

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5

# Longitudinal changes in muscle mass, muscle strength and physical performance in acutely hospitalized older adults

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## Abstract

**Objectives:** Acute hospitalization may lead to a decrease in muscle measures, but limited studies are reporting on the changes after discharge. The aim of this study was to determine longitudinal changes in muscle mass, muscle strength, and physical performance in acutely hospitalized older adults from admission up to 3 months post-discharge

**Design:** A prospective observational cohort study was conducted.

**Setting and Participants:** This study included 401 participants aged ≥70 years who were acutely hospitalized in 6 hospitals. All variables were assessed at hospital admission, discharge, and 1- and 3-months post-discharge.

**Methods:** Muscle mass in kilograms was assessed by multifrequency Bio-electrical Impedance Analysis (MF-BIA) (Bodystat; Quadscan 4000) and muscle strength by handgrip strength (JAMAR). Chair stand and gait speed test were assessed as part of the Short Physical Performance Battery (SPPB). Norm values were based on the consensus statement of the European Working Group on Sarcopenia in Older People.

**Results:** A total of 343 acute hospitalized older adults were included in the analyses with a mean (SD) age of 79.3 (6.6) years, 49.3% were women. From admission up to 3 months post-discharge, muscle mass (-0.1 kg/m2; $P = .03$) decreased significantly and muscle strength (-0.5 kg; $P = .08$) decreased nonsignificantly. The chair stand (+0.7 points; $P < .001$) and gait speed test (+0.9 points; $P < .001$) improved significantly up to 3 months post-discharge. At 3 months post-discharge, 80%, 18%, and 43% of the older adults scored below the cutoff points for muscle mass, muscle strength, and physical performance, respectively.

**Conclusions and Implications:** Physical performance improved during and after acute hospitalization, although muscle mass decreased, and muscle strength did not change. At 3 months post-discharge, muscle mass, muscle strength, and physical performance did not reach normative levels on a population level. Further research is needed to examine the role of exercise interventions for improving muscle measures and physical performance after hospitalization.

## Introduction

Low muscle mass, muscle strength, and physical performance are diagnostic measures of sarcopenia.[1,2] The prevalence of sarcopenia in hospitalized older adults is up to 40% depending on the diagnostic criteria.[3] Sarcopenia is associated with poor health outcomes such as loss of activities in daily living (ADLs),[4] falls, fractures,[5] and mortality.[1] Approximately one-third of acutely hospitalized older adults experience a loss of ADLs during their hospital stay,[6,7] despite the successful treatment of the primary medical illness.[8] Physical inactivity and bed rest may lead to a loss of muscle mass and muscle strength.[9] Bed rest studies in healthy older adults reported more than 10% loss of muscle mass and up to 13% of knee extensor muscle strength over 7 to 10 days of inactivity.[9,10] Medical illness with acute hospitalization as a result, might affect muscle mass and muscle strength even more in older adults; this could be a facilitator of functional decline and loss of physical performance.[8,11,12]

Detailed information is lacking on longitudinal changes in muscle mass, muscle strength, and physical performance from admission to post-discharge. A systematic review concluded that muscle mass and muscle strength did not change in acute hospitalized older adults during hospitalization.[13] Few studies reported on the changes in muscle mass, muscle strength, and physical performance in older adults after acute hospitalization. Studies on the changes in muscle mass and muscle strength post-discharge were inconclusive; muscle strength was unchanged[14] or improved at 1 month post-discharge.[15] Physical performance improved at 1 month post-discharge, but remained below reference levels for independent living.[14,15] It has been shown that it is important to regain functionality within 3 months after hospitalization to prevent permanent functional decline.[16] Insight in the changes in muscle mass, muscle strength, and physical performance may help to understand the underlying mechanisms of how older adults lose functionality after acute hospitalization. Recent publications from our Hospital Associated Disability and impact on daily Life (Hospital-ADL) study showed that psychosocial factors, such as depressive symptoms, fatigue, and fear of falling are highly prevalent and persistent after hospitalization and are associated with functional decline.[17,18] Information on the changes in muscle mass, muscle strength, and physical performance from admission to post-discharge and which factors could confound these changes, may provide specific starting points for tailored interventions to counteract sarcopenia and to prevent functional decline after acute hospitalization.

This study aimed to determine the longitudinal changes in muscle mass, handgrip strength, and physical performance from hospital admission up to 3 months post-discharge, adjusted for depressive symptoms, cognition, fatigue, fear of falling, risk of malnutrition, and comorbidity, in acutely hospitalized older adults.

## Methods

### Study design and setting

This multicenter observational prospective cohort study was conducted by a multidisciplinary team.[19] Participants were recruited among those admitted to the internal medicine, cardiology, or geriatric wards at 6 participating hospitals between October 1, 2015, and June 1, 2017. The study was approved by the institutional review board and performed according to the Medical Research Involving Human Subjects Act and the ethical standards laid down in the Declaration of Helsinki (1964) and its later amendments.

### Study population

Older adults aged ≥70 years who were acutely admitted for at least 48 hours to the hospitals were approached for participation. In addition, further inclusion criteria were applied: (1) approval of the treating medical doctor; (2) Mini-Mental State Examination (MMSE) score ≥15 points; (3) sufficient Dutch language proficiency to complete questionnaires. Older adults were excluded if (1) they had a life expectancy of fewer than 3 months, as assessed by the treating medical doctor; or (2) were disabled in all 6 basic ADLs as determined with the Katz-6 ADL index.

### Data collection

A geriatric team, consisting of a psychologist and physical therapist, visited the participating wards and contacted all eligible older adults within 48 hours after hospital admission. Participants were enrolled in the study after written informed consent was obtained. The psychologist completed the questionnaires and the physical therapist carried out performance tests at baseline (within 48 hours after admission) and on discharge. Highly trained students visited the participant's home or residence to perform the assessments at 1- and 3-months post-discharge. All assessors were trained to administer the study protocol in a standardized way to prevent variability. All measurements were taken at the same time points.

### Muscle mass

Muscle mass was assessed with multifrequency Bio-electrical Impedance Analysis (MF-BIA; Bodystat; Quadscan 4000). The participant had to lie in a supine position with legs and arms not touching the body with 2 surface electrodes placed on the right foot and hand, with a distance of 5 cm between both electrodes. This test was not conducted in case of a pacemaker or Implantable Cardioverter Defibrillator because the risk of dysregulation of the device. The MF-BIA Quadscan 4000 was reported reliable and interchangeable at the population level with the dual-energy X-ray absorptiometry methods.[20] Skeletal muscle mass in kilograms was calculated with the formula as used by Janssen et al.[21] and divided by the squared height (m2) to calculate the skeletal muscle mass index (SMI). The cutoff points for the SMI for low muscle mass were ≤10.70 kg/m2 for men and ≤6.75 kg/m2 for women as a diagnostic measure for sarcopenia.[2,22]

**Muscle strength**

Handgrip strength was used as a measure of general upper body strength[2,23] and assessed using a JAMAR handgrip strength dynamometer (Lafayette Instrument Company, Lafayette, IN), expressed in kilograms. Participants were assessed, encouraged, and performed the task 3 times alternating bilaterally.[23] The highest score of either hand was used for the analysis. Handgrip strength showed good to excellent reliability and validity among hospitalized older adults.[24] The cutoff points for low handgrip strength are <16 kg for women and <27 kg for men.[1]

**Physical performance**

Physical performance was assessed by the Short Physical Performance Battery (SPPB) was used.[25] The SPPB is a reliable and valid measurement tool and consists of the balance test, gait speed test, and chair stand test. Balance was assessed by side-side, semi-tandem, and tandem stands. Participants received a score of 0 points if they were unable to complete the task and 4 points when all tests were held for 10 seconds.[25] Gait speed was assessed with the 4-m walking test at usual walking speed.[1,25] Participants received a score of 0 points if they were unable to complete the task, 1 point when the time over 4 m was more than 8.70 seconds, 2 points between 6.2 and 8.7 seconds, 3 points between 4.8 and 6.2 seconds, and 4 points under 4.8 seconds.[25] A cutoff value of lower than 1.2 m per second (1, 2, or 3 points) is considered as low.[26,27] For the chair stand test,[1,25] participants were asked to rise 5 times as fast as possible with the arms crossed on the chest. Participants received a score of 0 if they were unable to complete the task, 1 point when the time for 5 rises was between 16.7 and 60.0 seconds, 2 points when the time was between 13.7 and 16.7 seconds, 3 points when the time was between 11.2 and 13.7 seconds, and 4 points when the time was less than 11.2 seconds. A cutoff value of higher than 13.7 seconds (0, 1, or 2 points) was considered as low physical performance.[27] For chair stand and gait speed test sub-scores were analyzed. For the complete SPPB test, a cutoff score of $\leq$ 8 points was considered as low physical performance.[1,25-28]

**Other variables**

Potential confounding variables on the longitudinal changes in muscle mass, handgrip strength, chair stand, and gait speed were assessed at admission, discharge, and 1- and 3-months post-discharge. Depressive symptoms were assessed with the geriatric depression scale-15 item (GDS-15),[29] cognitive impairment with the MMSE,[30] fatigue and fear of falling on a numeric rating scale, and the Short Nutritional Assessment Questionnaire (SNAQ) was used to identify the risk of malnutrition.[31] The Charlson Comorbidity Index (CCI) was used to assess the number and severity of comorbidities at baseline.[32] Additional data were collected at baseline for age, sex, marital status, living arrangement, length of stay (LOS) in hospital, and body mass index (BMI). Sarcopenia was defined as reported by the revised consensus statement of the European Working Group on Sarcopenia in Older People (EWGSOP2) using the cutoff points as outlined previously.[2]

Functional decline was defined as experienced loss of 1 point on the Katz-6 ADL index (bathing, dressing, toileting, transferring, continence, and feeding) between 2 weeks before hospitalization and 3 months post-discharge.[33]

**Statistical analysis**

Baseline characteristics were presented with mean and SD or median and interquartile range using descriptive statistics and stratified by sex. Linear mixed models (LMM)[34] were performed to analyze the longitudinal changes in muscle mass, handgrip strength, chair stand, and gait speed. First, interaction effects of time, sex, and age were analyzed to decide if stratification was needed for these variables was needed. Second, for every potential confounder, such as age, sex, LOS, BMI, cognition, comorbidity, depressive symptoms, fatigue, nutrition, and fear of falling, it was determined if the beta of muscle mass, handgrip strength, chair stand, and gait speed changed >10%.[35] Third, confounding factors were then included in the adjusted model. Variables had to be present minimally at one time point to be included in the final analysis. To analyze the effect of missing data, a sensitivity analysis was performed with data at all time points. To compare the variables, standardization was performed using Z-scores and tested on differences over time by multivariate analysis, with a baseline score of zero for all variables. All parameter estimates were expressed with 95% confidence interval and were considered statistically significant if $P < .05$. A trend was defined as P value ≥ .05 and < .10. Analyses were conducted with the Statistical Package for the Social Sciences for Mac (version 24; SPSS Inc., Chicago, IL).

## Results

**Participant characteristics**

Of the 1024 acute hospitalized older adults admitted for ≥48 hours between October 2015 and February 2017, 519 (50.7%) did meet the inclusion criteria (Figure 1) and of these 118 (22.7%) were not interested in participating. Of the 401 older adults who agreed to participate, 40 participants (10%) were deceased, and 87 participants (21.7%) were lost to follow-up at 3 months post-discharge. In the analysis, 58 participants were excluded because no data were available at any time-point due to no permission or not able to perform the tests at all. Therefore, 343 of 401 older adults with a mean age (SD) of 79.3 (6.6), 49.3% women, were included. Table 1 shows the baseline characteristics of all participants stratified by sex. In Supplementary Table 1 the proportions of older adults below the norm values are presented.

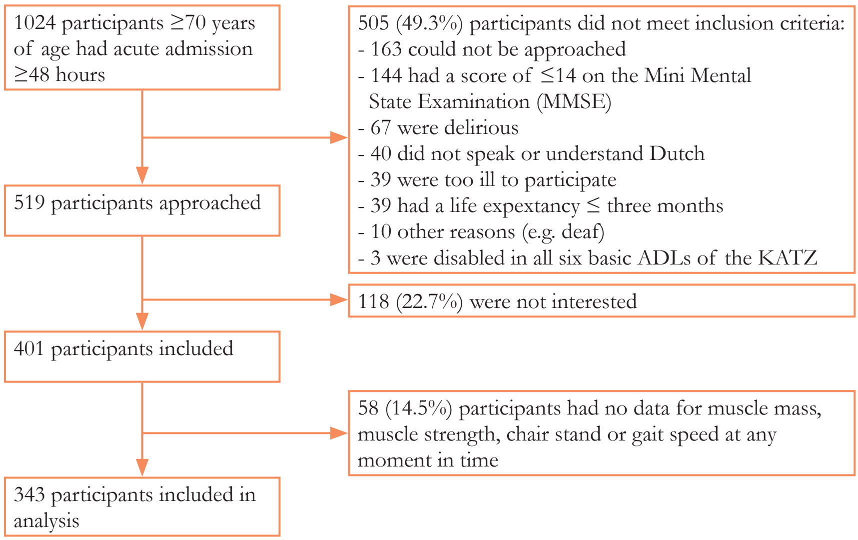


**Figure 1.** Flowchart of the acute hospitalized older adults included in the analysis of this study

**Table 1.** Baseline characteristics of acute hospitalized older adults at admission

| | All (N=343) | Female (n=169) | Male (n=174) |
|---|---|---|---|
| **Demographics** | | | |
| Age in years, mean (SD) | 79.3 (6.6) | 79.8 (6.8) | 78.9 (6.4) |
| Living arrangements before admission n (%) | | | |
| Independent | 291 (84.8) | 135 (79.9) | 156 (89.7) |
| Nursing home | 7 (2.0) | 5 (3.0) | 2 (1.1) |
| Senior residence/assisted living | 45 (13.1) | 29 (17.1) | 16 (9.2) |
| Marital status n (%) | | | |
| Married or living together | 182 (53.1) | 60 (35.5) | 122 (70.1) |
| Single or divorced | 54 (15.7) | 35 (20.7) | 96 (10.9) |
| Widow/widower | 107 (31.2) | 74 (43.8) | 33 (19.0) |
| Primary admission diagnosis, n (%) | | | |
| Cardiovascular disease | 100 (29.2) | 48 (28.4) | 52 (29.9) |
| Gastrointestinal disease | 42 (12.2) | 21 (12.4) | 21 (12.1) |
| Pulmonary disease | 66 (19.2) | 33 (19.5) | 32 (18.4) |
| Infection | 51 (14.9) | 23 (13.6) | 28 (16.1) |
| Other | 84 (24.5) | 44 (26.0) | 41 (23.6) |
| BMI, mean (SD) | 25.5 (4.9) | 25.7 (5.2) | 25.3 (4.6) |
| Length of stay, median (IQR) | 5.7 (3.9-8.7) | 5.6 (3.9-8.9) | 5.5 (3.9-8.2) |

**Table 1.** *Continued*

| | All (N=343) | Female (n=169) | Male (n=174) |
|---|---|---|---|
| Charlson comorbidity index (CCI), median (IQR) | 2 (1-3) | 2 (1-3) | 2 (1-3) |
| **Diagnostic measures of sarcopenia** | | | |
| Muscle mass SMI (BIA), mean (SD) | 8.0 (1.8) | 6.7 (1.1) | 9.2 (1.5) |
| Handgrip strength (JAMAR), mean (SD) | 27.4 (10.2) | 20.5 (5.8) | 34.0 (9.1) |
| Chair stand test (SPPB), median score (IQR) | 1 (0-2) | 0 (0-2) | 1 (0-3) |
| Gait speed test (SPPB), median score (IQR) | 2 (0-3) | 2 (0-3) | 2 (1-3) |
| **Other variables** | | | |
| Cognitive level (MMSE), median (IQR) | 26 (25-28) | 27 (24-28) | 27 (25-27) |
| Depressive symptoms (GDS), median (IQR) | 3 (2-5) | 4 (2-6) | 3 (2-5) |
| Fatigue (NRS), mean ± SD | 5.4 (2.9) | 6.0 (2.8) | 4.9 (3.0) |
| Severe risk of malnutrition (SNAQ), n (%) | 132 (32.9) | 69 (33.5) | 63 (32.3) |
| ADL score (KATZ 6), median (IQR) | 1 (0-3) | 1 (1-3) | 0 (0-2) |
| Sarcopenia n (%) | 45/283 (14.1) | 17/156 (10.1) | 28/163 (17.2) |
| Functional decline n (%) | 35/239 (10.2) | 18/115 (10.7) | 17/124 (9.8) |

Abbreviations: SD = Standard Deviation; IQR=Inter Quartile Range ; Body Mass Index (BMI) = square of the body height in kg/m2; CCI = Charlson comorbidity index range 0-31; SMI = Skeletal Muscle Index in kilograms/meter2; BIA= Bioelectrical Impedance Analysis; SPPB = Short Physical Performance Battery in points MMSE = Mini Mental State Examination range 0-30; SNAQ = Short Nutritional Assessment Questionnaire; GDS = Geriatric Depression Scale range 0-15 ; Fatigue and Fear of Falling NRS = Numeric Rating Scale range 0-10; KATZ 6 ADL = Activities of Daily Living range 0-6.

### Longitudinal changes of muscle mass, handgrip strength, chair stand and gait speed

Table 2 shows an overview of the data based on the unadjusted LMM analysis. Muscle mass significantly decreased from admission up to 3 months post-discharge (−0.1 kg/m2; P = .03) with the lowest value at 1-month post-discharge. Both women and men decreased nonsignificant in muscle mass (resp. −0.2 kg/m2; P = .08 and −0.1 kg/m2; P = .13). Handgrip strength did not decrease significantly from acute hospitalization up to 3 months post-discharge (−0.5 kg; P = .08) with also the lowest value at 1-month post-discharge. For women, handgrip strength decreased significantly (resp. −0.7 kg; P = .03) and not significantly for men (−0.2 kg; P = .55) at 3 months post-discharge. Chair stand increased significantly (+0.7 points; P < .001) either for all participants as for women and men separately (resp. +0.8 points; P < .001 and +0.5 points; P < .001), from admission up to 3 months post-discharge. Gait speed increased significantly (+0.9 points; P = .00) for all participants and women and men separately (resp. +0.7 points; P < .001 and +1.0 points; P < .001), from admission up to 3 months post-discharge.

**Table 2.** Unstandardized linear mixed model analysis for the longitudinal changes in muscle mass, handgrip strength, the chair stand test and the gait speed test at admission, discharge, one- and three months post-discharge in acute hospitalized older adults

| Diagnostic measure* | Admission | Discharge | One-month | Three months | P-value* |
|---|---|---|---|---|---|
| Muscle mass SMI (kg/m2) | 7.9 (7.8-8.2) | 7.9 (7.7-8.1) | 7.7 (7.5-7.9) | 7.8 (7.6-8.0) | 0.03† |
| ♀ Muscle mass SMI (kg/m2) | 6.7 (6.5-6.9) | 6.7 (6.5-6.9) | 6.5 (6.3-6.7) | 6.5 (6.3-6.7) | 0.08 |
| ♂ Muscle mass SMI (kg/m2) | 9.1 (8.9-9.4) | 9.1 (8.9-9.3) | 8.8 (8.6-9.0) | 9.0 (8.7-9.2) | 0.13 |
| Handgrip strength (kg) | 27.1 (26.1-28.1) | 27.2 (26.1-28.2) | 26.1 (25.1-27.2) | 26.6 (25.6-27.7) | 0.08 |
| ♀ Handgrip strength (kg) | 20.2 (19.4-21.1) | 20.3 (19.4-21.1) | 19.4 (18.5-20.3) | 19.5 (18.6-20.5) | 0.03* |
| ♂ Handgrip strength (kg) | 33.6 (32.3-34.9) | 33.7 (32.4-35.5) | 32.6 (31.3-33.9) | 33.4 (32.1-34.7) | 0.55 |
| Chair stand (pts) | 1.1 (1.0-1.3) | 1.5 (1.3-1.6) | 1.6 (1.4-1.7) | 1.8 (1.7-2.0) | <0.001* |
| ♀ Chair stand (pts) | 0.9 (0.7-1.1) | 1.2 (1.0-1.4) | 1.4 (1.2-1.6) | 1.7 (1.5-2.0) | <0.001* |
| ♂ Chair stand (pts) | 1.4 (1.2-1.6) | 1.7 (1.5-1.9) | 1.8 (1.6-2.0) | 1.9 (1.7-2.2) | <0.001* |
| Gait speed (pts) | 1.9 (1.8-2.1) | 2.3 (2.2-2.5) | 2.1 (2.0-2.3) | 2.8 (2.6-3.0) | <0.001* |
| ♀ Gait speed (pts) | 1.7 (1.5-1.9) | 2.0 (1.8-2.1) | 1.8 (1.6-2.1) | 2.4 (2.2-2.7) | <0.001* |
| ♂ Gait speed (pts) | 2.1 (1.9-2.3) | 2.6 (2.4-2.8) | 2.4 (2.2-2.6) | 3.1 (2.9-3.3) | <0.001* |

*Presented with mean (95% confidence interval). † P-value shows the significance level (alpha = 0.05) between hospital admission - three months post-discharge. Abbreviations: ♀= female; ♂=male; SMI= Skeletal Muscle Index; kg = kilogram; m2=squared meters; pts: points.

Table 3 presents the confounders on the longitudinal changes of muscle mass, handgrip strength, chair stand, and gait speed. Fatigue was identified as a confounder for the longitudinal changes in muscle mass. Fatigue, BMI, and nutrition were identified as confounders and depressive symptoms as an effect modifier in the longitudinal changes of handgrip strength. Fatigue, depressive symptoms, and cognitive impairment were identified as confounders in the longitudinal changes of chair stand and depressive symptoms, BMI, cognitive impairment, and fear of falling were identified as confounders in the longitudinal changes of gait speed. Depressive symptoms were identified as an effect modifier in the longitudinal changes in muscle mass.

**Table 3.** Longitudinal change in muscle mass, handgrip strength, chair stand and gait speed, controlled for confounding factors.

| | Model 1: Crude model | | | Model 2: Adjusted model | | |
|---|---|---|---|---|---|---|
| | B | 95% CI | | B | 95% CI | |
| | | lower bound | upper bound | | lower bound | upper bound |
| Muscle mass | -0.08 | -0.12 | -0.03 | -0.10[1] | -0.15 | -0.01 |
| Handgrip strength | -0.17 | -0.33 | -0.00 | -0.19[1-3] | -0.39 | 0.02 |
| Chair stand | 0.23 | 0.18 | 0.28 | 0.12[1,4,5] | 0.05 | 0.18 |
| Gait speed | 0.24 | 0.17 | 0.30 | 0.27[2,4-7] | 0.20 | 0.33 |

Abbreviations: B=unstandardized beta regression coefficient; CI=confidence interval. Unstandardized beta controlled for: 1=fatigue; 2=body mass index; 3=nutrition; 4=depressive symptoms; 5=cognitive impairment; 6=nutrition; 7=fear of falling.

### Standardized longitudinal changes in muscle mass, handgrip strength, chair stand and gait speed

Figure 2 shows the standardized longitudinal changes in muscle mass, handgrip strength, chair stand test, and gait speed. Muscle mass and handgrip strength were not significantly different from each other. The longitudinal changes in muscle mass and handgrip strength were significantly different as for chair stand and gait speed ($P < .001$).

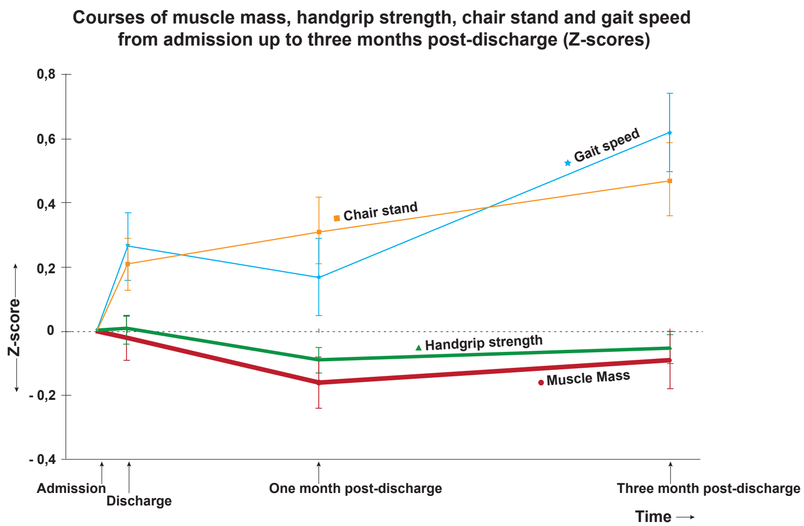


**Figure 2.** Standardized (Z-scores) longitudinal changes in muscle mass, handgrip strength, chair stand and gait speed from hospital admission up to three months post-discharge in acute hospitalized older adults.

**Sensitivity analysis**

Supplementary Table 2 show the complete cases with data at all timepoints for 108 older adults. The mean age (SD) for the complete cases was 77.8 years (6.0), 43% women. The mean (SD) value for muscle mass (SMI) was 8.1 kg/m2 (1.7), for handgrip strength 30.5 kg (10.0) and the median (IQR) value for chair stand was 1 point (0–3), for gait speed 3 points (1–4) and for the complete SPPB was 7 points (3–10). For the complete cases, longitudinal changes in muscle mass and handgrip strength showed a nonsignificant decrease up to 3 months post-discharge.

## Discussion

This multicenter prospective cohort study determined the longitudinal changes of the diagnostic measures of sarcopenia: muscle mass, handgrip strength, chair stand, and gait speed after hospitalization up to 3 months post-discharge. Physical performance improved although muscle mass decreased and handgrip strength did not change from acute hospitalization up to 3 months post-discharge, with differences between women and men. The lowest level of muscle mass was determined at 1-month post-discharge. Chair stand and gait speed improved from admission up to 3 months post-discharge. A considerable part of the older adults stayed below the normative levels of muscle mass, handgrip strength, and physical performance, at 3 months post-discharge.

The decline in muscle mass and absence of improvement in handgrip strength can be explained by the combination of inactivity and inflammation of older adults during and after acute hospitalization.[9,10,36] During hospitalization, muscle mass and handgrip strength did not change. The relatively short admission period, which is comparable to other studies,[6] and the ongoing deterioration could explain that a decline in muscle mass and muscle strength were observed only after 1-month post-discharge and not during hospitalization. In addition, low muscle function, recognized as sarcopenia, might already have been developed before hospitalization.[12,13] However, this cannot be confirmed in this study. The decline in muscle mass and handgrip may have relevance for clinical practice because the first month after discharge is reported as a critical period,[16] after which disabilities have a high chance of becoming permanent among older hospitalized adults. It can be hypothesized that the decline in muscle mass and handgrip strength have an impact on the physical performance. In this study, the improvement of the physical performance can be seen as part of the expected recovery after acute illness with hospitalization, where older adults are at their lowest level of functioning at hospital admission. A similar improvement was seen in a previous study,[15] in which the physical performance improved up to 3 weeks following discharge, but aberrant to another study[14] where no difference was reported 30 days post-discharge. Our study showed additionally that this improvement continued up to 3 months post-discharge with different patterns between gait speed and chair stand. An explanation for the different patterns for gait speed and chair stand might be that chair stand is conditional to the complex task of walking.[37] Although physical performance improved, not all older adults reach normative level. This means that older adults are still at risk for being (re)hospitalized with deteriorating health, at 3 months after discharge from hospital.[1,25,38]

The transition from hospital to the home situation seems to be crucial and older adults need specific guidance during this critical period. Previous studies from the Hospital-ADL study group reported that geriatric syndromes are highly prevalent after discharge from the hospital and are associated with functional decline.[17,18] The current study confirmed the involvement of psychosocial factors such as depressive symptoms, but also fatigue, nutrition, and BMI on the longitudinal changes in muscle mass, muscle strength and physical performance. The finding that depressive symptoms is an effect modifier in the longitudinal change of handgrip strength might indicate the role in the recovery of physical performance but needs further investigation.

The clinical implications of this study can be significant, because a substantial part of the older adults does not return to their level at which they can live independently. Current standard care after discharge from the hospital does not include an exercise program. It could be hypothesized that an exercise intervention is indicated to increase muscle mass and muscle strength in order to improve physical performances. This hypothesis is in accordance with the growing body of knowledge about the effect of exercise interventions for older adults.[39- 42] However, it is unclear if an exercise intervention could have a similar effect on an acutely hospitalized population with geriatric syndromes.[17,18] These syndromes, may be barriers to regain muscle mass and strength and recover to a higher level of functioning after acute hospitalization. Recent research has demonstrated that an exercise intervention during hospitalization could be an effective therapy for improving muscle strength and reducing functional decline.[42,43] Future research for this specific population with complex care needs, should focus on the transitional period after hospitalization to improve muscle mass, muscle strength and physical performances in the home situation to prevent functional decline and achieve normative levels of independent living. The role of geriatric syndromes, such as depressive symptoms, apathy, and nutrition, should be considered in the development of this intervention.[17,18,44-46]

This study has several limitations. First, measurements were taken in a standardized way according to a strict protocol.[19] However, some limitations need to be addressed. Second, data were missing due to several reasons such as inability to perform the test or not available for follow-up which is a known challenge in aging research.[47] The missing data might have introduced bias. A sensitivity analysis on the complete cases (Supplementary Table 2) showed nonsignificant differences in muscle mass and handgrip strength and differences in the temporal pattern of gait speed in comparison with the overall LMM analysis including all cases. However, LMM analysis is a sophisticated statistical technique which handles missing values very well.[34] Third, measurements were taken both in hospital and in the home situation, where the protocol was sometimes adjusted in some cases due to the organization in the hospital (patients were not always available at the same moment or in fasting condition) or in the home situation (not enough space to perform tests) which might have been influenced the results. Fourth, generalizability of the study might be limited because patients dependent in all 6 basic ADLs were excluded from this study, although this occurred in 3 patients only. Fifth, detailed information on additional treatment and use of medication of the patients is lacking. It remains unknown whether these factors might have influenced the results.

**Conclusions and Implications**

In conclusion, muscle mass and handgrip strength decrease, and physical performance improves after discharge from the hospital. At three months post-discharge, muscle mass, handgrip strength and physical performance do not reach normative levels. Our results underscore that in the transition from hospital to the home situation, improvement of muscle mass, muscle strength and physical performance is warranted, which could be possible by tailor-made exercises.

**Conflicts of interest**

All authors declare no potential conflicts of interest to disclose.

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6

# Factors associated with step numbers in acutely hospitalized older adults: The Hospital-ADL study


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## Abstract

**Objectives:** To determine the number of steps taken by older patients in hospital and one week after discharge; to identify factors associated with step numbers after discharge; and to examine the association between functional decline and step numbers after discharge.

**Design:** Prospective observational cohort study conducted in 2015–2017.

**Setting and Participants:** Older adults (≥ 70 years) acutely hospitalized for at least 48 hours at internal, cardiology, or geriatric wards in six Dutch hospitals.

**Methods:** Steps were counted using the Fitbit Flex® accelerometer during hospitalization and one week after discharge. Demographic, somatic, physical, and psychosocial factors were assessed during hospitalization. Functional decline was determined one month after discharge using the Katz-ADL index.

**Results:** The analytic sample included 188 participants [mean age (standard deviation) 79.1 (6.7)]. One month post discharge, 33/174 participants (19%) experienced functional decline. The median number of steps was 656 (interquartile range [IQR], 250–1146) at the last day of hospitalization. This increased to 1,750 (IQR, 675–4,114) steps one day post discharge, and to 1,997 (IQR, 938–4,098) steps seven days post discharge. Age (β = -57.93; 95% confidence interval [CI], -111.15 to -4.71), physical performance (β = 224.95; 95% CI, 117.79–332.11), and steps in hospital (β = 0.76; 95% CI, 0.46–1.06) were associated with steps post discharge. There was a significant association between step numbers after discharge and functional decline one month after discharge (β = -1400; 95% CI, -2380 to -420; P = .005).

**Conclusions and Implications:** Among acutely hospitalized older adults, step numbers double one day post discharge, indicating that their capacity is underutilized during hospitalization. Physical performance and physical activity during hospitalization are key to increasing the number of steps post discharge. The number of steps one week after discharge is a promising indicator of functional decline one month after discharge.

## Introduction

Physical activity is very limited in hospitalized older adults,[1-5] and is associated with functional decline,[1,6-8] readmissions,[9,10] and mortality.[4,11,12] Functional decline, described as new or additional difficulties performing one or more activities of daily living (ADL),[13] is a major problem and is highly prevalent in older adults after acute hospitalization.[8,14-17] More than 30% of acutely hospitalized older adults experience functional decline at discharge, and only one-third of these adults recover their premorbid functional level one month after discharge.[14] The first month after discharge is a critical recovery period, during which new functional disabilities have a high risk of becoming permanent.[14]

To prevent functional decline, the World Health Organization (WHO) recommends keeping older adults as physically active as their abilities and conditions allow.[18] However, physical condition and the ability to be physically active are greatly affected in acutely ill older adults during hospitalization.[19] It is known that physical activity is reduced during hospitalization, but levels of physical activity after discharge have not been well studied.[20] Physical activity, defined as "any bodily movement produced by skeletal muscles that requires energy expenditure",[21] can be objectively monitored as step numbers in older adults, using accelerometers.[4,6,10,20] One study using accelerometers showed that taking less than 900 steps per day during hospitalization is associated with functional decline at discharge.[6] Several studies have shown that physical activity interventions can improve physical performance in older adults,[15,22-24] but reversing functional decline in the first month after discharge remains challenging.[15]

To optimize in-hospital and post-discharge rehabilitation strategies to prevent or reverse eventual functional decline, we need more information on the number of steps taken after discharge and how the number of steps taken relates to functional decline. A previous study[20] showed that the number of steps taken in the first week after discharge was associated with 30-day readmission in older adults, indicating that the level of physical activity soon after discharge is a physical marker of readmission risk and overall health. Based on these findings, we hypothesized that step numbers one week after discharge are associated with functional decline one month after discharge. The aims of this study were to: i) determine step numbers in hospital and up to one week after discharge in acutely hospitalized older adults; ii) identify independent predictors of step numbers after discharge; and iii) examine the association between functional decline and step numbers after discharge.

## Methods

### Study Participants

Participants were from the Hospital-Associated Disability and impact on daily Life (Hospital-ADL) study, a multicenter observational prospective cohort study evaluating the mechanism of hospital-associated functional decline among 401 older adults aged 70 years and over, who were acutely admitted to six Dutch hospitals for ≥ 48 hours between October 2015 and June 2017.[25] Further inclusion criteria were: 1] approval of the medical doctor; 2] Mini-Mental State Examination (MMSE) score ≥ 15;[26] and 3] sufficient understanding of the Dutch language to answer the questionnaires. Persons were excluded if they: 1] had a life expectancy of less than 3 months or 2] were dependent on help for all six basic ADLs (bathing, dressing, eating, toileting, transferring, and maintaining continence).[27] There were no further exclusion criteria regarding walking ability. To determine whether a patient was eligible for inclusion, the researcher asked the attending medical doctor for approval before approaching the patient. Participants were recruited from internal medicine, cardiology, and geriatric wards and were asked to provide written consent before inclusion. All participants gave additional consent to wear an activity tracker during hospitalization and after discharge. The study was approved by the institutional review board. The study was conducted according to the Dutch Medical Research Involving Human Subjects Act and principles of the Declaration of Helsinki (1964). Local approval was provided by all participating hospitals.

**Assessments**
Demographics, malnutrition, and cognitive functioning of participants were assessed at admission. Comorbidities were retrieved from medical records. Other variables in physical, functional, and psychological domains that might change during hospitalization were assessed at discharge, which was considered the most optimal time-point to identify older adults at risk of insufficient recovery post discharge. Trained researchers administered the standardized study protocol. At one month post discharge, all participants were asked to rate their functionality in performing ADLs.

**Counting Steps**
The primary outcome was the number of steps taken per day in hospital and up to one week after discharge. For the second and third study aims, the primary outcome was the number of steps taken post discharge. Steps were counted using the Fitbit Flex® activity tracker (Fitbit®, Inc., San Francisco); an accurate activity tracker to estimate step counts compared to the gold standard Actigraph (r =.96).[28] The Fitbit Flex® is worn on the non-dominant wrist[29] and is user-friendly, which limits study withdrawal.[30] The activity tracker was worn continuously from hospital admission to one week after discharge. Participants were asked to wear the device at all times, except during charging (1–2 hours per week). Step data were frequently synced to the Fitbit platform and exported at the end of the study. Step numbers were counted every 24 hours, starting at the time of discharge (e.g., discharge at 3:00 PM until 3:00 PM the next day was the first day counted after discharge) up to seven days post discharge. Steps taken in hospital were counted in the same way, backwards from the time of discharge up to the time of study

inclusion for a maximum of seven days. Incomplete days (e.g., day of inclusion) and days when no steps were counted were omitted from analyses.

**Assessment of Functional Decline**

We assessed functional decline based on the ability to perform basic ADLs using the Katz-ADL index score.[27] At admission, we asked participants to retrospectively rate their ability to perform ADLs during the two weeks before hospital admission. This assessment was repeated at discharge and one month after discharge. Participants were asked whether they needed assistance to perform each ADL. A summary score was calculated ranging from 0 (independent in all ADLs) to 6 (dependent on help for all ADLs). Functional decline was defined as a higher dependency on help in one or more ADLs one month after discharge compared with baseline (two weeks before admission).

**Assessment of Other Variables**

Potential predictors for step numbers were identified based on Fried's theoretical cycle of physical frailty.[19] Comorbidities were assessed with the Charlson comorbidity index, (range, 0–31), where higher scores indicate higher one-year mortality risk.[31] Malnutrition was assessed with the short nutritional assessment questionnaire (SNAQ), and was categorized as no malnutrition, mild malnutrition, and severe malnutrition.[32] Handgrip strength was measured three times using a dynamometer.[33,34] The highest score (in kilograms) from both hands was used. Physical performance was assessed with the short physical performance battery (SPPB), which measures walking speed, chair stand, and balance. Scores range from 0 to 12, and higher scores indicate better physical performance.[35] The number of steps taken in hospital, counted using the Fitbit Flex®, was also a potential predictor of steps taken after discharge and was calculated as an average number of steps taken during hospitalization. Functionality in performing ADLs at discharge was assessed using the Katz-ADL, and scores ranged from 0 (independent at all ADLs) to 6 (dependent on all ADLs).[27] Somatic geriatric syndromes (fear of falling, pain, fatigue, and mobility impairment), which are prevalent after discharge[36] and may impair physical activity, were assessed.[37] Fear of falling, pain, and fatigue were measured using the numeric rating scale, which is a continuous scale from 0 (no symptoms) to 10 (severe symptoms).[38,39] Mobility impairment was assessed using the Functional Ambulation Categories test; scores range from 0 to 5, with higher scores indicating greater dependency.[40] We assessed psychological geriatric syndromes (cognitive functioning, depressive symptoms, and apathy) because they are 1] highly prevalent in this population;[36] 2] associated with physical activity;[41] and 3] potential barriers for functional recovery after acute hospitalization.[42,43] Cognitive functioning was assessed with the MMSE, with a score of ≤ 23 indicating cognitive impairment.[44] Apathy was measured with the Geriatric Depression Scale-3A (GDS-3A) subscale of the GDS-15.[45] Depressive symptoms were measured with the GDS-15 subscale (GDS-12D).[46] Higher scores indicated more symptoms of apathy and depression (range, GDS-3A: 0–3; GDS-

12D: 0–12).[45,46]

**Statistical Analyses**

Statistical analyses were performed in four phases: 1] descriptive analysis; 2] linear regression analysis of potential predictors of step numbers post discharge; 3] multivariable regression analysis of potential predictors of step numbers post discharge using a backwards selection procedure; and 4] multivariable regression analysis of functional decline and step numbers post discharge. For the first study aim, baseline variables and potential predictors were described with a mean and standard deviation (SD) or median and interquartile range (IQR) for continuous variables, and a number (n) and percentage (%) for categorical variables. The primary outcome was number of steps taken per day in hospital and one week after discharge and were presented as medians and IQR. Step numbers were also presented separately for older adults with and without functional decline. We assessed potential predictors of steps numbers taken after discharge using linear mixed models because these can account for correlations between repeated step measures. Factors associated with the primary outcome ($P < .10$) were retained for further analysis. The remaining factors were included in the multivariable linear mixed models. Because of high collinearity between physical factors, we used backward elimination to identify independent predictors using a cut-off P value of .05.[47] The results are presented as an unstandardized regression coefficient (beta), 95% confidence interval (CI), and P value. To evaluate the association of functional decline with step numbers, we used linear mixed models and adjusted for the independent predictors of steps numbers. We analyzed functional decline as the independent variable to assess differences in post-discharge step numbers between older adults with and without functional decline.

Mixed linear models can handle missing values in the dependent variable – missing values in the independent variables were imputed.[48] Based on the missing value patterns and percentage of missing values, we multiply imputed 50 datasets using the multiple imputation chained equations by fully conditional specification with predictive mean matching with K of 10 to the nearest neighbor. Results were pooled using Rubin's rules and used in the linear regression analyses.[49] Sensitivity analyses were conducted to check for selection bias. All baseline variables were compared between participants included in our analyses versus participants not included in our analyses. Additionally, a complete case analysis was performed to identify all risk factors associated with the number of steps taken after discharge. All statistical analyses were performed in Stata SE/15.1 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

## Results

Of the 401 participants, 55 did not consent to wear the activity tracker and post-discharge activity measurements were not available for 158 participants (see Figure 1). In total, 188 participants were included in the analysis. The sensitivity analysis showed that participants not included in the analysis (n = 213) had a significant lower body mass index, step number during hospitalization, handgrip strength, and SPPB score. Participants not included in the analyses also had a longer hospital stay, more frequent cognitive impairment, and a higher Katz-ADL score at discharge.

The mean (SD) age of participants was 79.1 (6.7) years, 106 (56.4%) participants were male, and 169 (89.9%) were born in the Netherlands (Table 1). At discharge, 57/188 (30.3%) participants experienced functional decline. 17/48 (35.4%) of these still had functional decline one month after discharge, and nine were lost to follow-up. Of the 131 participants without functional decline at discharge, 16/126 (12.7%) had functional decline one month after discharge, and five were lost to follow-up. In total 33/174 (18.9%) of the participants experienced functional decline one month post discharge.

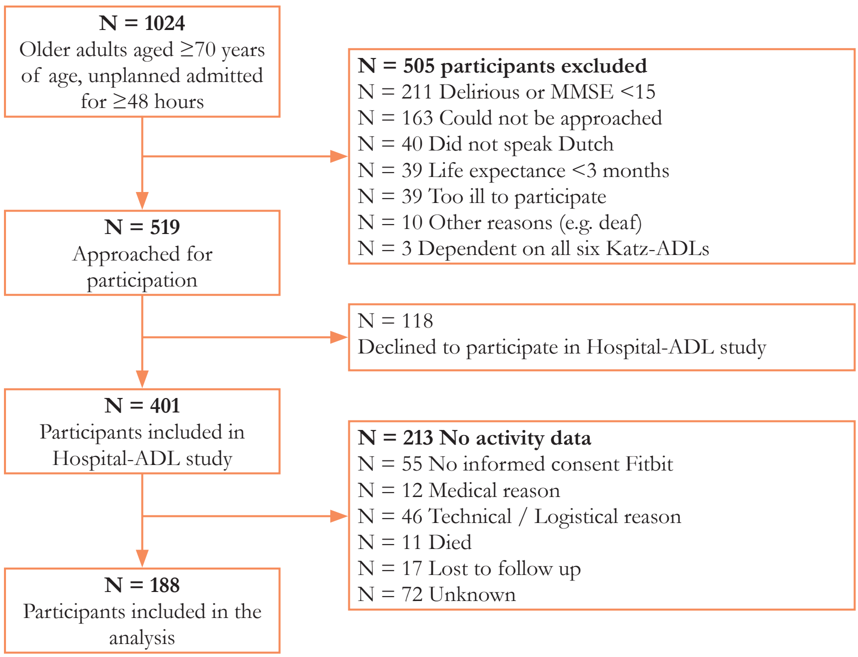



**Figure 1.** Derivation of the analytic sample

**Table 1.** Study sample characteristics during hospitalization (N = 188)

| **Patient characteristics** | |
|---|---|
| Age, mean (SD), y | 79.1 (6.7) |
| Male, No. (%) | 106 (56.4) |
| BMI, * mean (SD) | 22 (19-25) |
| Marital status, No. (%) | |
| Married or living together | 106 (56.4) |
| Widow/widower | 27 (14.4) |
| Single or divorced | 55 (29.3) |
| Born in the Netherlands, No. (%) | 169 (89.9) |
| Education, No. (%) | |
| Primary school | 44 (23.4) |
| Elementary technical/domestic science school | 42 (22.3) |
| Secondary vocational education | 58 (30.9) |
| Higher level high school/third-level education | 44 (23.4) |
| Polypharmacy, † No. (%), (n=186) | 121 (65.1) |
| Hearing impairment, No. (%) | 22 (11.7) |
| Vision impairment, No. (%) | 20 (10.7) |
| Primary admission diagnosis, No. (%) | |
| Cardiac | 60 (31.9) |
| Respiratory | 31 (16.5) |
| Other | 28 (14.9) |
| Infection | 24 (12.8) |
| Gastrointestinal | 22 (11.7) |
| Renal | 9 (4.8) |
| Cancer (including hematology) | 8 (4.3) |
| Electrolyte disturbance | 6 (3.2) |
| Length of hospital stay, median (IQR), d | 5 (4-8) |
| Charlson comorbidity index, ‡ median (IQR) | 2 (1-3) |
| SNAQ, No. (%) | |
| No malnutrition | 120 (63.8) |
| Mild malnutrition | 10 (5.3) |
| Severe malnutrition | 58 (30.9) |
| Handgrip strength, mean (SD), kg, (n=177) | 28.9 (10.6) |
| Physical performance, § median (IQR), (n=169) | 7 (4-10) |
| Steps taken in hospital, median (IQR), (n=166) | 922 (407-1633) |
| Katz-ADL score, ‖ median (IQR), (n=182) | 1 (0-2) |
| Fear of falling, median (IQR), NRS score, (n=183) | 0 (0-5) |

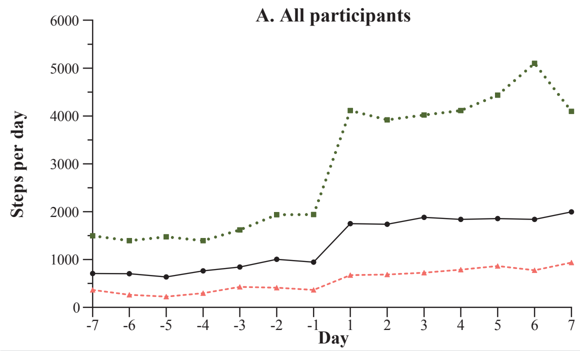
Table 1. *Continued*

| Patient characteristics | |
|---|---|
| Pain, median (IQR), NRS score, (n=184) | 0 (0-4) |
| Fatigue, median (IQR), NRS score, (n=183) | 5 (2-7) |
| FAC, No. (%), (n=176) | |
| Independent | 43 (22.9) |
| Independent on level surfaces | 95 (50.5) |
| Dependent for supervision | 28 (14.9) |
| Dependent for physical assistance I | 4 (2.1) |
| Dependent for physical assistance II | 2 (1.1) |
| Non-functional ambulation | 4 (2.1) |
| Cognitive impairment, ** No. (%), (n=169) | 13 (7.7) |
| Depressive symptoms, †† No. (%), (n=179) | 33 (17.6) |
| Apathy, ‡‡ No. (%), (n=179) | 96 (51.1) |
| Living independently after discharge, No. (%) | 147 (78.2) |

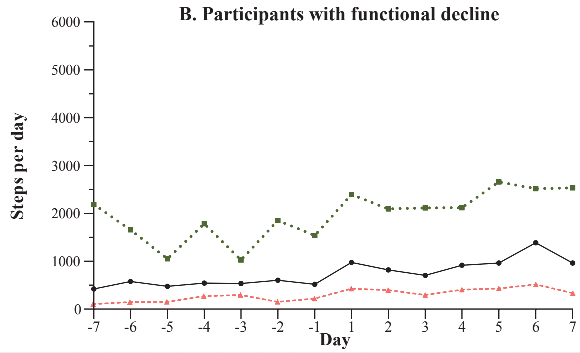
Abbreviations: SD, standard deviation; BMI, body mass index; IQR, interquartile range; SNAQ, short nutritional assessment questionnaire; ADL, activities of daily living; NRS, numeric rating scale; FAC, functional ambulation categories.
*Calculated as weight in kilograms divided by height in meters squared.
† Use of 5 or more different medications.
‡ Range of 0-31, with a higher score indicating more or severe comorbidity.
§ Assessed with the short physical performance battery. The score ranges of 0-12, a higher score indicates a better physical performance.
ll Ranging from 0 (independent at all ADLs) to 6 (dependent on all ADLs).
** If a score of <24 on the Mini-Mental State Examination.
†† If a score of ≥6 on the Geriatric Depression Scale.
‡‡ If a score of ≥2 on three items on the Geriatric Depression Scale.

Figure 2A shows the number of steps per day in hospital and after discharge. The median number of steps was 656 (IQR, 250–1146) on the last day before discharge and this more than doubled to a median of 1,750 (IQR, 675–4,114) steps on the first day after discharge. From the second day post discharge, the number of steps slightly increased to 1,997 (IQR, 938–4098) on the seventh day post discharge. Figures 2B and 2C show the number of steps separately for older adults with (n = 33) and without (n = 141) functional decline. In older adults with functional decline, the median was 518 (IQR, 229–1,541) steps on the last day before discharge, 978 (IQR, 437–2395) steps on the first day after discharge, and 965 (IQR, 344–2,535) steps on the seventh day after discharge. In older adults without functional decline, the median was 1,189 (IQR, 407–2,007) steps on the last day before discharge, 1,908 (IQR, 763–4,421) steps on the first day after discharge, and 2,289 (IQR, 1,222–4,727) on the seventh day after discharge.

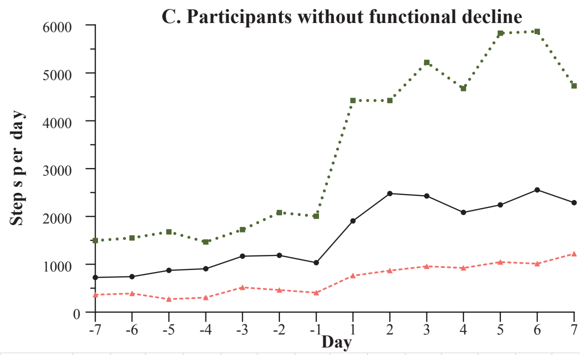
Table 2 shows the linear regression analysis of the potential predictors and the number of steps after discharge. Age, comorbidities, living independently,




| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| p75 | 1497 | 1397 | 1477 | 1394 | 1620 | 1939 | 1943 | 4114 | 3918 | 4022 | 4114 | 4435 | 5099 | 4098 |
| Median | 710 | 704 | 639 | 766 | 843 | 1004 | 945 | 1750 | 1740 | 1883 | 1840 | 1858 | 1840 | 1997 |
| p25 | 366 | 265 | 225 | 298 | 431 | 413 | 367 | 675 | 687 | 727 | 789 | 866 | 777 | 938 |
| n = | 46 | 56 | 74 | 92 | 108 | 132 | 147 | 103 | 123 | 146 | 162 | 167 | 163 | 157 |




| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| p75 | 2185 | 1656 | 1053 | 1784 | 1025 | 1852 | 1541 | 2395 | 2095 | 2117 | 2119 | 2656 | 2519 | 2535 |
| Median | 420 | 579 | 476 | 544 | 534 | 605 | 518 | 978 | 820 | 707 | 916 | 964 | 1388 | 965 |
| p25 | 115 | 160 | 162 | 281 | 309 | 162 | 229 | 437 | 409 | 308 | 419 | 444 | 526 | 344 |
| n = | 9 | 13 | 17 | 16 | 20 | 23 | 24 | 17 | 20 | 26 | 29 | 30 | 27 | 27 |




| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| p75 | 1497 | 1551 | 1681 | 1469 | 1726 | 2080 | 2007 | 4421 | 4424 | 5220 | 4674 | 5829 | 5866 | 4727 |
| Median | 725 | 742 | 873 | 910 | 1169 | 1189 | 1037 | 1908 | 2480 | 2427 | 2086 | 2242 | 2557 | 2289 |
| p25 | 366 | 390 | 274 | 305 | 520 | 463 | 407 | 763 | 872 | 958 | 927 | 1049 | 1014 | 1222 |
| n = | 31 | 35 | 49 | 68 | 79 | 97 | 111 | 77 | 93 | 109 | 121 | 124 | 125 | 120 |

**Figure 2A-C.** Number of steps* for (A) all participants (N = 188), (B) participants with functional decline (n = 33), and (C) participants without functional decline (N = 141)

**Table 2.** Univariable (model A) and multivariable (model B) linear regression analyses of predictors and step numbers after discharge

| | | Model A | | | | Model B | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Variables*** | **Reference** | **β†** | **95% confidence interval** | | **P value‡** | **β†** | **95% confidence interval** | | **P value§** |
| Age | Year | -147.68 | -200.63 | -94.73 | <.001 | -57.93 | -111.15 | -4.71 | .03 |
| Gender | Male | 265.00 | -492.3 | 1023.15 | .49 | | | | |
| Charlson comorbidity index | Score | -259.92 | -455.90 | -63.94 | .009 | | | | |
| SNAQ | No malnutrition | | | | | | | | |
| Mild malnutrition | | 871.23 | -770.63 | 2513.10 | .30 | | | | |
| Severe malnutrition | | -1292.68 | -2097.45 | -487.92 | .002 | | | | |
| Handgrip strength | Kilogram | 59.92 | 24.88 | 94.96 | .001 | | | | |
| Physical performance | Score | 362.57 | 261.96 | 463.19 | <.001 | 224.95 | 117.79 | 332.11 | <.001 |
| Steps taken in hospital | Step | 1.07 | 0.77 | 1.37 | <.001 | 0.76 | 0.46 | 1.06 | <.001 |
| Katz-ADL score | Score | -560.73 | -853.22 | -268.23 | <.001 | | | | |
| Fear of falling | Score | -172.00 | -293.39 | -50.63 | .005 | | | | |
| Pain | Score | -64.26 | -209.74 | 81.21 | .39 | | | | |
| Fatigue | Score | -184.63 | -324.81 | -44.46 | .01 | | | | |
| FAC | Non-functional | | | | | | | | |
| Dependent for physical assistance II | | -117.58 | -3846.98 | 3611.82 | .95 | | | | |
| Dependent for physical assistance I | | 365.99 | -2686.08 | 3418.06 | .81 | | | | |
| Dependent for supervision | | 794.6 | -1566.12 | 3155.33 | .51 | | | | |
| Independent on level surfaces | | 1636.18 | -621.53 | 3893.90 | .16 | | | | |
| Independent | | 4215.36 | 1902.45 | 6528.27 | <.001 | | | | |

**Table 2.** *Continued*

| Variables* | Reference | Model A | | | | Model B | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | β† | 95% confidence interval | | P value‡ | β† | 95% confidence interval | | P value§ |
| Cognitive impairment | No | -1987.33 | -3422.87 | -551.78 | .007 | | | | |
| Depressive symptoms | No | -1025.03 | -2002.02 | -48.05 | .04 | | | | |
| Apathy | No | -579.28 | -1360.52 | 201.96 | .15 | | | | |
| Living independent after discharge | No | 1301.93 | 402.09 | 2201.77 | .005 | | | | |

Abbreviations: See Table 1. *Refer to Table 1 for definitions.
†Unstandardized regression coefficients for continuous variables are per 1-point increase.
‡ Variables with a value <.10 were retained for further analysis.
§ Using a backward selection procedure variable with a P value <.05 were included in the model.

**Table 3.** Unadjusted (model A) and adjusted (model B) association of functional decline after discharge with steps numbers after discharge (N = 174)

| Variables* | Reference | Model A | | | | Model B | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | β† | 95% confidence interval | | P value | β† | 95% confidence interval | | P value |
| Functional decline at 1-month | No functional decline | -1400 | -2380 | -420 | .005 | -671 | -1668 | 325 | .19 |
| Age | Year | | | | | -58 | -125 | 9 | .09 |
| Physical performance | Score | | | | | 188 | 57 | 318 | .005 |
| Steps taken in hospital | Step | | | | | 0.9 | 0.6 | 1.3 | <.001 |

Abbreviations: See Table 1. *Refer to Table 1 for definitions.
†Unstandardized regression coefficients are per 1-point increase.

cognitive functioning, depressive symptoms, fear of falling, fatigue, handgrip strength, physical performance, malnutrition, functional disabilities, and steps taken in hospital had a p value < .10 and were retained for further analysis. In the multivariable linear regression analysis, we found that age (β = -57.93; 95% CI, -111.15 to -4.71), physical performance (β = 224.95; 95% CI, 117.79–332.11), and steps taken in hospital (β = 0.76; 95% CI, 0.46–1.06) were independent predictors of physical activity after discharge. This means that for every one-year increase in age, there was a reduction in steps after discharge, and for every 1-point increase in physical performance and every one-step increase in hospital, there was an increase in steps taken post discharge. These results differed slightly to the complete case analysis, which found comorbidities (β = -247.07; 95% CI, -443.84 to -50.3) to also be a significant predictor of steps taken post discharge.

Table 3 shows the unadjusted and adjusted association of functional decline one month after discharge with step numbers after discharge. Older adults with functional decline took significantly fewer steps after discharge than older adults without functional decline did (β = -1400; 95% CI, -2380 to -420; P = .005). Following adjustment for age, physical performance, and steps taken in hospital, there was no significant association between functional decline and step numbers after discharge (β = -671; 95% CI, -1667 to 325; P = .19).

## Discussion

This study aimed to assess the number of steps taken by older adults in hospital up to one week after discharge, to identify factors associated with step numbers after discharge, and to determine if functional decline one month after discharge is associated with step numbers after discharge. Our results showed that the number of steps taken one day after discharge was double those taken prior to discharge. This finding suggests the physical capacity of older adults may be underused during hospitalization, regardless of their (dis)ability. Moreover, the number of steps taken slightly increased for up to seven days post discharge, but the number of steps remained low in the majority of older adults. These results demonstrated that, at a younger age, better physical performance and more steps taken in hospital were independently associated with higher post-discharge step numbers. The number of steps taken one week after discharge was significantly lower in participants with functional decline one month post discharge compared with in those who experienced no functional decline. This association was not significant after correcting for age, physical performance, and steps taken in hospital.

The median number of steps taken in hospital was consistent with results from previous studies in similar patient populations.[4,5] We found that approximately 50% of older adults did not take the recommended 900 steps per day during hospitalization, which is associated with a higher risk of functional decline at discharge.[6] Compared with a study by Fisher et al., we counted fewer steps in the first week post discharge. A possible explanation for this discrepancy is the different exclusion criteria; in our study, older adults were not excluded if they could not walk safely without assistance, which was an exclusion criterion in the study of Fisher et al.[20] Although low step numbers are common during hospitalization in our population,[4,5] the increase in step numbers that we observed immediately after discharge shows that older adults do not use their full physical capacity during hospitalization. This important finding implies that older adults can be more physically active during hospitalization and underlines the need for in-hospital interventions to stimulate physical activity.[50,51]

Our findings suggest that, of the of physical frailty factors described by Fried et al.,[19] only age,[41] physical performance, and in-hospital step numbers are predictors of post-discharge step numbers. These findings support the theory that acute illness and age-related changes can lead to loss of muscle mass and physical performance, resulting in functional decline and reduced physical activity.[19] In this light, our results suggest that particularly frail older adults, who are more likely to be functionally vulnerable to an acute illness,[52] become less active after an acute illness.[20] Offering targeted interventions to these vulnerable individuals to improve their physical performance and physical activity while they are in hospital may improve post-discharge activity levels.[15]

The present study has also shown that a large proportion of acutely hospitalized older adults experience functional decline one month after discharge.[14] We also showed that these older adults accrued significantly fewer steps in the first week after discharge compared to older adults without functional decline after discharge. This association between functional decline and physical activity has already been shown during hospitalization.[6,8] In line with the findings of Fisher et al., our results support the idea that the level of physical activity in the first week after discharge may predict recovery after acute hospitalization.[20] However, our results also suggested there is no direct association between physical activity and functional decline, and that age and physical performance may confound this relationship.[19] Further research is needed to determine whether modifiable factors like physical activity and physical performance can predict functional decline or recovery after discharge. This information may lead to the development of more effective interventions to prevent or reverse functional decline during the post-discharge recovery period.

**Limitations**

This study has several potential limitations. First, we aimed to include a cohort of older adults with a wide range of vulnerability. However, we had to exclude participants without post-discharge activity data, which may have resulted in selection bias; this means that participants who stayed in hospital longer, whose physical performance was poor, and who took fewer steps in hospital, and who might have been more vulnerable as a result, were excluded. This may have led to an underestimation of the observed associations and reduced the generalizability of our findings to these older, more vulnerable adults. Secondly, we assessed physical activity using the Fitbit Flex® activity tracker because of its practical applicability, user-friendly wristband, and high reliability in measuring steps. Fitbit Flex® wearing was controlled using logbooks and regular checks. However, the Fitbit Flex® does not detect non-wear time, so physical activity would have been underestimated if the participant was not wearing the tracker. A major strength of this study was the continuous assessment of physical activity during hospitalization up to the first week post discharge in a heterogeneous cohort of acutely hospitalized older adults. A large cohort of older adults with a wide range of diagnoses was included. During hospitalization, we assessed a broad set of potential predictors of physical activity.

**Conclusions and Implications**

This study shows that step numbers taken by acutely hospitalized older adults double immediately after discharge, indicating that the physical capacity of older persons is underutilized during hospitalization. Acutely hospitalized older adults with a younger age, better physical performance, and higher in-hospital physical activity levels have better post-discharge physical activity levels. Interventions focusing on physical performance and physical activity during hospitalization may optimize post-discharge physical activity and should continue during the critical post-discharge recovery period. The level of physical activity in the first week after discharge is a promising indicator of functional decline one month after discharge. Further research is needed to determine whether physical activity and physical performance can predict recovery after acute hospitalization.

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7

# Recommendations for an exercise intervention and core outcome set for older patients after hospital discharge: results of an international Delphi study

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## Abstract

For older adults, acute hospitalization is a high-risk event with poor health outcomes, including functional decline. In absence of practical guidelines and high quality randomized controlled trials, this Delphi study was conducted. The aim of this study was to obtain consensus on an exercise intervention program, a core outcome set (COS) and handover information to prevent functional decline or restore physical function in acutely hospitalized older patients transitioning from hospital to home. An internal panel of experts (n=16) in the field of exercise interventions for acutely hospitalized older adults were invited to join the study. In the Delphi study, relevant topics were recognized, statements were formulated and ranked on a 9-point Likert scale in two additional rounds. To reaching consensus, a score of 7–9 was classified as essential. Results were expressed as median and semi-interquartile range (SIQR), and consensus threshold was set at SIQR≤0.5. Fifteen international experts from eight countries participated in the panel. The response rate was 93%, 93% and 80% for the three rounds respectively. After three rounds, consensus was reached on 167 of the 185 (90.3%) statements, of which ninety-five (51.4%) were ranked as essential (median Likert-score ≥7.0, SIQR ≤0.5). This Delphi study provides starting points for developing an exercise intervention, a COS and handover information. The results of this Delphi study can assist physical therapists to provide a tailored Resistance Exercise Training (RET) intervention for older patients with complex care needs after hospital discharge, to prevent functional decline and/or restore physical function.

For older adults, acute hospitalization is a high-risk event with poor health outcomes, including functional decline, readmission and mortality.[1] More than 30% of older adults experience physical deconditioning and functional decline after acute hospitalization.[2,3] Several factors are associated with functional decline, including severity of the acute disease, immobility,[4,5] reduced physical activity,[6,7] low muscle mass/strength,[8,9] nutritional deficiency[10] and geriatric syndromes.[11,12] These factors are highly prevalent in older patients after acute hospitalization and might hinder recovery, reduce physical functioning and promote functional decline.[3,11]

Functional decline is the loss of activities of daily living with worsening self-care skills[13] and can be reduced during hospitalization with an exercise program.[14] In this study, in-hospital exercise programmes to prevent functional decline were performed twice per day. These programmes included multiple components that focused on the patients' individual needs.[14] Providing older patients with an exercise programme when they transition from the hospital to home has been associated with better recovery and less functional decline. However, this association has not been confirmed.[15-17] Exercise interventions started in the hospital are often not continued at home, despite the importance of these interventions to the patients.[2]

A seamless transition of exercise interventions from the hospital to home might stimulate recovery and prevent functional decline.[1,11,13] However, practical guidelines on the frequency, intensity, time, and type (FITT) of home-based exercise interventions in older patients after hospitalization are lacking. Also important to a seamless transition in rehabilitation care from hospital to home are recommendations for handover information and measurement tools as part of a core outcome set (COS) for clinical practice. It has been suggested that a COS would increase uniformity[18-21] in research and clinical practice and might help create exercise intervention programmes that are tailored to the individual needs and goals of the patient.

In the absence of practical guidelines and high-quality randomized controlled trials, the Delphi methodology is often applied to obtain expert consensus on interventions for different populations.[22,23] If experts could agree on practical guidelines for an exercise intervention, a COS and handover information for older patients after acute hospitalization in the home situation, this would guide physical therapists in their clinical decision-making. The aim of this Delphi study was to develop a consensus statement on 1) the characteristics of a home-based exercise intervention, 2) a COS of measurements on daily functioning and 3) handover information for older, acutely hospitalized patients transitioning from hospital to home that can prevent functional decline or restore physical function.

## Methods

To determine topics relevant to the objective of this Delphi study, a scoping literature review was conducted on measurement tools and exercise interventions for older adults. After this, a three round Delphi method was applied. A steering committee consisting of experts in complex care and rehabilitation after acute hospitalization from the Amsterdam University Medical Centers (Amsterdam UMC), location AMC supervised the Delphi project. The project was registered with the Core Outcome Measures in Effectiveness Trials (COMET) initiative (study reference: http://www.comet-initiative.org/Studies/Details/1294).

We conducted a scoping literature review searching PubMed, Medline, PEDro, CINAHL, Science Direct and ProQuest Social Sciences to summarize the current state of the art.[24,25] This scoping review included studies on characteristics of exercise interventions and measurement tools within the domains of the International Classification of Functioning (ICF)[26] for older patients after acute hospitalization. Articles were considered for review if they were systematic reviews or clinical trials and published in the last 10 years and if exercise for older adults was the studied intervention. Based on the scoping review, the following three topics were recognized: 1) characteristics of the exercise intervention, 2) COS of measurement tools and 3) handover information. Statements on the three topics were formulated and then discussed by the panel.

**Expert panel**

Delphi panel members were recruited based on their clinical and scientific expertise in exercise interventions, their professional background, their research output, and their geographical location. Eligible panellists were invited to participate via email, and informed consent for publication of the results was obtained when they agreed to participate.

**Delphi rounds**

The Delphi rounds were conducted between January and April 2019. It was decided, a priori, to conduct a minimum of three rounds because this is considered appropriate when limited scientific evidence is available.[23] Panellists were asked to rank statements on a 9-point Likert scale, as per Delphi methodology recommendations.[18] A score of 1–3 was given to items of limited importance; a score of 4–6 to items ranked as important but not essential; and a score of 7–9 to items deemed essential (Figure 1). Panellists could also give a score of 0 (unable to score) if they felt a topic or statement fell outside of their scope of expertise. For each statement scored in the second and third Delphi rounds, a median Likert-score and semi-interquartile range (SIQR) were computed based on the first and third quarters of the SIQR.[27] Results from the second Delphi round were imputed into the final round results if no third-round score was given. Consensus was defined a priori as an SIQR ≤0.5. Statements with consensus and a median Likert score ≥7.0 were used for further analysis. Consensus was reached on ≥80% of the statements after round three, so no extra Delphi round was deemed necessary.[22-24]

| Unable to score | Limited importance | | | Importance, but not essential | | | Essential | | |
|---|---|---|---|---|---|---|---|---|---|
| O | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |

**Figure 1.** Scoring of each statement on a 0-9 Likert Scale

**Delphi round 1: collecting expert opinions**

The aim of the first round was to collect expert opinions on the three topics identified in the scoping review (exercise intervention, COS, and handover information). A case description of an acutely hospitalized older adult transitioning home from hospital provided the context and was the starting point for each panel member (supplementary material). The questions were related to the different aspects of the ICF and used a standard description of health and health-related status.[25] In this first round, 22 closed questions on the three topics were asked with multiple possible answers. Additional information was also collected from 17 open questions on topics such as the intensity of training or involvement of other healthcare professionals (supplementary material). All items checked as relevant by the panel members were included in the following rounds. Answers to the open questions were examined to check whether they raised new questions or identified different topics. All input was categorized, and statements were drafted for each of the topics and approved by the steering committee.

**Delphi round 2: Ranking statements**

After the first Delphi round, 185 statements were formulated: 74 on exercise interventions, 86 on measurement tools and COS, and 25 on handover information.

**Delphi round 3: Consensus round**

In the third Delphi round, each panellist received their results from the second Delphi round together with the panel's median Likert scores and SIQR for each of the statements. If an individual panel member's scores differed from the panel's median scores, they were asked to consider re-ranking the statement towards the median to reach consensus. Participants were motivated further if they chose not to re-rank their statements.

## Results

All invited experts agreed to participate in the Delphi panel (n=16). One panellist did not respond within the allocated time for the first Delphi round so 15 panellists were included in the analysis. The response rates were 93% for round one, 93% for round two and 80% for round three. Table 1 presents the panellists' nationalities, profession, field of expertise, years of clinical experience and response. The panel consisted of nine physical therapists, two exercise physiologists, two sports scientists, one physician and one occupational therapist.

**Table 1.** International Delphi panel characteristics

| | Country | Gender | Title | Field of Expertise | Years of Clinical experience | Number of Publications in PubMed | Round 1 | Round 2 | Round 3 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Australia | Male | Professor | Exercise physiologist | >20 | 127 | ✓ | ✓ | ✓ |
| 2 | Belgium | Male | MSc | Physical therapist | >20 | 2 | ✓ | ✓ | ✓ |
| 3 | Belgium | Male | Professor | Exercise Physiologist | 10-15 | 82 | ✓ | ✓ | ✓ |
| 4 | Canada | Female | PhD | Physical therapist | 5-10 | 14 | ✓ | ✓ | ✓ |
| 5 | Denmark | Female | PhD | Physical therapist | 15-20 | 7 | ✓ | - | - |
| 6 | Netherlands | Female | MSc | Physical therapist | 15-20 | 0 | ✓ | ✓ | ✓ |
| 7 | Netherlands | Female | MSc | Physical therapist | 15-20 | 0 | ✓ | ✓ | ✓ |
| 8 | Netherlands | Female | PhD | Physical therapist | 10-15 | 28 | ✓ | ✓ | ✓ |
| 9 | Netherlands | Male | PhD | Exercise physiologist | 10-15 | 45 | ✓ | ✓ | ✓ |
| 10 | Netherlands | Female | MSc | Physical therapist | >20 | 0 | ✓ | ✓ | ✓ |
| 11 | Spain | Female | Associate professor | Physical therapist Sport scientist | 10-15 | 50 | ✓ | ✓ | ✓ |
| 12 | Spain | Male | Professor | Sport scientist | 15-20 | 104 | ✓ | ✓ | - |
| 13 | Spain | Male | Associate professor | Medical doctor | >20 | 71 | ✓ | ✓ | - |
| 14 | USA | Female | Associate professor | Occupational therapist | 10-15 | 23 | ✓ | ✓ | ✓ |
| 15 | USA | Male | Associate professor | Physical therapist | 5-10 | 10 | - | ✓ | ✓ |

– = no response; ✓= response obtained

After round three, consensus was reached on 185 statements, warranting the end of the Delphi consensus process. Ninety-five of the 185 statements (51.4%) were consensually ranked between 7 and 9 on the Likert scale and therefore considered essential for implication in clinical practice by the Delphi panel.

**Theme 1: Exercise intervention**

Seventy-four of the 185 (40.0%) statements were about exercise interventions to prevent functional decline after hospital discharge. Of these, 55 statements (74.3%) were consensually ranked as essential (supplementary material). Statements covered topics such as FITT of training, the need for supervised exercise programmes, importance of exercise programmes, and whether exercise interventions should be combined with nutritional and behavioural interventions. Regarding training frequency, daily exercise interventions in the acute phase (up to 7 days post-discharge) and 1–2 times weekly interventions in the sub-acute phase (up to 12 weeks post-discharge) and long-term phase (>12 weeks post-discharge) were consensually ranked as essential for preventing functional decline. The panel agreed that exercise intensity levels up to 70–80% of the maximum heart rate are essential for preventing functional decline and that contra-indications should be absent. With regards to the type of training in the acute phase, the panel ranked early mobilization, supervised tailor-made exercise interventions, and combined exercise interventions (including strength, aerobic and functional training, either individual or in a group) as essential. Furthermore, co-creation of a training program by the patient and healthcare professional, functional training, building up physiological reserves, coaching, and reassessment and treatment by a geriatrician post-discharge were all ranked as essential during the recovery phases. Figure 2 summarizes these exercise intervention characteristics and existing recommendations.

**Theme 2: Core Outcome Set**

Eighty-six of the 185 (46.5%) statements were related to measurement tools for the COS. Of these statements, 25.6% (22 statements) were consensually ranked as essential. For activities of daily living, functional exercise capacity, performance, and muscle strength, more than one measurement outcome was ranked as essential. Figure 3 presents an overview of the measurement tools across all ICF domains. A COS of measurement tools was consensually ranked as essential for identifying risk factors of functional decline.

**Theme 3: Handover information**

Of the 185 statements, 25 (13.5%) were related to the handover information provided when the patient is discharged from hospital. The panel consensually ranked five demographic aspects as essential for inclusion in handover information: age, gender, weight, height and living situation. Panellists also ranked the following 13 items as essential for inclusion in the handover information: hospital length of stay, number of days of bedrest and sedentary behaviour, comorbidities, reason

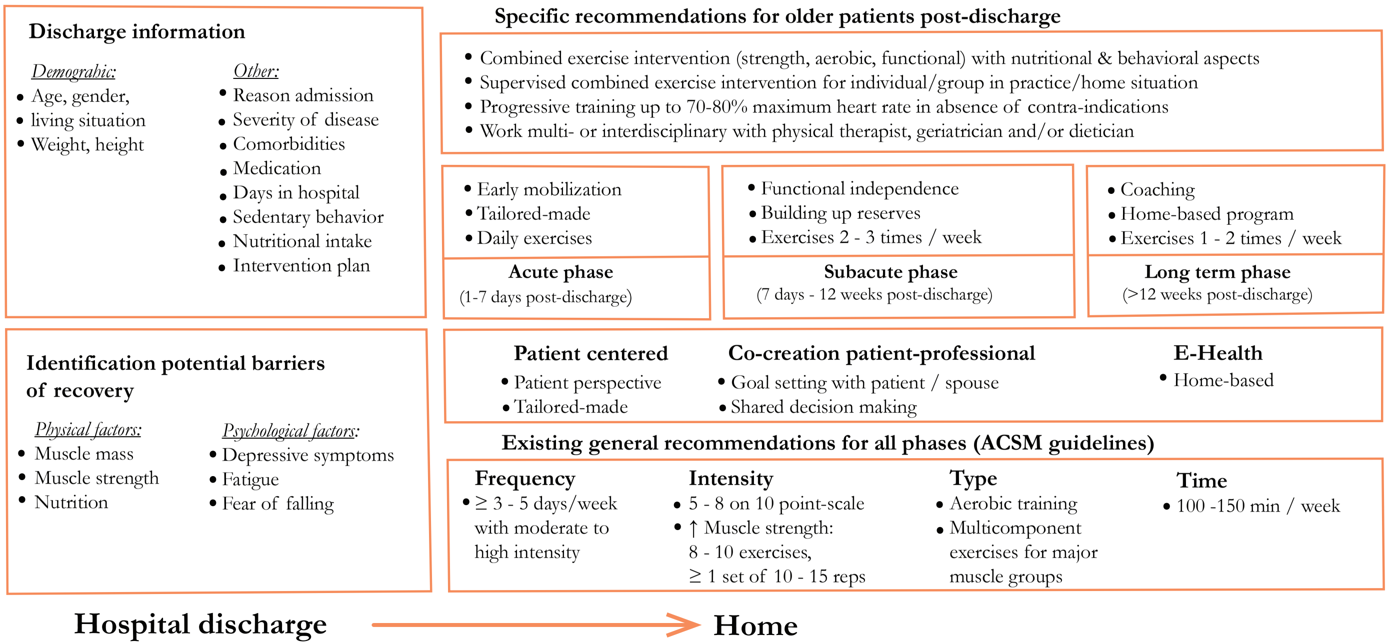


**Figure 2.** Recommended exercise intervention characteristics and handover information derived from this Delphi consensus process in addition to general recommendations for older patients after discharge from hospital

for hospital admission and/or severity of illness, medication usage, physical therapy interventions, level of (physical) functioning at hospital discharge, premorbid level of functioning, nutritional intake, and treatment goals. Detailed ranking results including median Likert scores and SIQRs can be found in the supplementary material.

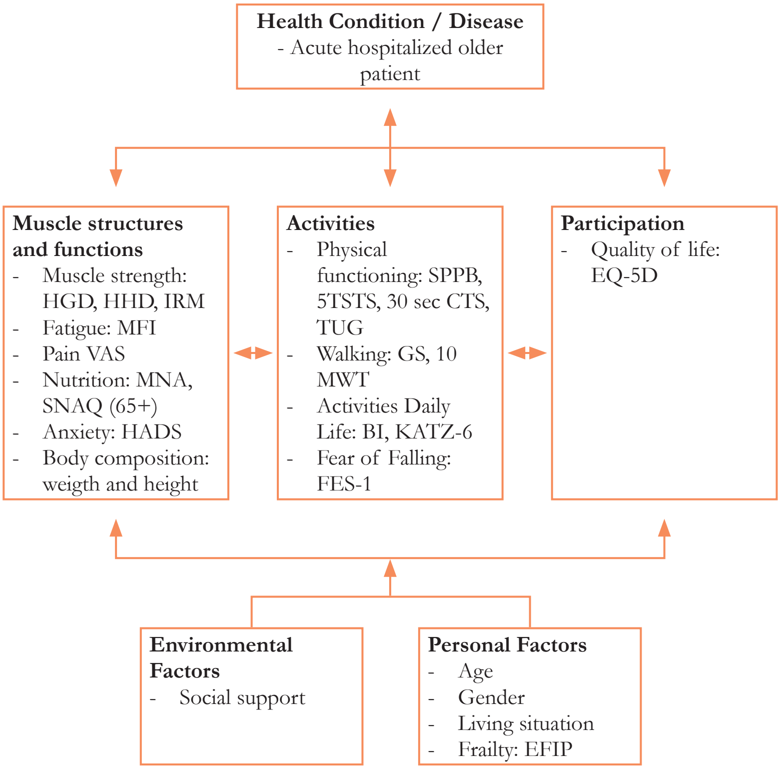


**Figure 3.** Core outcome set (COS) of measurement tools per ICF domain post-discharge. Abbreviations: BI: Barthel Index; CTS: Chair to Stand; EFIP: Evaluation Frailty Index for Physical activity; EQ-5D; EuroQol Health Questionnaire; FES: Fall Efficacy Scale; GS: Gait Speed; HADS: Hospital Anxiety Depression; HGD: Hand Grip Dynamometer; HHD: Hand Held Dynamometer; MFI: Multidimensional Fatigue Inventory; MNA: Mini Nutritional Assessment; MWT: Meter Walk Test; RM: Repetition Maximum; SNAQ: Short Nutritional Assessment Questionnaire; SPPB: Short Physical Performance Battery; TUG: Timed Up and Go; VAS: Visual Analogue Scale; 5 TSTS: 5 Times Sit To Stand.

## Discussion

This Delphi study provides practice guidelines for an exercise intervention, a COS and handover information to facilitate the seamless transition of exercise interventions when older patients are discharged from hospital. Experts agreed that supervised intensive exercise programmes should continue after hospital discharge and that these interventions should be tailored to the specific needs of the patient. COS measurement tools in all domains of the ICF and handover information from the hospital can help to tailor the exercise intervention to promote recovery, prevent functional decline, and restore physical function.

After discharge from hospital, exercises and physical activity are often not continued because stimulus[21] and self-discipline[17] are lacking. The expert panel agreed that an exercise intervention with FITT criteria should be continued after discharge to prevent functional decline or restore physical function. This is consistent with the guidelines on exercise from the American College of Sports Medicine.[26,27] Exercise interventions are associated with higher activities of daily living,[28] better mental health[29] and improved quality of life in older adults. Our panellists also agreed that high-intensity exercise interventions are suitable in this population if no contra-indications are present such as decompensated congestive heart failure or severe aortic stenosis.[30] Exercise interventions to regain physical functioning should be supervised by a physical therapist in older patients who are discharged from hospital with multiple chronic diseases. This is in line with the recommendation from Echeverria et al.[17] that home-based programmes require self-discipline, and that group exercise may have an important social element. A novel finding of our study is the expert consensus that exercise interventions should be tuned to the specific needs and goals (such as independent self-care, cooking or gardening) of the patient. Previous research has also suggested setting collaborative goals for complex care interventions in older patients with chronic diseases or multimorbidities.[31,32]

A COS in all domains of the ICF can give a complete overview of an older patient's physical functioning when they return home. Geriatric syndromes such as apathy, fear of falling, fatigue, depressive symptoms[11] or undernutrition[10] are highly prevalent in older patients and prevent recovery of functioning after acute hospitalization.[11] Indicating that these syndromes are present in the handover information when a patient is discharged home from hospital might increase the success of an exercise intervention. Our expert panel agreed that if multiple risk factors are identified, other healthcare professionals should be involved in the interventions. However, it can be difficult to collect information on all ICF domains of patient functioning because this is time-consuming and burdensome for older patients. Future studies could investigate how to collect this information using wearables.[33,34]

To optimize transitional care, a seamless transition with handover information is important. However, this does not automatically prevent functional decline in older patients.[35,36] It has been shown that exercise interventions during hospitalization can prevent functional decline or restore physical function,[14,15,37] but the effects of exercise interventions at home after discharge have not been properly defined.[16] In older patients, the cardiopulmonary and musculoskeletal systems are often not appropriately challenged or loaded by exercise interventions. Finding the optimal FITT training parameters is crucial for recovery.[38] Future research should investigate the effectiveness and appropriateness of exercise interventions and determine how to tailor these interventions to the patient's goals. Our expert panel agreed that eHealth should be investigated in future studies to see whether it can improve the post-discharge care of older patients with complex care needs. Evidence-based knowledge of how psychometric sound assessment tools with normative sex-related values and proper clinical reasoning can be used to tailor exercise interventions to individual older patients who have been acutely hospitalized might reduce the pathophysiological disease process and restore physical functioning.

**Study strengths and limitations**

The strengths of this study were the international panel with expertise in exercise interventions, the high response rate, the structured methodology and the relevance of the topic. The study also had limitations. First, although the Delphi panel was chosen with care, all panel members were from Western countries, so recommendations from this study cannot be easily extrapolated to the healthcare systems of non-Western countries. Second, most panel members have a primary background in physical therapy, so the physical therapy profession may be overrepresented in the practice recommendations. However, the panel had a broad view on this topic and underscored the involvement of other healthcare professionals for optimal intervention.

**Conclusion**

This Delphi study has provided starting points for developing an exercise intervention, COS and handover information that can prevent functional decline or restore physical functioning in older patients after discharge from hospital. The results of this Delphi study might help physical therapists to develop an exercise intervention for older patients with complex care needs after hospital discharge.

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8

# General discussion

“Despite my handicap,
I can still have fun"
(Henk, 81 years)

## Introduction

Acute hospitalized older patients frequently experience disabilities when they return home after being discharged from hospital – this is known as hospital-associated disability (HAD). HAD may lead to permanent functional decline and loss of independency.[1,2] Multiple factors contribute to this deterioration in health. Covinsky et al.[2] developed a model to describe the main risk factors for HAD; these risk factors were pre-illness determinants of functional reserve, severity of the acute illness, hospitalization factors and post-hospitalization factors.[2]

This thesis determined demographic, physical and psychosocial factors and their interaction, in acutely hospitalized older patients. These factors were measured during and after hospitalization to determine their longitudinal development and their effect on physical functioning. Previous research from our study group,[4] looked at the role of psychosocial factors in the development of HAD after acute hospitalization. In this thesis, we focused on physical risk factors of HAD and examined their impact on physical functioning and disability after acute hospitalization. The results described in this thesis, together with our previous findings, will guide healthcare providers to develop a tailored exercise intervention to prevent HAD in acutely hospitalized older patients with complex care needs. The physical and psychosocial risk factors we identified complement those in the model of Covinsky et al.[2]

The aims of this thesis were to:

1. Examine changes in physical functioning, muscle mass and muscle strength after acute hospitalization.
2. Identify physical risk factors for poor health outcomes.
3. Provide evidence to develop a Resistance Exercise Training (RET) intervention tailored to acute hospitalized older patients to prevent HAD and improve independent living.

To realize these aims, we addressed several knowledge gaps in relation to physical functioning, physical activity, muscle mass and muscle strength in acutely hospitalized older patients.

In this discussion, we reflect on the main findings of this thesis. Implications and presumed adaptations of the model by Covinsky et al.[2] will be presented along with methodological considerations and the implications of our findings on future research, education, and healthcare. Finally, we will present the general conclusions.

## Reflections on the main findings of this thesis

Several previous studies have reported HAD in older patients after hospitalization.[1,5,6,7] Our results were consistent with these reported findings. In **Chapter 2**, we showed that 27% of older patients died within one year after discharge from hospital and most of the older patients experienced severe disability. Patients with a hip fracture followed one of three distinct disability trajectories: mild, moderate, or severe. Most recovery took place in the first months after discharge from hospital and the patient's condition then stabilized between three months and one year after discharge. Patients with a mild disability trajectory almost completely returned to baseline physical functioning after one year, whereas patients with a moderate or severe trajectory developed more disabilities in the first year after discharge. These observations suggest that a different treatment approach is needed for each trajectory. Patients with a moderate or severe disability trajectory may need a tailored exercise intervention to prevent functional decline, while patients with a mild trajectory may recover independently with limited support from healthcare professionals. Different recovery trajectories have also been identified in other studies of older patients after hospitalization.[8-10] These studies confirmed that the first months after hospitalization are critical for recovery5 and should be used to start an exercise intervention to promote recovery and prevent functional decline. To collect more detailed information on the recovery of older patients after an acute hospitalization from a multifactorial perspective, we performed the Hospital-ADL study, described in **Chapter 3**. The aim of this study was to identify demographic, physical and psychosocial factors that contribute to HAD within three months after hospital discharge. These findings might help to specify starting points for developing a suitable exercise intervention for older patients after an acute hospitalization.

**Muscle mass and muscle strength decreases after discharge and is associated with physical functioning**

Acute hospitalization with a medical illness may reduce muscle mass and muscle strength in older patients because of physical inactivity. Muscle strength is an essential prerequisite for physical functioning and its decline is associated with HAD.[11] In **Chapter 4**, we determined a longitudinal association between muscle strength and physical functioning, which indicated that increasing muscle strength can improve physical functioning in older patients during and/or after hospitalization. We assessed physical functioning using the De Morton Mobility Index (DEMMI), in which the patient was asked to demonstrate several activities such as rolling to the side of the bed, standing up from a chair and walking.[12] Performance tests like these have been more frequently included in geriatric assessments in the last decade and provide important complementary information to self-reported assessments about physical functioning.[13,14] We found that age, cognitive impairment, fear of falling and depressive symptoms reduced the longitudinal association between muscle strength and physical functioning. While the importance of muscle strength on recovery after hospitalization had been shown,[15] the role of psychosocial factors such as fear of falling and depressive symptoms in interaction with physical factors had not been identified previously. Our findings showed that muscle strength interacts with fear of falling and depressive symptoms during recovery and that these factors should be considered when developing a resistance exercise intervention for this older population after hospitalization. In **Chapter 5**, we showed that muscle mass and muscle strength decreased in the three months after discharge from hospital while physical functioning improved. This might contradict with the longitudinal association between muscle strength and physical functioning we identified in **Chapter 4**. Possible explanations for this discrepancy are i) the different measurement tools used to measure physical functioning in the two chapters (de Morton Mobility Index in Chapter 4 versus the Short Physical Performance Battery (SPPB) in Chapter 5), ii) different values for missing data in the studies due to the statistical procedure and iii) the correction for psychosocial factors in the longitudinal association between muscle strength and physical functioning in **Chapter 5**.

In **Chapter 5**, improvements in physical functioning were observed where over 40% of older patients scored below normal levels of physical functioning three months after discharge from hospital. Physical functioning is a prerequisite for normal independent living as described by the ICF. A below normal score for physical functioning indicates that patients are not completely independent in ADLs such as cooking, self-care and/or shopping.[16] Although physical functioning partially recovers, the lack of improvement in muscle mass and muscle strength might prevent complete recovery after discharge from hospital. It is noteworthy that muscle mass and muscle strength are lowest one month after discharge. The reason for this is unknown, but may involve prolonged deconditioning after acute medical illness, short stay in hospital and undernutrition.[17-19] Low muscle mass and muscle strength one month after discharge might prevent further recovery to self-supported living[20] whereas higher muscle mass and muscle strength after discharge might promote recovery and prevent HAD. Low muscle mass and muscle strength before acute hospitalization may also have been caused by an existing vulnerability – indeed, 80% of older adults had low muscle mass when they were admitted to the hospital. However, only 20% of older adults showed handgrip strength below the reference level when admitted to hospital. Although the cut-off points for sarcopenia (low muscle mass and low muscle strength) are not established, most of the older patients in the Hospital-ADL study were sarcopenic and at risk of poor hospital outcomes with permanent functional decline.[11] These older sarcopenic patients should receive a tailored exercise intervention to promote recovery. Based on the findings reported in **Chapters 4** and **5** and the results of the Hospital-ADL studies,[3,4,19] any future exercise interventions should address physical, psychosocial, and nutritional factors. Previous Hospital-ADL studies[3,4,19] have demonstrated a 50% prevalence of fatigue, apathy, fear of falling and depressive symptoms as well as undernutrition in acute hospitalized older patients. These factors are potential barriers to recovery.[3] Exercises during hospitalization are safe and can help older patients to improve their functional independence.[21-23] Although research into promoting recovery of older patients after hospital discharge is growing,[24,25] research into multifactorial exercise interventions to prevent functional decline is lacking. Improving muscle mass and muscle strength by an exercise intervention, considering the potential psychosocial barriers to recover can improve physical functioning and prevent functional decline after discharge from hospital.

**Number of steps after acute hospitalization and the association with HAD**

In **Chapter 6**, physical activity was assessed by an activity tracker (Fitbit Flex®), expressed in step numbers. A median (IQR) number of 656 (250–1146) steps during hospitalization and 1997 (938–4098) steps at seven days post-discharge was considered very low and 50% of older patients did not reach the recommended 900 steps per day during hospitalization.[26] In our study, the number of steps was associated with HAD one month after discharge, which is consistent with the results of other studies.[26-29] Patients with HAD took significantly fewer steps one week after discharge than patients without HAD did. This suggests that patients with HAD might be under-stimulated during hospitalization and during the first week after discharge. Lower number of steps and lower SPPB in hospital increased the risk of HAD.30 These findings might have clinical implications because the number of steps is easy to assess, can be modified, and can help to identify older patients at risk for HAD.[31,32] These findings are consistent with those of a consensus study, which recommended increasing physical activity during hospitalization by a minimum of 900 steps per day in acutely hospitalized older patients[33] to prevent HAD. Monitoring and promoting physical activity in older patients after acute hospitalization should be included in an exercise intervention.

**Resistance exercise training (RET) intervention for older patients after discharge from hospital**

**Chapter 7** describes a Delphi study involving 15 experts in the field of geriatrics and Exercise Training. This Delphi study recommended a core outcome set (COS) of measurement tools in all domains of the ICF and gave starting points for a Resistance Exercise Training (RET) intervention for older patients after discharge from hospital. The COS included measurement tools in all ICF domains to determine factors that can be modified to promote recovery. The experts agreed that an RET intervention immediately after discharge from hospital is critical for recovery, in line with ACSM recommendations.[34] The RET intervention should be based on the older patient's specific situation, and barriers to recovery such as fear of falling and malnutrition should be identified before the RET intervention is started. The high prevalence of psychosocial factors and undernutrition in acute hospitalized older patients requires a holistic multifactorial solution. This is supported by findings from the Hospital-ADL study, which showed that psychosocial factors such as fear of falling might prevent recovery.[3,4,19] This approach should be tuned to the specific goals and activities of patient to promote recovery and prevent functional decline.[35,36]

### Contributing factors to hospital-associated disability

Numerous physical factors contribute to HAD in older patients after discharge from hospital. These include a low number of steps and poor physical functioning during hospitalization as well as low muscle mass and low muscle strength during and after hospitalization. Our study group showed that psychosocial factors such as fatigue, fear of falling and depressive symptoms, apathy also increase the risk of HAD. Therefore, physical factors like muscle mass, muscle strength, physical activity and physical functioning should be studied along with psychosocial factors such as apathy, fatigue, depressive symptoms, fear of falling and undernutrition when assessing the risk of HAD. This thesis, as part of the Hospital-ADL study group, complements the HAD model of Covinsky et al.[2] by emphasizing the importance of physical and psychosocial factors and their interactions. Our proposed modifications to the model of Covinsky et al.[2] are indicated in red in the figure below.

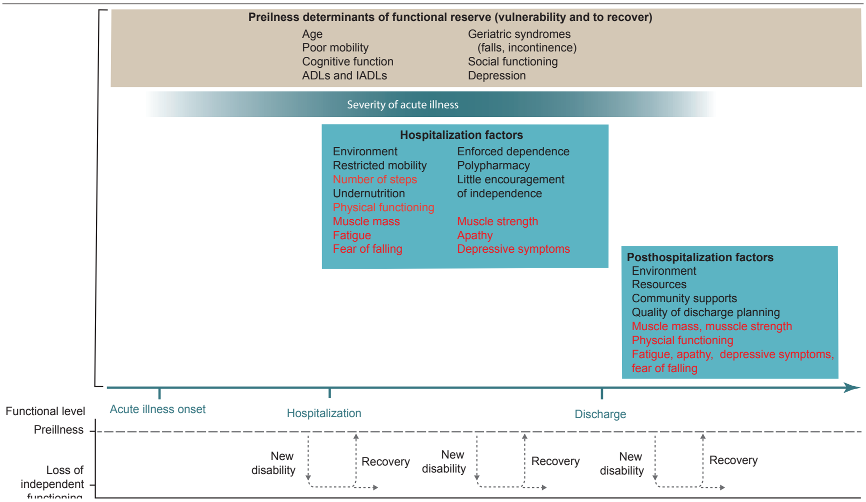


**Figure 1.** Proposed modifications to the Model of Covinsky

## Methodological considerations

### Study population

The population studied in Chapters 3–5 was part of the Hospital-ADL study population and were older patients (≥70 years of age) admitted to hospital with an acute medical illness. There are several strengths of the population of our study. First, it was a representative sample of 401 participants (50% female) from internal, cardiac, and geriatric departments of six university and generic hospitals in the Netherlands. Second, 80% of invited patients participated in the study. Third, measurements were collected longitudinally, both during hospitalization and up to three months after discharge. Fourth, demographic, physical, nutritional, and psychosocial measurements were collected along with self-reports and assessments of physical functioning.

There are also some limitations to the used methodology in this thesis. First, the Hospital-ADL study was an observational study, so causal relationships could not be determined. Second, we could not measure physical functioning before admission to hospital, so functional decline was based on recall of the older patient at hospital admission. Using a performance assessment might give a complete overview of the patients physical functioning. Third, older patients with low cognitive level (MMSE<15) were excluded from the Hospital-ADL study,[37] so the most vulnerable patients were not included. This might have led to a selection bias and an underestimation of the outcomes. Fourth, patients who could not speak or write Dutch were excluded from the study, which might have excluded patients with a migration background, leading to selection bias. Patients with a migration background experience more health problems, partly because of a lower socioeconomic status.[38] Fifth, some data were missing, either because the patient died or became unavailable during the study or because the patient or their spouse refused to participate further. This is a common challenge in longitudinal studies on clinical aging[39] and might have introduced bias. To minimize the effect of this limitation, linear mixed models were used to handle missing values.[40] Sixth, information on additional treatments by physical- or occupational therapists was lacking, although we asked for this information from the patient or their spouse. Seventh, data were collected from six hospitals in the Netherlands. These may be representative of the Netherlands but not worldwide, and specifically not of non-Western countries. This should be considered when transferring our results to clinical practice in different settings and countries.

**Outcome measures**

The outcome measures studied in **Chapters 4–6** were assessed by researchers with a background in physical therapy or psychology. Demographic, psychosocial, nutritional, and physical factors were self-reported by the patients and evaluated in performance assessments. This thesis focused on physical functioning, muscle mass and muscle strength, including capacity (what an older patient can do) and performance (what an older patient does).[41] This complements previous research of the Hospital-ADL study group, which focused on the psychosocial domain of physical recovery.[3,4] The complete findings of the Hospital-ADL study have provided outcome measures for assessing older patients after acute hospitalization. A holistic view of the complex care needs of older patients after discharge from hospital is critical to identify which factors should be considered in the exercise intervention. Measuring physical functioning, muscle mass and muscle strength is clinically applicable and relevant for acute hospitalized older patients.

A strength of this thesis is that physical factors were measured over time (longitudinal) and that physical and psychosocial factors were analysed together using self-reported and objective performance measures. Using an accelerometer

(Fitbit Flex®), to assess the physical activity of a patient in hospital and after discharge has not been done previously. The advantage of the accelerometer is that it can capture continuous information on physical activity.[42] The combination of all these measurements gave a detailed insight into the physical functioning of older patients in all ICF domains. Because the study investigated patients both in hospital and at home, the outcome measures give a realistic view of which factors promote recovery in older patients after acute hospitalization and which factors promote HAD. A complete overview of relevant outcome measures will help us to design multifactorial exercise interventions that are specific to individual patients.

## Implications for clinical practice

**Assessment of older patients after hospital discharge**

Healthcare in the hospital setting often focuses on the medical diagnosis, but the physical function of the patient after acute hospitalization is also very important. The Hospital ADL study showed that both physical factors (muscle mass, muscle strength, physical functioning, physical activity, and nutritional status) and psychosocial factors (apathy, fatigue, fear of falling, and depressive symptoms) should be assessed to determine the physical functioning of an older patient. **Chapters 4–6** showed that physical functioning, physical activity, and muscle mass and muscle strength are low in older adults during acute hospitalization. Physical functioning is at its lowest level in older patients upon admission to hospital and then gradually improves. Once older patients are discharged from hospital, their physical functioning improves but over 40% cannot live independently.

Recovery of physical functioning is accompanied by psychosocial factors such as fatigue, apathy, depressive symptoms and fear of falling,[2,3] which might hinder physical activity and reduce stimulation of the muscular system. Older patients might be sedentary and may not start increasing their physical activity without specific instructions, motivation, or guidance.4 A multifactorial assessment can help by providing an overview of the physical functioning of the older patient and identifying specific physical or psychosocial risk factors for delayed recovery and HAD after discharge from hospital.[3,4,30]

Knowing which patients are at risk for HAD and which factors may be preventing recovery can optimize post-discharge exercise interventions. The comprehensive geriatric assessment (GCA) that is performed in the hospital already provides information on different ICF domains. Handing over this information to healthcare professionals when the patient transitions from hospital to home is essential for optimal continuation of care. This GCA can be complemented with performance tests for muscle mass and muscle strength and physical functioning[43-46] and/or additional psychological and nutritional tests to collect information on all ICF domains. In the Delphi study in **Chapter 7**, experts agreed on measurement tools for all ICF domains, which can be used to monitor older patients after discharge from hospital.

Multiple assessments may be a burden to older patients. To reduce this burden, we need to find alternative, easier ways to collect information about the patient. Wearables and other sensors are being used increasingly in research and practice and offer new and easier ways to assess patients.[46] The accelerometer was studied in **Chapter 6** and is already frequently used and accepted in the medical field.[42] More wearables will become available in the future to measure physical and psychosocial functioning. Wearables can collect measurements 24 hours a day/7 day a week, making it possible to monitor the patient in real time.[46] Collecting information continuously and in real time can identify changes in physical functioning earlier, based on validated algorithms using Machine Learning. This can detect potential health issues that may lead to HAD, allowing patients and healthcare professionals to intervene. Wearables and technology might also reduce the burden on patients and healthcare professionals.[47,48] However, these innovations are not always easy, and a clear plan is needed to use this technology to its full potential.[49] To better organize post-discharge healthcare for the growing number of older patients, patients should be encouraged to use these wearables to self-manage their disease. Vulnerable older patients need support and feedback about their health situation from a healthcare professional. This support should be close to the patient's home or via eHealth.[50] This new technology is promising but the accessibility is not always optimal for older patients with low digital or self-management skills. More attention is needed to design technology that it is accessible to all patients. A hybrid approach that combines technology with personal attention would likely be best for older patients after acute hospitalization at their home.[51]

**Exercise interventions for older patients after hospital discharge**

In the Delphi study described in **Chapter 7**, experts agreed that a supervised Resistance Exercise Training (RET) intervention should be offered to vulnerable older patients by a physical therapist when they are discharged from hospital. This intervention should be tailored to the patient and should consider any potential barriers to recovery. Multiple barriers in an older patient may require help from a dietician, psychologist, general practitioner, or geriatrician. Our Delphi study, along with other studies showing the benefit of exercise interventions,[52-55] suggests that a tailored RET intervention should be offered to vulnerable older patients at home after acute hospitalization. The findings described in **Chapter 4** show that recovery trajectories can be different. It is important to identify patients at risk for HAD based on these trajectories and to start the RET intervention as soon as the patient is discharged to improve physical functioning and prevent HAD.

## Implications for education

Optimal healthcare for older patients is multifactorial and requires expertise from multiple professions.[57] Therefore, healthcare students should learn about multiple specializations to improve their communication and collaboration with other healthcare professionals. To this end, universities should facilitate interprofessional education (IPE) and interprofessional collaborative practice (IPEC) to help healthcare students deliver high interdisciplinary quality of care to patients with complex care needs. Specific training is needed in four core competencies: i) values/ethics for interprofessional practice, ii) role/responsibilities, iii) interprofessional communication and iv) teams and teamwork.[58]

Another important implication is the increasing demand for healthcare due to the growing number of older patients and that the number of healthcare professionals does not match this demand. eHealth technology may help to meet this growing demand for care. Healthcare professionals and their patients should be prepared to use information and communication technology (ICT) to deliver and receive healthcare, which will require different competences.[59] Barakat et al.[60] defined five competences for healthcare providers: i) ICT attitude and skills, ii) interpretation and analysis of eHealth data, iii) support and guidance of patients using eHealth, iv) effective communication with patients and other healthcare professionals and v) privacy and confidentiality. Digital technologies will play a major role in improving future health. Self-monitoring wearables, virtual assistants, artificial intelligence, and machine learning will be used to construct algorithms and support decisions about the healthcare process.[57] These tools will help to identify problems early on, allowing timely intervention and helping patients to be as independent as possible without care. Universities of applied sciences for healthcare professionals all over the world should facilitate and implement IPE/IPEC and ICT competences in their courses to prepare students for their future in healthcare. This will be a huge challenge for universities of applied sciences in the (para)medical field.

## Implications for future research

This thesis offers several starting points for future research in geriatric healthcare, particularly regarding physical functioning and muscle mass and muscle strength after discharge from hospital. We highly recommend a randomized controlled trial to investigate the value of RET interventions as part of a transitional rehabilitation programme. This intervention should be based on a personalized analysis of the barriers (for example malnutrition or fear of falling) and should facilitate recovery of the patient after discharge from hospital. Future studies should also investigate how to offer these interventions with eHealth or as a combination of eHealth and personal support. Using technology (such as wearables and eHealth) may reduce the burden on patients and healthcare professionals by collecting information on the health status of the patient. Future studies should also investigate whether this technology can be used to monitor patients and compare with other patients to identify older patients at risk for HAD to prevent further deterioration. Research should also investigate the changing role of the healthcare professional in guiding the patient digitally.[59,60]

## General conclusions

This thesis has investigated the changes in muscle mass, muscle strength physical activity and physical functioning, has identified risk factors for HAD and has created a starting point for developing an RET intervention to prevent HAD. The findings have illustrated that physical factors contribute to HAD and should be assessed along with psychosocial and nutritional factors. A holistic assessment of the patient in all ICF domains is advised to identify barriers to and facilitators of recovery. After a thorough assessment and risk stratification, an RET intervention that considers these barriers should be implemented to prevent HAD. If risk factors in multiple domains are present, an interdisciplinary intervention may be required to facilitate optimal recovery.

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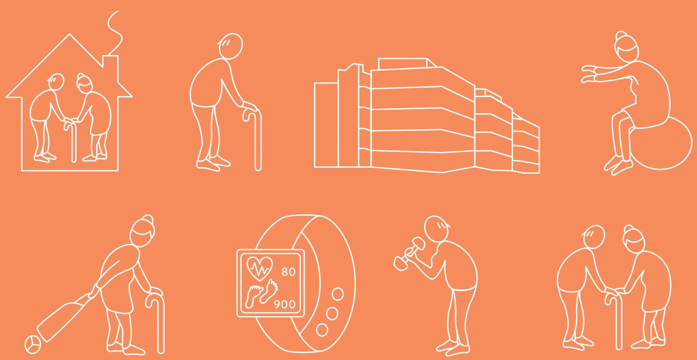
# Summary
# Samenvatting



# Summary

## Unravelling decline of physical functioning in acutely hospitalized older patients
### From risk factors to targeted intervention

**Chapter 1** provides an overview of the framework in which this research was conducted is presented. The number of older adults with chronic diseases and consequent disabilities is increasing and leads to one of the biggest global challenges in healthcare. Older adults are frequently admitted to a hospital for acute illness or falls with 30-60% of the older adults experiencing Hospital Associated Disability (HAD), even when the illness is successfully managed. The loss of activities of daily life (ADLs) after hospitalization reduces for self-care, independent living as well as participation in society which are often challenged by a higher dependency of care and/or caregivers. This negative spiral leads to increase in demands for long-term healthcare services and costs for society. This thesis aimed to unravel the mechanisms of HAD by determining changes in muscle mass and strength, physical functioning during and after hospitalization in relation with psychosocial functioning in acutely hospitalized older patients.

**Chapter 2** describes the impact of hospitalization after hip fracture surgery in older patients on physical functioning and the recovery in different trajectories. A retrospective study was conducted with 267 patients with a mean age (standard deviation) of 84.0 (6.9) years. Three disability trajectories, based on the Katz ADL-index, were identified from hospital admission until one-year follow-up. Patients in all three trajectories showed an increase of disabilities at three months in relation to baseline. 80% of the older patients did not return to baseline one-year post-discharge.

**Chapter 3** presents the protocol for the Hospital-ADL study with an overview of the study design and assessments which were performed. The Hospital-ADL study is a multicentred, observational, prospective cohort study aiming to recruit 400 patients aged ≥70 years that are acutely hospitalized at departments of Internal Medicine, Cardiology or Geriatrics, involving six hospitals in the Netherlands. Data was collected at hospital admission, hospital discharge, at one-, two- and three-months post-discharge. The aim of the Hospital-ADL study is to unravel the mechanism of Hospital Associated Disability (HAD) by performing social, physical, and psychological assessments by a multidisciplinary research group.

**Chapter 4** describes the longitudinal association between muscle strength and mobility in acutely hospitalized older patients. In a multicenter, prospective, observational cohort study, measurements of 391 older patients with a mean (standard deviation) age of 79.6 (6.7) were taken at admission, discharge, one-and three months post-discharge. Mobility was assessed by the De Morton Mobility Index (DEMMI) and muscle strength by the JAMAR. The longitudinal association between muscle strength and mobility was analysed with a Linear Mixed Model and controlled for potential confounders. Muscle strength was longitudinally associated with mobility, even after controlling for factors as age, cognitive impairment, fear of falling and depressive symptoms. Interventions to improve mobility including muscle strength are warranted, in acute hospitalized older adults.

**Chapter 5** focuses on the longitudinal changes of muscle mass, muscle strength and physical performance in older patients during hospitalization up to three months after discharge from hospital. In this prospective observational cohort study 343 patients, with a mean (standard deviation) age of 79.3 (6.6) years and 49% being female, were assessed at admission, discharge, one- and three months post-discharge. Muscle mass and handgrip strength decrease, and physical performance improve during and after hospitalization. At three months post-discharge, muscle mass, handgrip strength and physical performance do not reach normative levels. Our results underscores, that in the transition from hospital to the home situation, improvement of muscle mass, muscle strength and physical performance is warranted, which could be possible by tailor-made exercises for the older patient.

The study in **Chapter 6** determined the number of steps taken by older patients during hospitalization and first week post-discharge and the association with functional decline post-discharge. In this study 188 patients with a mean age (standard deviation) of 79.1 (6.7) were included. At one-month post-discharge 33/174 (19%) experienced functional decline. The median number of steps was 656 (interquartile range (IQR), 250–1146) at the last day of hospitalization. This increased to 1750 (IQR, 675–4,114) steps one day post discharge to 1997 (IQR, 938–4,098) steps seven days post discharge. There was a significant association between step numbers after discharge and functional decline one month after discharge. Physical performance and physical activity during hospitalization are key to increasing the number of steps post discharge. The number of steps one week after discharge is a promising indicator of functional decline one month after discharge.

**Chapter 7** describes a three round Delphi consensus study by an international panel on an exercise intervention program, a core outcome set (COS) of measurement tools and handover information to prevent functional decline, for acutely hospitalized older patients in transition from hospital towards home. Fifteen experts of eight countries participated in the panel with consensus on 90% of the statements. Continuation of an exercise intervention for older patients in transition from hospital to home, was consensually deemed essential by our expert panel. This Delphi study provides starting points for a personalized exercise intervention, COS, and handover information, aiming to prevent functional decline in older patients after discharge from hospital.

In **Chapter 8**, the results of the studies are summarized, the methodological considerations of the studies presented and the clinical, educational, and scientific implications for future research are discussed. This thesis demonstrates the importance of physical factors such as muscle mass, muscle strength and physical performance in the development of functional decline after hospitalization. In the development of functional decline after acute hospitalization, physical factors play an important role. It was proposed to include physical factors in the model of Covinsky. Measuring all factors of the model including the physical factors, might help physical therapists and other healthcare providers to identify patients who may benefit from tailored-made exercise intervention to prevent or restore functional decline.

# Samenvatting

## Ontrafelen van verlies van fysiek functioneren bij acuut opgenomen ouderen

### Van risicofactoren naar gepersonaliseerde behandeling

In **hoofdstuk 1** wordt een overzicht gegeven van het kader waarin dit onderzoek is uitgevoerd. Het toenemend aantal oudere volwassenen met chronische ziekten en daaruit voortvloeiende beperkingen leidt tot een van de grootste wereldwijde uitdagingen in gezondheidszorg. Ouderen worden vaak opgenomen in een ziekenhuis voor acute ziekte of vallen, waarbij 30-60% van de ouderen een 'Hospital Associated Disability (HAD)' ervaart, zelfs wanneer de ziekte met succes wordt behandeld. Het verlies van het uitvoeren van activiteiten in het dagelijks leven (ADL's) na een ziekenhuisopname heeft gevolgen voor zelfzorg, zelfstandig wonen en participatie in de samenleving, die vaak op de proef worden gesteld door een grotere afhankelijkheid van zorg en/of mantelzorgers. Deze negatieve spiraal leidt tot een toename van de vraag naar langdurige gezondheidszorg en tot kosten voor de samenleving. Dit proefschrift had tot doel de mechanismen van HAD te ontrafelen door veranderingen in spiermassa, spierkracht en fysiek functioneren tijdens en na ziekenhuisopname in samenhang met psychosociaal functioneren bij acuut opgenomen oudere patiënten vast te stellen.

**Hoofdstuk 2** van deze thesis beschrijft de impact van ziekenhuisopname na een heupfractuuroperatie bij oudere patiënten op het herstel van het fysiek functioneren. Er is een retrospectieve studie uitgevoerd met 267 patiënten met een gemiddelde leeftijd (standaarddeviatie) van 84,0 (6,9) jaar. Deze studie laat zien dat verschillend trajecten van herstel op basis van de Katz ADL-index werden geïdentificeerd vanaf ziekenhuisopname tot een jaar follow-up. Deze studie laat zien dat er een toename van het aantal beperkingen is te zien na een heupoperatie en dat 80% van de ouderen na een heupfractuuroperatie niet terugkeert op het niveau van voor ziekenhuisopname.

**Hoofdstuk 3** presenteert het protocol voor de Hospital-ADL studie met een overzicht van de onderzoeksopzet en de uitgevoerde metingen. De Hospital-ADL-studie is een multicenter, observationele, prospectieve cohortstudie met 400 patiënten (>70 jaar) die acuut zijn opgenomen op afdelingen Interne Geneeskunde, Cardiologie of Geriatrie van zes ziekenhuizen in Nederland. Gegevens zijn verzameld bij ziekenhuisopname, ontslag uit het ziekenhuis en op één, twee en drie maanden na ontslag. Het doel van de Hospital-ADL-studie is om het mechanisme van 'Hospital Associated Disability' (HAD) te ontrafelen door het uitvoeren van sociale, fysieke en psychologische metingen door een multidisciplinaire onderzoeksgroep.

**Hoofdstuk 4** beschrijft de longitudinale associatie tussen spierkracht en mobiliteit bij acuut gehospitaliseerde oudere patiënten. In een multicenter, prospectieve, observationele cohortstudie werden metingen gedaan bij 391 oudere patiënten met een gemiddelde (standaarddeviatie) leeftijd van 79,6 (6,7) bij opname, ontslag, één en drie maanden na ontslag. Mobiliteit werd beoordeeld door de De Morton Mobility Index (DEMMI) en spierkracht door de JAMAR. De longitudinale associatie tussen spierkracht en mobiliteit werd geanalyseerd met een Linear Mixed Model en gecontroleerd op mogelijke confounders. Spierkracht was longitudinaal geassocieerd met mobiliteit, zelfs na correctie voor factoren als leeftijd, cognitieve stoornissen, angst om te vallen en depressieve symptomen. Interventies om de mobiliteit te verbeteren, inclusief spierkracht, zijn aanbevolen bij acute gehospitaliseerde oudere volwassenen.

**Hoofdstuk 5** richt zich op de longitudinale veranderingen van spiermassa, spierkracht en fysieke prestaties bij oudere patiënten tijdens ziekenhuisopname tot drie maanden na ontslag uit het ziekenhuis. In deze prospectieve observationele cohortstudie werden 343 patiënten, met een gemiddelde (standaarddeviatie) leeftijd van 79,3 (6,6) jaar en 49% vrouw, beoordeeld bij opname, ontslag, één en drie maanden na ontslag. Spiermassa en handknijpkracht nemen af en fysieke prestaties verbeteren tijdens en na ziekenhuisopname. Drie maanden na ontslag bereiken spiermassa, handknijpkracht en fysieke prestaties niet de normatieve niveaus. Onze resultaten benadrukken dat in de overgang van het ziekenhuis naar de thuissituatie verbetering van spiermassa, spierkracht en fysieke prestaties aanbevolen is, wat mogelijk zou kunnen zijn door oefeningen op maat voor de oudere patiënt.

De studie in **Hoofdstuk 6** beschrijft het aantal stappen dat oudere patiënten zetten tijdens ziekenhuisopname en de eerste week na ontslag en de associatie met functionele achteruitgang na ontslag. In deze studie werden 188 patiënten geïncludeerd met een gemiddelde leeftijd (standaarddeviatie) van 79,1 (6,7). Een maand na ontslag ondervond 33/174 (19%) functionele achteruitgang. Het mediane aantal stappen was 656 (interkwartiel bereik (IQR), 250-1146) op de laatste dag van ziekenhuisopname. Het aantal stappen nam toe tot 1750 (IQR, 675–4.114) één dag na ontslag tot 1997 (IQR, 938–4.098) stappen zeven dagen na ontslag. Er was een significant verband tussen het aantal stappen na ontslag en functionele achteruitgang een maand na ontslag. Fysieke prestaties en fysieke activiteit tijdens ziekenhuisopname zijn mogelijk de sleutel tot het verhogen van het aantal stappen na ontslag. Het aantal stappen een week na ontslag is een veelbelovende indicator voor functionele achteruitgang een maand na ontslag.

**Hoofdstuk 7** beschrijft een Delphi-consensus studie met drie rondes door een internationaal panel over een oefeninterventie, een Core Outcome Set (COS) van meetinstrumenten en overdrachtsinformatie om functionele achteruitgang te voorkomen, voor acuut opgenomen oudere patiënten in de overgang van ziekenhuis naar huis. Vijftien experts uit acht landen namen deel aan het panel met consensus voor 90% van de stellingen. Continuering van een oefeninterventie voor oudere patiënten in de overgang van ziekenhuis naar huis, werd door ons panel van deskundigen als essentieel beschouwd. Deze Delphi-studie biedt aanknopingspunten voor een gepersonaliseerde oefeninterventie, COS en overdrachtsinformatie, gericht op het voorkomen van functionele achteruitgang bij oudere patiënten na ontslag uit het ziekenhuis.

In **Hoofdstuk 8** worden de resultaten van de studies samengevat, de gepresenteerde methodologische overwegingen over de studies en de klinische, educatieve en wetenschappelijke implicaties voor toekomstig onderzoek besproken. Dit proefschrift toont het belang aan van fysieke factoren zoals spiermassa, spierkracht en fysieke prestaties bij het ontstaan van functionele achteruitgang na ziekenhuisopname. In het ontstaan van functieverlies na een acute ziekenhuisopname bij ouderen spelen de fysieke factoren een belangrijke rol en het voorstel is om fysieke factoren op te nemen in het model van Covinsky. Het meten van alle factoren van het model inclusief de fysieke factoren, zou fysiotherapeuten en andere zorgverleners kunnen helpen om patiënten te identificeren die baat kunnen hebben bij op maat gemaakte bewegingsinterventie om functionele achteruitgang te voorkomen of te herstellen.

# Addendum

Portfolio
Scientific Publications
Dankwoord
About the author

# Portfolio

Name PhD student: Jesse Jeen Aarden
PhD period: 2015-2022
Name PhD supervisor: Prof. dr. R.H.H. Engelbert and Prof. dr. B.M. Buurman
Name Co-supervisors: Dr. M. van der Schaaf and Dr. M. van der Esch

| PhD training | Year | Workload (ECTS*) |
|---|---|---|
| **General courses** | | |
| Update basic course legislation and organization (BROK). Graduate school for medical sciences, University of Amsterdam, Amsterdam, Netherlands | 2020 | 0.5 |
| Introduction courses University of Melbourne: Office ergonomics, manual handling, and gas safety. | 2019 | 0.5 |
| Project management. Graduate school for medical sciences, University of Amsterdam, Amsterdam, Netherlands | 2018 | 0.6 |
| Scientific writing in English for publication. Graduate School for medical sciences, University of Amsterdam, Amsterdam, Netherlands | 2017 | 1.5 |
| Basic course legislation and organization (BROK). Graduate school for medical sciences, University of Amsterdam, Amsterdam, Netherlands | 2016 | 1.5 |
| Practical Biostatistics. Graduate school for medical sciences, University of Amsterdam, Amsterdam, Netherlands | 2016 | 1 |
| Systematic reviews. Graduate School for medical sciences, University of Amsterdam, Amsterdam, Netherlands | 2015 | 0.7 |
| Longitudinal data analysis. EpidM, Amsterdam University Medical Centers, VUMC, Amsterdam, Netherlands | 2017 | 3 |
| **Seminars, workshops, and master classes** | | |
| Monthly Hospital-ADL study research meeting department of internal medicine, Amsterdam UMC, Amsterdam, the Netherlands | 2015-Present | 3 |

| | | |
|---|---|---|
| Monthly research meeting Amsterdam University of Applied Sciences, Faculty of Health, School of Physiotherapy, Amsterdam, the Netherlands | 2015-Present | 3 |
| Workshop Sarcopenia, professional in the lead School of Physiotherapy Amsterdam University of Applied Sciences, Amsterdam, the Netherlands | 2018 | 0.5 |

**Oral presentations**

| | | |
|---|---|---|
| Hospital-ADL study. Dag van de Fysiotherapeut, KNGF congress, Utrecht, the Netherlands | 2015 | 0.5 |
| Ver van huis na het ziekenhuis: minisymposium. Oral presentation, Dag van de Fysiotherapeut, KNGF, Den Bosch, the Netherlands | 2019 | 0.5 |
| Functieverlies na ziekenhuisopname: eerste inzichten uit de Hospital-ADL studie. Geriatriedagen. Den Bosch, the Netherlands | 2017 | 0.5 |
| Functieverlies na ziekenhuisopname. Nederlandse Vereniging van Ziekenhuis Fysiotherapie (NVZF), Utrecht, the Netherlands | 2019 | 0.5 |
| Changes in muscle mass, muscle strength and physical performance in acutely hospitalized older patients. Research meeting University of Melbourne, Melbourne, Australia | 2019 | 0.5 |

**Poster presentation**

| | | |
|---|---|---|
| Poster presentation European Union of Geriatric Medicine Society (EUGMS), Nice, France | 2017 | 0.5 |
| Poster presentation European Union of Geriatric Medicine Society (EUGMS), Berlin, Germany | 2018 | 0.5 |
| Poster presentation KNGF congress. Dag van de Fysiotherapie, Utrecht, the Netherlands | 2016 | 0.5 |
| Poster presentation NVZF congress. Utrecht, the Netherlands | 2016 | 0.5 |

**(Inter)national conferences**

| | | |
|---|---|---|
| Australian and NewZealand Society for Sarcopenia and Frailty Research, Syndey, Australia | 2019 | 0.5 |
| Annual Congress Royal Dutch Society of Physiotherapy, KNGF. Barneveld, the Netherlands | 2019 | 0.5 |

| | | |
|---|---|---|
| Annual Congress Royal Dutch Society of Physiotherapy, KNGF. Barneveld, the Netherlands | 2018 | 0.5 |
| World Confederation for Physical Therapy Congress. Singapore | 2015 | 0.5 |

**Teaching**

**Lecturing**

| | | |
|---|---|---|
| Clinical Reasoning, Evidence Based Practice, Complex care, Amsterdam University of Applied Sciences, European School of Physiotherapy, Amsterdam, the Netherlands | 2014-Present | 4 |
| Training Standardized Operating Procedures students at the Amsterdam University of Applied Sciences, Amsterdam, the Netherlands | 2015 | 1 |
| Functional decline in acute hospitalized older patients. Minor Rehabilitation. Amsterdam University of Applied Sciences, Amsterdam, the Netherlands | 2019 | 0.5 |

Mentoring

| | | |
|---|---|---|
| Student bachelor thesis: Resistance training for acutely hospitalized older patients A systematic review (Croix & Goodyear), European School of Physiotherapy, Amsterdam University of Amsterdam, Amsterdam, the Netherlands | 2020 | 1 |
| Student master thesis: an international expert consensus statement regarding a post-discharge exercise program for acutely hospitalized older adults, Physiotherapy Science, Utrecht University, Utrecht, the Netherlands | 2019 | 1 |
| Student bachelor thesis: Predictors of functional declinein older acutely hospitalized adults (McPhilips), European School of Physiotherapy, Amsterdam University of Amsterdam, Amsterdam, the Netherlands | 2019 | 1 |

| | | |
|---|---|---|
| Student bachelor thesis: A double pronged approach for predicting functional decline among entrants to homes for the elderly: a geriatric screening tool (Strebel), European School of Physiotherapy, Amsterdam University of Amsterdam, Amsterdam, the Netherlands | 2019 | 1 |
| Student bachelor thesis: Prevalence of sarcopenia in acutely hospitalized patients in hospital and after discharge (Brajovic) European School of Physiotherapy, Amsterdam University of Amsterdam, Amsterdam, the Netherlands | 2018 | 1 |
| Student bachelor thesis: Functional outcomes of acute hospitalized sarcopenic patients after hospital discharge compared to non-sarcopenic patients (Stevens) European School of Physiotherapy, Amsterdam University of Amsterdam, Amsterdam, the Netherlands | 2018 | 1 |
| Student master thesis: Insight into the level of physical activity in older patients during and after acute hospitalization – an observation prospective cohort study. (Kolk), Evidence Based Master University of Amsterdam, Amsterdam, the Netherlands | 2017 | 1 |
| Student master thesis: Unravelling risk factors predicting the course of physical performance in acute, hospitalized elderly: a multicentre prospective cohort study. (Schilder), Evidence Based Master, University of Amsterdam, Amsterdam, the Netherlands. | 2017 | 1 |

| **Grants** | **Year** |
|---|---|
| Doctoral grant for teachers from the Dutch Research Council (NWO), The Hague, the Netherlands. | 2018 |

*ECTS: European Credit Transfer System (1 ECTS = 28 hours)

# Scientific Publications

1. **Aarden JJ**, Major M, Aghina CMWA, van der Esch M, Buurman BM, Engelbert RHH, van der Schaaf M. An international expert consensus statement regarding a post-discharge exercise intervention program for acutely hospitalized older adults (Submitted).
2. **Aarden JJ**, Reijnierse EM, van der Schaaf M, van der Esch M, Reichardt LA, van Seben R, Bosch JA, Twisk JWR, Maier AB, Engelbert RHH, Buurman BM. Longitudinal changes in muscle mass, muscle strength and physical performance in acutely hospitalized older adults. J Am Med Dir Assoc 2021; S1525-8610(20)31055-0.
3. van der Velde M, Valkenet K, Geleijn E, Kruisselbrink M, Marsman M, Janssen LM, Ruurda JP, van der Peet DL, **Aarden JJ**, Veenhof C, van der Leeden M. Usability and preliminary effectiveness of a preoperative mHealth app for people undergoing major surgery: pilot randomized controlled trial. JMIR Mhealth Uhealth 2021:7;9(1):e23402.
4. Reichardt LA, Nederveen FE, van Seben R, **Aarden JJ**, van der Schaaf M, Engelbert RHH, van der Esch M, Twisk JWR, Bosch JA, Buurman BM; Hospital-ADL study group. The longitudinal association between depressive symptoms and functional abilities in older patients. J Psychosom Res. 2020:23;137;110195.
5. Kolk D, **Aarden JJ**, MacNeil-Vroomen JL, Reichardt LA, van Seben R, van der Schaaf M, van der Esch M, Twisk JWR, Bosch JA, Buurman BM, Engelbert RHH. Factors associated with the number of steps taken in the recovery period post-discharge in acutely hospitalized older adults: The Hospital-ADL study. J Am Med Dir Assoc. 2021;22(2);425-32.
6. Reichardt LA, **Aarden JJ**, van Seben R, van der Schaaf M, Engelbert RHH, van der Esch M, Twisk JWR, Bosch JA, Buurman BM. Motivational Factors Mediate the Association of General Self-Efficacy and Performance Outcomes in Acutely Hospitalised Older Patients. Age Ageing 2020:24;49(5):837-42.
7. van Seben R, Covinsky KE, Reichardt LA, **Aarden JJ**, van der Schaaf M, van der Esch M, Engelbert RHH, Twisk JWR, Bosch JA, Buurman BM. J Gerontol. Insight into the Posthospital Syndrome: A 3-Month Longitudinal Follow up on Geriatric Syndromes and Their Association With Functional Decline, Readmission, and Mortality. A Biol Sci Med Sci.2020;18;75(7): 1403-10.
8. **Aarden JJ**, van der Schaaf M, van der Esch M, Reichardt LA, van Seben R, Bosch JA, Twisk JWR, Buurman BM, Engelbert RHH. Muscle strength is longitudinally associated with mobility among older adults after acute hospitalization: The Hospital-ADL study. PLoS One 2019: 5;14(7).

9. Ribbink ME, van Seben R, Reichardt LA, **Aarden JJ**, van der Schaaf M, van der Esch M, Engelbert RHH, Twisk JWR, Bosch JA, MacNeil Vroomen JL, Buurman BM. Determinants of Post-acute Care Costs in Acutely Hospitalized Older Adults: The Hospital-ADL Study. J Am Med Dir Assoc 2019:20(10):1300-6.
10. Van Dronkelaar C, Tieland M, **Aarden JJ**, Reichardt LA, van Seben R, van der Schaaf M, van der Esch M, Engelbert RHH, Twisk JWR, Bosch JA, Buurman BM. Decreased Appetite is Associated with Sarcopenia-Related Outcomes in Acute Hospitalized Older Adults. Nutrients 2019: 25;11(4).
11. Reichardt LA, Nederveen FE, van Seben R, **Aarden JJ**, van der Schaaf M, Engelbert RHH, van der Esch M, Henstra MJ, Twisk JWR, Bosch JA, Buurman BM. Hopelessness and Other Depressive Symptoms in Adults 70 Years and Older as Predictors of All-Cause Mortality Within 3 Months After Acute Hospitalization: The Hospital-ADL Study. Psychosom Med 2019:81(5):477-85.
12. Reichardt LA, van Seben R, **Aarden JJ**, van der Esch M, van der Schaaf M, Engelbert RHH, Twisk JWR, Bosch JA, Buurman BM. Trajectories of cognitive-affective depressive symptoms in acutely hospitalized older adults: The Hospital-ADL study. J Psychosom Res 2019; 120:66-73.
13. Van Seben R, Reichardt LA, **Aarden JJ**, van der Schaaf M, van der Esch M, Engelbert RHH, Twisk JWR, Bosch JA, Buurman BM. The Course of Geriatric Syndromes in Acutely Hospitalized Older Adults: The Hospital-ADL Study. J Am Med Dir Assoc. 2019;20(2):152-8.
14. **Aarden JJ**, van der Esch M, Engelbert RHH, van der Schaaf M, de Rooij SE, Buurman BM. Hip Fractures in Older Patients: Trajectories of Disability after Surgery. J Nutr Health Aging 2017;21(7):837-42.
15. Reichardt LA, **Aarden JJ**, van Seben R, van der Schaaf M, Engelbert RHH, Bosch JA, Buurman BM. Unravelling the potential mechanisms behind hospitalization-associated disability in older patients; the Hospital-Associated Disability and impact on daily Life (Hospital-ADL) cohort study protocol. BMC Geriatr. 2016:5;16:59.

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## About the author

Jesse Aarden was born on August 5th, 1971, in Amsterdam, the Netherlands. In 1994 he graduated with a bachelor's degree in Physical Therapy at the Amsterdam University of Applied Sciences (AUAS), the Netherlands. In 1997, he received his master's degree in Healthcare Science at the University Maastricht, the Netherlands. From 1994 – 2010 he worked as a physical therapist in a private practice in Amsterdam with different patient populations. From 2005 – 2010 he combined his work as physical therapist with lecturing at the European School of Physiotherapy of the AUAS.

In 2007 Jesse became part of the management of the School of Physiotherapy. In 2010, Jesse focused completely on management of the School of Physical Therapy of the AUAS. In 2015, Jesse had the opportunity to start in a PhD position at the rehabilitation department of the Amsterdam UMC, location AMC in close collaboration with the geriatrics department of the Amsterdam UMC. He decided to resign from the management role and focus on research and education from that moment. In 2018, he received a Doctoral Grant for Teachers of the Netherlands Organisation for Scientific Research (NWO) which gave him the financial support to continue with his PhD. In the first part of 2019, Jesse joined the research group of Prof. dr. A.B. Maier from the University of Melbourne, Australia. He moved to Australia together with his family which was a special experience for both work and private. During his PhD, Jesse was also working as lecturer/coordinator at the European School of Physiotherapy, as part of the Faculty of Health of the AUAS.

From the moment that Jesse started with his PhD his ambition was to contribute to the healthcare with a focus on older patients. Recently, in September 2021, Jesse got the opportunity to join the Centre of Expertise of Artificial Intelligence (CoE AAI) of the AUAS. The AUAS started with 7 Artificial Intelligence (AI) labs and Jesse was requested to start the Smart Health and Vitality Lab which is closely connected to the Faculty of Health and Faculty of Sports and Nutrition. The aim of this lab is to prepare and facilitate lecturers, researchers, and students to use AI in their (future) work and support healthcare with the challenges of the growing ageing population the coming decades.

In his spare time, Jesse loves to travel through Europe with his Mercedes ambulance from 1986 together with his family. He loves climbing in the mountains, playing tennis, and playing and watching football. Jesse lives together with Marianne and together they are proud parents of three fabulous children: Ila (2002), Loeta (2005) and Obi (2007).

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