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PhD thesis

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Mobility in older acutely admitted and primary care patients – in-hospital physical activity and simple strength training

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Acknowledgements

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List of papers and manuscripts

This thesis consists of 3 papers and 1 manuscript, which will be referred to with roman numerals.

I. Pedersen MM, Bodilsen C, Petersen J, Beyer N, Andersen O, Lawson-Smith L, Kehlet H, Bandholm T. 24-hour mobility during hospitalization in older medical patients. J Gerontol A Biol Sci Med Sci. 2013 Mar;68(3):331-337. doi: 10.1093/gerona/gls165.

II. Pedersen MM. Petersen J, Bean JF, Damkjær L, Juhl-Larsen HG, Andersen O, Beyer N, Bandholm T. Feasibility of progressive sit-to-stand training among older hospitalized patients. Accepted for publication in PeerJ, November 2015.

III. Pedersen MM, Beyer N, Petersen J, Bandholm T. Supervised progressive in-hospital and post-discharge strength training compared with usual care in older medical patients: study protocol for a randomized controlled trial (the STAND-Cph trial). Submitted to Trials, November 2015.

IV. Pedersen MM, Holt NE, Grande L, Kurlinski LA, Beauchamp MK, Kiely D, Petersen J, Leveille S, Bean JF. Mild Cognitive Impairment Status and Mobility Performance: An Analysis from the Boston RISE Study. J Gerontol A Biol Sci Med Sci. 2014 Dec; 69(12):1511-1508; doi: 10.1093/gerona/glu063

Papers I-II and Manuscript III represent Studies I, II and III, which were performed at Clinical Research Centre, Copenhagen University Hospital, Hvidovre from November 2012 to December 2015. In the initial plan for the PhD, Study III should have been reported as an RCT, but due to slow inclusion the last patients are currently being recruited. To keep the study blinded, data analyses will await completion of the data collection. Consequently, only the methods of Study III are presented, in the form of a trial protocol-manuscript currently submitted for publication. Paper IV represents Study IV, which was performed at the Department of Physical Medicine and Rehabilitation, Spaulding Rehabilitation Hospital (SRH), Boston, Massachusetts, in the spring of 2013. Paper IV was not originally a part of the PhD plan. It has been included in the thesis because it reflects work performed at SRH during the PhD study, and because it provides information about the association between mobility and cognition in older adults, which is of importance when designing rehabilitation for older medical patients.

The following papers are not included in the thesis, but reflect work done while being a PhD student:

1) Bodilsen C, Pedersen MM, Petersen J, Beyer N, Andersen O, Lawson-Smith L, Kehlet H, Bandholm T. Acute hospitalization of the old medical patient: changes in muscle strength and functional performance during hospitalization and 30 days after discharge. Am J Phys Med Rehabil. 2013 Sep;92(9):789-96. Doi: 10.1097/PHM.0b013e31828cd2b6.
2) Buhl SF, Andersen AL, Andersen JR, Andersen O, Jensen JB, Rasmussen AM, Pedersen MM, Damkjær L, Gilkes H, Petersen J. The effect of protein intake and resistance training on muscle mass in acutely ill old medical patients – A randomized controlled trial. Clin Nutr. 2015 Mar 5. pii: S0261-5614(15)00073-4. doi: 10.1016/j.clnu.2015.02.015. [Epub ahead of print]
3) Marla K Beauchamp, Cathy Schmidt, Mette Pedersen, Jonathan F Bean, Alan Jette. Psychometric properties of the Late-Life Function and Disability Instrument: a systematic review. BMC Geriatrics 2014, 14:12. doi: 10.1186/1471-2318-14-12.
4) Schepker CA, Leveille SG, Pedersen MM, Ward RE, Kurlinski LA, Grande L, Kiely DK, Bean JF. The Association of Pain and Mild Cognitive Impairment with Mobility. Submitted.
5) Lawson-Smith L, Petersen J, Jensen PS, Sivertsen DM, Pedersen MM, Ellekilde G, Lindhardt T, Andersen O. Nutritional risk in acutely admitted older medical patients. American Journal of Food and Nutrition, 2015, Vol. 3, No.3, 84-89. doi:10.12691/ajfn-3-3-4
6) Bjerre MCK & Ingstrup L. ActivPAL3™: A valid tool for quantifying slow gait in frail elderly populations? An explorative validity study. (Bachelor Thesis in Danish; role as a study supervisor for MCK Bjerre and L Ingstrup).

List of abbreviations

ADL	Activities of Daily Living
aMCI	Amnestic mild cognitive impairment
CAS	Cumulated Ambulation Score
DEMMI	The de Morton Mobility Index
DSST	Digit Symbol Substitution Test
F8W	Figure of 8 Walk
HG	Hand Grip strength
HGS	Habitual Gait Speed
HVLT	Hopkins Verbal Learning Test
iADL	Instrumental Activities of Daily Living
ICF	The World Health Organization's International Classification of Functioning, Disability and Health
LLFDI	Late Life Function and Disability Index
mdMCI	Multiple domain mild cognitive impairment
MCI	Mild cognitive impairment
MMSE	Mini Mental State Examination
naMCI	Non-amnestic mild cognitive impairment
NMS	New Mobility Score
No-MCI	No mild cognitive impairment/cognitively intact
RM	Repetition Maximum
SPPB	Short Physical Performance Battery
STS	Sit-To-Stand
VRS	Verbal Ranking Scale

1. Terminology and definitions

The World Health Organization's International Classification of Functioning, Disability and Health (ICF) provides a framework for classification of disability and health and for the description of health and health-related conditions across populations (Figure 1)(1,2). The ICF was developed to be a scientific basis for understanding and studying health and for standardizing data on health and disability (1,3) and the concepts of the ICF will be used throughout this thesis.

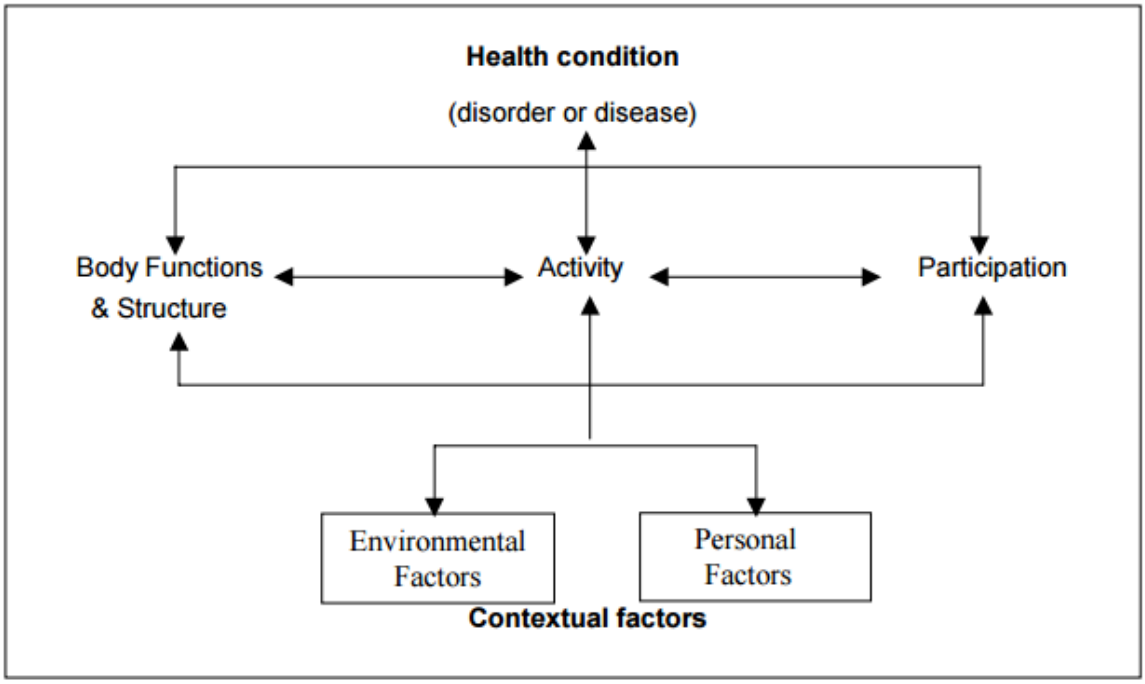


Figure 1. The International Classification of Functioning, Disability and Health (2).

In the ICF, functioning is an umbrella term for human functioning on three levels: the body (all body functions and structures), the whole person (activities), and the person in a social context (participation). Body functions and structures cover the physiological functions of body systems and anatomical parts of the body, activity covers how the individual performs a task or an action, and participation covers how the individual is involved in a life situation (2,3). Like functioning, disability is an umbrella term for dys-functioning on the three levels: impairments (in body functions), limitations (in activities) and restrictions (in participation). Both functioning and disability result from interactions between health conditions and contextual factors that can influence an individual's level of functioning and disability (1–3). Contextual factors cover environmental factors, e.g. the social and physical environment, and personal factors, e.g. age, gender, background, behavior (1–3).

Different nomenclatures have been used to describe the disablement process, amongst others Nagi's disablement model from the 1960's and the precursor of the ICF, the WHO's International Classification of Impairments, Disabilities, and Handicaps (ICIDH) from 1980 (1,3). Moreover, in the WHO classification, a shift has taken place from focusing on disability to focusing on health and functioning. This use of different nomenclatures is reflected in a great variation in the use of concepts like disability, impairment etc. throughout studies. Thus, in the ICF model disability is used as an umbrella termt for dys-functioning, in the ICIDH disability is used to describe lack of ability to perform an activity (individual level), and in the Nagi-model disability describes a limitation in performing social roles and tasks (1,3). When referring to the results of the included studies in this thesis, the terminology used by the authors will be used even though the terminology does not correspond with the terminology of the ICF model. Instead, wherever possible an ICF definition will be added in parenthesis, e.g. functional impairments (ICF: activity limitations). Also, in research literature "mobility", which is a sub-dimension of both the Activities and Participation components of the ICF (1,3), is used to describe abilities on all levels of the ICF, i.e. mobility disability, mobility impairments, mobility limitations, and mobility restrictions. Mobility is described by Drs. Brown and Flood as "more than a person's physical ability to walk or move and encompasses considerations of a person's environment and his or her ability to adapt to it" and mobility disability as "the gap between an individual's physical ability (e.g., muscle strength or balance) and environmental challenges such as walking outdoors on uneven surfaces" (4). Throughout this thesis, the term mobility will be referenced as used in the literature, with the terms "disability", "impairments", "limitations" and "restrictions" as indicators of the corresponding level of the ICF, and will not be followed by a parenthesis with corresponding ICF definitions. The terms "level of mobility", "mobility level" and "24-hour mobility" will be used to denote time spent active and "mobility" to describe abilities as mentioned above, that is the ability to climb stairs, walk, transfer, rise from a chair etc.

Rehabilitation is defined as "a set of measures that assists individuals who experience, or are likely to experience, disability to achieve and maintain optimal functioning in interaction with their environments" (5).

Basic mobility is defined as the ability to get in and out of bed, sit and stand from a chair and walk, as measured by the Cumulated Ambulation Score (CAS)(6).

2. Introduction

2.1 The aging population

In Denmark, as in the rest of the world, the population is aging (7,8) and the number of adults ≥65 years is expected to double over the next 30 years (9). Today, older adults ≥65 years constitute 18% of the population (1 million) in Denmark (10) and this number is estimated to increase to 25% in 2040 (11). The prevalence of disability increases with age (5,8), which along with increasing life expectancy, challenges the health care system (7,8) due to increasing expenses for health related services like hospitalization, medications, public health insurance, and home care (12). Among older Danes (≥65 yrs) in 2005, 37.4% reported mobility limitations, i.e. difficulty walking 400 meters, climbing a flight of stairs without rest or carrying 5 kg (13), compared to 17.4 % in the younger population.

2.2 Age related changes – functioning and disability

2.2.1 Muscle mass and aging

Aging is associated with loss of muscle mass, -strength and -power (14–16) increasing the risk of adverse outcomes like falls, mobility limitations, and disability (14,16,17). From the age of 20 to 80, muscle mass declines by 30% as a result of normal aging processes (18). This decline results from a loss of both slow (Type I) and fast (Type II) muscle fibers (14,19), combined with a conversion of Type II fibers to Type I fibers, due to an accelerated loss of fast motor units (14,18). This is reflected by a shift in activities favoring activities of daily living and submaximal exercises like walking, requiring primarily Type I fibers (18).

The maintenance of skeletal muscle mass requires a balance between muscle synthesis and muscle breakdown (14,20,21), and the decline in muscle mass seen with age is due to a reduction in the rate of protein synthesis, e.g. due to decline in growth hormone (14,22), or a rise in breakdown due to increased levels of inflammatory markers (e.g. inflammatory cytokines), and increased levels of catabolic hormones (e.g. cortisol) (14,21), or a combination of the two (20,22,23). This imbalance can be explained by anabolic resistance, i.e. a decreased ability of diet and exercise to stimulate muscle protein synthesis (21–24), which can possibly be reversed by the intake of protein or performing exercise (18,20,21,24,25). Therefore, older adults depend more on exercise than young to maintain a balance between breakdown and synthesis (25).

2.2.2 Muscle mass, muscle strength and functioning

The age-related change in muscle mass and loss of fast muscle fibers, along with infiltration of fat in the muscle and impairments in neural activation, can explain the loss seen in muscle strength and the loss of ability to generate the strength needed to perform everyday activities like rising from a chair, climbing stairs, or maintaining balance (14,26). From the age of 30, a decline in muscle strength of 10-15% per decade is seen (27). It is well recognized that muscle mass is related to muscle strength (14,17,19,27–29), and that the decline in strength goes beyond the decline in mass, suggesting a change in muscle quality (28–32). The Health ABC study, a large cohort study following 1880 initially well-functioning older adults, evaluated changes in muscle mass and muscle strength in the knee extensors over three years (28). The loss of muscle strength was three fold greater (3% per year) than the loss of muscle mass (1% per year), indicating a decline in muscle quality (28). In the same cohort study, both lower muscle mass and lower muscle strength were found to be associated with increased risk of mobility limitations (17), and lower muscle strength was associated with greater risk of hospitalization and death (33,34). A review on the influence of muscle mass and muscle strength on physical performance (26) found that a higher proportion of studies on muscle strength, than studies on muscle mass, found an association with physical performance.

Several studies have evaluated characteristics associated with disability and other adverse events. The InCHIANTI study has evaluated risk factors for mobility disability in old age (16) in a cohort of 1030 adults (20-102 yrs) living in Tuscany, Italy. Independent of age, they found low muscle strength and -power to be associated with poor mobility defined by a gait speed below 0.8 m/s and inability to walk 1 km (16). Similarly, a systematic review investigating physical performance characteristics related to disability in older adults (35) found an association both between upper and lower body strength, lower gait speed and a sedentary lifestyle, respectively, and a higher probability of disability. Furthermore, the relationship between muscle strength and self-reported Activities of Daily Living (ADL) performance has been elucidated. A prospective study in 567 older adults (≥75 yrs), independent in ADL at baseline, showed muscle strength to be associated with future (5 years) ADL dependence (36). Also, in the EPESE study (37), a longitudinal study of 4588 community-dwelling older adults (≥65 yrs), who initially reported no disability in ADLs, walking a half mile, and climbing stairs, physical performance measures (gait speed, balance, sit-to-stand) were found to be significant predictors of developing mobility disability and ADL disability up to 6 years later (37), as well as institutionalization and death (38). Also, a systematic review by Cooper et al (39) found that those who performed less well on four measures of physical capability

- grip strength, gait speed, chair rise time, and balance – were at higher mortality risk. Taken together, this indicates that maintaining muscle strength, physical performance and activity is important in older adults to avoid disability, dependence, hospitalization and death.

2.2.3 Functional reserve capacity

The age-related decline in muscle strength and mobility implies that older adults do not possess the same functional reserve capacity as younger adults (16,40–43) putting them at risk of falling beneath a threshold for muscle strength where functioning is limited (44). Functional reserve capacity has been defined as ”the difference between a person’s maximal capacity and the minimal capacity required to perform a specific task or maintain a specific level of activity” (45). Thus, older adults with low functional reserve capacity are at greater risk of developing disability and loosing independence (45,46). This risk of losing independence when having a low reserve capacity, is illustrated in a study examining the role of strength in rising from a chair in both young adults and functionally impaired (ICF: activity limited) older adults, characterized by inability to descend stairs without using the handrail and inability to rise from a 33 cm chair (47). The study showed that the older adults required 78% of their available knee extension strength, compared to 34% in the young, to successfully rise from a chair at knee height, and up to 97% to rise at the lowest possible chair height, compared to 39% in the young (47). Thus, in these older adults knee extension strength was a limiting factor in functional performance (i.e. chair rise ability) and additional loss of strength could lead to disability and reduced functional reserve capacity inducing a risk of falling beneath a threshold for independence. Especially maintaining independence and mobility are considered important health outcomes by older adults (48,49).

A greater functional reserve capacity may provide the individual with more resistance towards disability, e.g. as a consequence of disease (36). Indeed, the increase in disability with age is closely related to the occurrence of various diseases, including hypertension, osteoarthritis, cardiovascular disease, lung dysfunction, diabetes and stroke (50), and additionally these diseases are given as self-reported causes of onset of disability in older adults (51).

2.2.4 Factors associated with disability – cognition and physical inactivity

Cognition

As mentioned, loss of muscle strength and the onset of disease are some of the factors associated with disability. Research has pointed to a range of other determinants including cognition and inactivity. Similar to a decline in muscle mass and -strength, a decline in brain weight of about 2-3% per decade is seen (52). A decline in cognitive function is part of the normal aging process and co-exists with decline in physical function (53–56). Thus, in community-dwelling older adults, cognitive impairments as well as mobility limitations, and the accumulation of both, can affect the ability to live independently (57–59). The relationship between cognition and functioning remains to be fully elucidated, but there is a growing body of literature on the subject. A systematic review (54) has found baseline physical functioning to be associated with future changes in cognition, whereas baseline cognition was only marginally associated with future physical functioning - according to the authors possibly due to a limited number of studies examining this association. However, in older adults bidirectional associations between cognition and functioning have been found, with signs of onset of ADL disability as an indicator of the rate of cognitive decline (60) and cognitive level as a predictor of incident mobility impairment (61). Also, functional decline and slowing of gait have been found to coexist with (56) or precede (62,63) cognitive decline in older adults.

It is estimated that among older adults (≥65 yrs) the prevalence of mild cognitive impairment (MCI) is between 10 and 20% (64). MCI is defined as cognitive decline greater than that expected for one's age and education level, but which does not interfere appreciably with daily function (64,65). Thus, MCI is considered a subclinical state, which may remain unreported or undetected for a period of time (66). MCI is a well-known risk factor for dementia (66,67), and people with MCI are at increased risk of gait impairments (ICF: gait limitations), and falls (68). Thus, older adults with MCI may be an especially vulnerable group, why it may be essential to better understand the association between cognitive status and mobility performance.

Physical inactivity

The level of physical activity decreases with age (69,70). In 2005, in Denmark, the percentage of adults who did not engage in leisure-time physical activity was 12.7% for those aged 65-74, compared to 10.6-11.2% for younger age groups, and 27% for those aged 75-84 (13,70).

As mentioned earlier, in older adults a sedentary lifestyle contributes to increased levels of inflammatory markers (71) known to increase muscle protein breakdown (14,21,71). Equally, studies in healthy older adults have shown that restricted activity and bed rest are associated with reduced protein synthesis and a decline in muscle mass and -strength (72–76) as well as a decline in instrumental Activities of Daily Living (iADL), mobility, and physical- and social activity (77). Even merely reducing the daily amount of steps to ≤1500 over a fortnight (≈76% reduction from 3500 steps/day) in 10 healthy older adults led to a 4% reduction in leg muscle mass, a 26% reduction in postprandial muscle protein synthesis, and a 43% reduction in insulin sensitivity (78), indicating that even less extreme forms of inactivity can have negative effects on skeletal muscle. Furthermore, older adults seem more sensitive to bed rest inactivity than younger adults (72,73,79,80) with an impaired ability to fully recover (72,79). In addition, it seems that in older adults episodes of bed rest are accompanied with a decline in physical activity (74,77), creating a possible vicious circle of inactivity.

The lower extremities are especially sensitive to bed rest and reduced activity (73,76,78,81). A study in 12 healthy older adults undergoing 10 days of induced bed rest found an average loss of 1.5 kg lean mass in the whole body, of which 0.95 kg were lost in the lower extremities (73). Also, reduced daily activity has been found to significantly affect lower extremity lean mass, but not upper extremity lean mass (78). This focus on loss of lower extremity muscle strength and –mass in bedrest and inactivity studies is possibly due to the importance of lower extremity strength on functional performance (e.g. mobility and the ability to perform ADL) (82–86). Also, in a study of 1462 older women (≥75 yrs), lower knee extension strength relative to body weight was associated with limitations in self-reported mobility, chair rise ability and usual and fast gait speed (86). Similarly, Manini et al. (87) found knee extensor strength to be indicative of future risk of mobility limitations.

Taken together, this illustrates that in older adults, inactivity and bed rest are associated with loss of muscle mass, muscle strength and functioning with the lower extremities being especially sensitive. Therefore, it seems reasonable to seek to avoid inactivity and maintain lower extremity strength to prevent disability. Indeed, a link has been shown between inactivity (88), lower muscle strength and functioning (i.e. gait speed and repeated chair stand time) (34) and increased risk of hospitalization.

2.3 Older medical patients

In Denmark, older adults (+65 yrs) are hospitalized more often than the rest of the population. In 2010, 90% of older Danes above the age of 90 were admitted to the hospital, compared to 40% between the age of 65 and 74 and 20% between the age of 15 and 64 (11).

The older medical patient (≥65 yrs) is characterized by one or more of the following: severe illness, co-morbidity, functional disability, cognitive impairments, polypharmacy, low self-care capacity, and a need for assistance from the municipality (9,89). In 2009, older medical patients accounted for 34% (115.000) of all hospital admissions, 53% of all admissions to Danish medical wards, and 66% of all in-patient days in Danish medical wards (9). More than 80% of the older medical patients were admitted acutely (90) and 18% of the acute admissions were re-admissions (9). Also, more than one third was hospitalized for one day or less (90).

2.3.1 Consequences of hospitalization

Inactivity and functional decline during hospitalization

In older adults (+65 yrs) a low level of mobility (91–96) and episodes of bed rest (91–94) are common during hospitalization, and a low in-hospital mobility level has been shown to be associated with a decline in ADL during and after hospitalization (92–94), new institutionalization (92) and increased risk of death (92,97). Moreover, associations have been found between pre-admission decline in ADL function and low in-hospital activity (96), which was low whether or not the patients were independent in ADL and walking ability before and on admission (91–96,98). Also, in healthy older adults episodes of bed rest have been shown to be associated with a subsequent decline in physical activity (74,77) - which is likely to be the case in hospitalized older adults as well - and may create a risk of re-admission within 30 days (99).

Throughout the last decade, a change has occurred in how the level of mobility is measured in older hospitalized adults. There has been a shift from assessing the level of mobility via hallway observations (98) and nurse reports (92) to objective measures like step counts (96) and accelerometer-based assessments of mobility level (91,95,100,101), enabling a more accurate assessment of mobility level throughout the entire hospital stay. However, by the time of designing Study I for this thesis, only one study had used accelerometers in assessing mobility level continuously throughout hospitalization in older adults (91), and none had compared the level of mobility with a daily assessment of basic mobility (ability to get in and out of bed, sit and stand

from a chair and walk). Since then, more studies have evaluated in-hospital mobility level in older adults using accelerometers (95,97). Common to these studies in hospitalized older adults is a picture of a low mobility level during hospitalization and an association between a low mobility level and adverse events like new institutionalization and death (91,95,97).

In two prospective cohort studies in 498 (92) and 684 (93,94) older medical patients, mobility level was assessed during hospitalization via nurse reports based on identical mobility index'. In both studies, 80% were independent in ADL before admission. Also, corresponding levels of in-hospital mobility were seen: sixteen percent and 18%, respectively, were classified with a low mobility level (bed rest or bed to chair transfers), 32% and 30.1% with an intermediate mobility level (ambulation one or two times per day with total assistance), and 52% and 51.9% with a high mobility level (ambulation two or more times with partial or no assistance). What is more, Brown et al. (92) found low and intermediate levels of mobility to be associated with an increased risk of decline in ADL, new institutionalization and death, even after controlling for illness severity and comorbidities (92). Zisberg et al. (93,94) found that 42% percent of the included patients reported decline in ADL function at discharge, and 46% at 1 month follow-up. Further, those who experienced decline in ADL before hospitalization were less likely to be highly mobile during their hospitalization than those who did not (45% vs 84%), and in-hospital mobility level was highly related to both ADL decline at discharge and at 1 month follow-up (94).

Self-reported functional decline (ADL function) is commonly reported in older adults before and during hospitalization (92,93,102–106). Moreover, a study investigating the effect of hospitalization in older adults not restricted to bed, who were not admitted with acute illness, but for diagnostic investigation (107), found that during 5 days of hospitalization, significant declines in functional capacity, i.e. upper extremity muscle strength, and 6-min walk test, were seen. Studies in older medical and geriatric patients have discovered that 43-64% experience a decline in ADL function in the two weeks prior to hospitalization (103,104,108), 1-17% experience a decline during hospitalization (103,104,106,108,109), and 39-40% are discharged with worse ADL function than two weeks before admission (102,104,108,110). This self-reported decline is seen even after short hospital stays (105). Moreover, it seems that more than 20% of older medical patients report new disabilities in ADL and iADL 3 months after discharge (102,110), which can increase the risk of institutionalization (111). Also, lack of ability to regain function during hospitalization is independently associated with 3-month mortality (112).

In a study by Boyd et al. (102) in 2279 older medical patients, evaluating independence in ADL 2 weeks prior to hospitalization, at admission, and 1,3,6 and 12 months post discharge, 35% were discharged with worse ADL than 2 weeks before admission, and had poorer functional outcomes at follow-up than those discharged without additional disability. Also, 41.3% of those who were discharged with additional disability had died within 1 year and barely one third of the patients returned to their pre-admission level within the first year after discharge. Also, those who had recovered to their baseline level within the first month after discharge had better long term outcomes than those not recovering by one month (102). However, those who decline in ADL before and during hospitalization have been reported to be less likely to recover within the first month after discharge, compared to those remaining stable in ADL (106), stressing the importance of avoiding functional decline during hospitalization. In addition, the significance of the first month after discharge is highlighted by the fact that in Denmark, 18% of admissions of older adults are readmissions (within 30 days after discharge) (89). Interestingly, older adults with cognitive impairment have been shown to have higher risk of functional decline during hospitalization (109,113,114) and after discharge and to be less likely to recover compared to patients without cognitive impairment (113,115), making them an especially vulnerable group.

Hospitalization has been linked with a general loss of functional reserve capacity, and thereby an increased risk of losing independence (46,116). Several risk factors for loss of function during and after hospitalization have been identified, amongst others age (103,104,114,117), cognitive impairment (104,109,113,117), functional status before hospitalization (104,114,117), co-morbidity and polypharmacy (114,117), mobility level (92,93,117,118), a history of falls (104) and nutritional status (93,117,118).

2.3.2 Rehabilitation

Functional status by the time of discharge from hospital seems important, as it has been shown to be associated with the ability to fully recover (102), readmission rate (119), and mortality (102). Moreover, in a cohort of older adults, hospitalization was associated with a subsequent loss of muscle strength (120), putting hospitalized older adults at a higher risk of losing independence as a consequence of their hospitalization, and in greater need of rehabilitation (46). Maintaining independence is considered the most important health outcome by many older adults (48). Therefore, preventing inactivity as well as loss of muscle strength and functional performance during hospitalization may well be a way of preventing adverse events including re-admissions, loss of independence, institutionalization, and death. Moreover, regaining function within the first

month after discharge seems especially important as one-month status can be indicative of functional status one year after discharge (102).

According to the Danish Healthcare Quality Programme (DDKM) (121), the functional level and nutritional status of hospitalized patients must be described within 24-48 hours after admission (89) and treatment planned accordingly. No standards exist for in-hospital training (89), but patients needing recovery (e.g. rehabilitation) should be identified and provided with a rehabilitation plan targeting the patient's impairments and limitations (122). In spite of this, of 4611 older medical patients admitted to Hvidovre Hospital in 2012, only 252 (5.5%) were discharged with a rehabilitation plan, indicating rehabilitation potential.

Exercise programs (strength training)

Systematic strength training has been shown to improve muscle strength and functional performance in healthy and frail older adults, and nursing home residents (23,123–126). However, only few studies have investigated the effect of strength training during (127) and after hospitalization (128) in older medical patients. Two of these studies found positive effects of 10 weeks of lower extremity strength training on leg muscle strength and functional performance in older patients recovering from acute illness on a geriatric ward (127) and older medical patients newly discharged from a geriatric ward (128). However, one study encountered recruitment problems and concluded that an in-patient exercise program for acutely admitted older medical patients was not feasible (129). Positive effects on strength and functional performance have been found in community-dwelling older adults performing at-home lower extremity strength training (130).

However, most exercise programs for older hospitalized or community-dwelling adults cover a range of exercises including upper- and lower body strength training, balance- and walking exercises and stretching exercises (129–136). Few have examined the effect of a program initiated during hospitalization and continued after discharge (129,135), and these studies have experienced problems with compliance. However, a recent systematic review suggests that "the recovery of patients could further benefit from a community based or an in-home intervention program which build on in-hospital programs" (137). In addition, acutely hospitalized older adults express that initiating exercise in the hospital or shortly after discharge is a good idea (129,138). Also, exercise than can be undertaken close to or at home is more likely to be taken up by older adults with mobility-related disability (139). The challenges with compliance might be reduced by ensuring

supervision and information about the importance of physical activity (137,140,141) as well providing recommendations for activity from a physiotherapist (142). Supervision may also be beneficial on the effect of training (143). This emphasizes the likely importance of supervision from trained staff both in the hospital and in the home setting.

A meta-analysis concludes that physical exercise therapy has a positive effect on mobility and physical functioning in mobility limited and physically disabled older adults, but that it is unclear which type of intervention is most effective although strength training seems important (144). Also, according to recent systematic reviews and meta-analyses, information is lacking about the appropriate dose of strength training in different settings for older adults as well as detailed descriptions of exercises and dosage (123,145,146). However, it seems that higher intensities are superior to lower intensities (144,145,147,148), but that research is required to elucidate the effect of higher intensities on older adults with chronic health conditions (147).

When constructing an exercise program for hospitalized older adults, it seems reasonable to focus on counteracting loss of strength and functional performance in the lower extremities thereby addressing the impairments (low muscle strength) and limitations (poor functional performance) seen in these patients (149,150). Especially since the lower extremities are sensitive to bed rest (73,81) and lower extremity strength is associated with functional performance, i.e. mobility, chair rise ability, and the ability to perform ADL (17,82–87,151,152), future risk of ADL and mobility limitations (35,87), hospitalization and death (17).

Combining strength training with protein supplementation may be even more beneficial than strength training alone as it may stimulate muscle protein synthesis and thus increase the exercise response on muscle mass and strength as seen in healthy older adults (153–155). In healthy adults, both strength training and amino acids have been shown to be potent anabolic agents, and the administration of amino acids and carbohydrates after strength training may induce a greater increase of muscle protein synthesis than either of the two (156). However, a consistent effect of protein supplementation on muscle mass and function is lacking (157).

A well-described, supervised and simple cross-continuum strength training program including repeated sit-to-stand exercises was chosen for Study III. The program was designed to: focus on the lower extremities and comply with the importance of both supervision and location (home) for adherence; be described in detail and ensure high intensity training; investigate if a minimum

treatment approach is sufficient; be feasible to perform within a busy care setting and in a home setting after discharge, requiring only minimal equipment; and be combined with protein supplementation to enhance the exercise response on muscle.

2.4 Summary

In summary, aging is associated with declines in muscle mass and –strength, physical performance and mobility, increasing the risk of adverse events like disability, hospitalization and death. Also, a decline in cognitive function is part of the normal aging process, and can affect the ability to live independently, why it may be important to better understand the association between cognitive status and physical performance. The increase in disability with age is related to the occurrence of various diseases, and older adults (+65 yrs) are hospitalized more often than the rest of the population. A low level of mobility during hospitalization is commonly reported in older adults and associated with adverse events; e.g. functional decline, institutionalization, and death. In-hospital levels of mobility have previously been assessed subjectively, but in the last decade objective measures have taken over. However, only few have assessed in-hospital mobility continuously throughout hospitalization in older adults, and combined this assessment with a daily assessment of basic mobility. Functional decline before and during hospitalization is often reported in older adults, and barely one third seem to return to their pre-admission level within the first year after discharge. Also, functional status by one month after discharge has been shown to be an indicator of long term outcome. Besides, hospitalization seems associated with a subsequent loss of muscle strength and functional performance putting hospitalized older adults at a higher risk of losing independence as a consequence of their hospitalization. Therefore, reducing inactivity and loss of muscle strength and functional performance in connection with hospitalization may be a way of preventing loss of independence. Older hospitalized adults have been shown to display poor muscle strength and functional performance. Systematic strength training can possibly prevent further loss of muscle strength and functional performance, but few studies have examined the effect of a cross-continuum exercise program initiated during hospitalization and continued after discharge. In addition, details are lacking regarding the appropriate nature and dose of training. Higher intensities seem superior to lower intensities, and supervision seems critical in enhancing compliance to training. Moreover, combining strength training with protein supplementation may enhance the muscular response to training (i.e. muscle mass and strength). Additionally, the lower extremities are most sensitive to bed rest and inactivity, why a strength training program focusing on the lower extremities may be the right choice in counteracting hospital-associated inactivity and functional decline.

3. Objectives and hypotheses

The main objectives of the studies included in this thesis were: to investigate 24-hour in-hospital mobility of older medical patients acutely admitted to Hvidovre Hospital, Denmark; to validate the accelerometers used; and to test the feasibility and effect of simple, supervised, cross continuum strength training aiming at avoiding mobility decline in connection with acute hospitalization. In addition, a secondary objective was to describe the association between mobility performance and MCI in older community-dwelling primary care patients.

3.1 Study I

3.1.1 Objectives

To quantify 24-hour mobility and the daily level of basic mobility during hospitalization both in a group of older medical patients who were able to walk independently before admission and in a reference of patients who were unable to walk independently, and to develop and validate an algorithm to quantify in-hospital mobility using accelerometers (Augmentec Inc., Pittsburgh, PA, USA).

3.1.2 Hypotheses

During hospitalization older medical patients spend the majority of their time sitting or lying. Accelerometers can validly quantify in-hospital mobility in older medical patients.

3.2 Study II

3.2.1 Objective

To test the feasibility of a model for progressive sit-to-stand training (STAND) in older medical patients in the hospital and in the patients' own homes.

3.2.2 Hypothesis

The STAND model can be used as a progression model for sit-to-stand strength training in older medical patients.

3.3 Study III (protocol manuscript for ongoing study)

3.3.1 Objective

To investigate if a simple, low technology, supervised strength training program for the lower extremities, combined with post-training protein supplementation initiated during hospitalization and continued for 4 weeks after discharge is superior to usual care on change in mobility 4 weeks after discharge.

3.3.2 Hypothesis

Strength training and protein supplementation will be superior to usual care on change in mobility 4 weeks after discharge.

3.4 Study IV

3.4.1 Objective

To examine the association between MCI and MCI subtypes and mobility in older primary care patients.

3.4.2 Hypothesis

Patients with MCI and all subtypes of MCI are more limited in performance-based and self-report measures of mobility than patients without MCI, and patients with non-amnestic MCI perform worse than those with amnestic MCI.

4. Methods

Inclusion of patients for Studies I-III took place in the Emergency Department at Copenhagen University Hospital, Hvidovre, Denmark. Patients were included by random sampling based on a computer-generated list using the patients' social security numbers. Patients for Study IV were recruited through primary care practices at the medical centers of Massachusetts General Hospital (MGH) and Brigham and Women's Hospital in Boston, Massachusetts, USA. An overview of the study designs in the four studies is presented in Table 1.

Table 1. Overview of study designs for Studies I-IV.

STUDY AIM	DESIGN	INVESTIGATORS	INCLUDED PATIENTS	STUDY SAMPLE	MAIN OUTCOMES
I. To quantify 24-hour mobility and the daily level of basic mobility during hospitalization both in a group of older medical patients who were able to walk independently before admission and in a reference of patients not able to walk independently, and to develop and validate an algorithm to quantify in-hospital mobility using accelerometers.	Prospective cohort study. Patients assessed on admission and daily throughout hospitalization.	Two skilled physiotherapists.	68 patients who gave written informed consent. 49 patients consented to wear accelerometers.	42 ambulatory and 6 non-ambulatory patients.	• In-hospital 24h mobility level assessed by accelerometers (Augmentec Inc) • The Cumulated Ambulation Score Explanatory variables: • The New Mobility Score • The Charlson Index • The Mini Mental State Examination • The Verbal Ranking Scale
II. To test the feasibility of a model for progressive sit-to-stand training (STAND) in older medical patients in the hospital and in the patients' own homes.	Prospective cohort study conducted as a feasibility study. Patients assessed once on admission and once in their own homes after discharge.	Two skilled physiotherapists.	24 patients who gave written informed consent.	23 tested on admission. 19 tested at home.	• Feasibility of STAND • Training load and level • The Borg Scale • The Verbal Ranking Scale Explanatory variables: • The de Morton Mobility Index • The Short Orientation-Memory-Concentration test
III. To investigate the effect of a simple, low technology, supervised strength training program for the lower extremities, combined with post-training protein supplementation, during hospitalization and continued for 4 weeks after discharge (protocol-manuscript).	Randomized, controlled, investigator-blinded trial.	Four skilled physiotherapists.	Aim: 80 patients giving written informed consent. Study still ongoing and data collection not completed.	Aim: 54 patients with complete data sets.	Primary outcome: • The de Morton Mobility Index Secondary outcomes: • 24h mobility level assessed by accelerometers (PAL Technologies Ltd) • Isometric knee extension strength. • Handgrip strength. • Habitual gait speed • 30-sec chair stand
IV. To investigate the association between mild cognitive impairment (MCI) and MCI subtypes and mobility in older primary care patients.	Prospective cohort study. Patient assessments at baseline.	A nurse practitioner and a research assistant.	430 patients who gave written informed consent.	430 with baseline data.	Dependent variables • Habitual gait speed • The Figure of 8 Walk • The Short Physical Performance Battery • The Late Life Function and Disability Index Explanatory variables • The Trail Making test • The Digit Symbol Substitution test • The Hopkins Verbal Learning test, revised

4.1 Inclusion and exclusion criteria

The inclusion and exclusion criteria for Studies I-IV are presented below (Table 2).

Table 2. Inclusion and exclusion criteria for Studies I-IV.

Common inclusion criteria for Studies I-III	**Common exclusion criteria for Studies I-III**
• ≥65 years of age • Acute medical admission from own home	• inability to give informed consent to participate • inability to co-operate in measurements • inability to understand or communicate in Danish • diagnosis of chronic obstructive pulmonary disease (COPD) and participation in a COPD rehabilitation program • isolation-room stay • transferal to intensive care • terminal illness
Additional inclusion criteria	**Additional exclusion criteria**
Study I • co-morbidity	Study I • an expected hospitalization of 2 days or less • inability to walk with or without a walking aid Studies II-III • an expected hospitalization of 1 day or less • inability to rise from a chair with assistance • in treatment for diagnosed cancer Study III • living outside the municipalities of Copenhagen, Broendby or Hvidovre • assigned to physical rehabilitation in the municipality by the time of admission
Inclusion criteria Study IV	**Exclusion criteria Study IV**
• ≥65 years of age • Community-dwelling • Ability to understand and communicate in English • self-reported difficulty with walking half a mile or climbing one flight of stairs	• inability to give informed consent to participate • terminal disease • significant visual impairment • uncontrolled hypertension • amputation of a lower extremity • use of supplemental oxygen • myocardial infarction or major surgery in the previous 6 months • planned major surgery • planned move from the Boston area within 2 years • Mini Mental State Examination (MMSE) score <18 • Short Physical Performance Battery (SPPB) score < 4

All patients gave written informed consent before participating in the studies. In Studies I-III a template from the National Committee on Health Research Ethics, Denmark, was used (available at: www.cvk.sum.dk). Studies I-III were approved by the Ethics Committee of the Capital Region of Denmark (numbers 06072010-1631 and H-2-2012-115) and by the Danish Data Protection Agency (2007-58-0015). Study III was registered at ClinicalTrials.gov (NCT01964482). All procedures in Study IV were approved by the Institutional Review Board of Spaulding Rehabilitation Hospital, Cambridge, Massachusetts.

4.2 Assessments and main outcome measures

All assessments followed standardized testing protocols to ensure assessment consensus. For Studies I-III the admission assessments were performed at the Emergency Department or an internal medicine ward at Hvidovre Hospital within the first 48 hours after admission. For Study I follow-up assessments were performed in the patient's bedroom at the hospital, and for Studies II-III follow-up assessments were performed in the patients' own homes. For Study IV the assessments took place at the Clinical Research Center of MGH and at Spaulding Rehabilitation Hospital Cambridge, Massachusetts. For all studies, descriptive data and self-report outcome measures were assessed via patient registries and by questionnaire based interviews (see Papers I-II+IV and Manuscript III for further details). Table 3 provides an overview of the main outcome measures.

4.2.1 Study I

Forty-nine patients were included in this prospective cohort study aiming at evaluating 24-hour mobility and basic mobility during hospitalization, and developing and validating an algorithm for quantifying mobility using accelerometers. Forty-three patients were ambulatory on admission (median age 84.7 (IQR 78.6; 87.2); 45% women) and 6 were non-ambulatory (median age 82.8 (IQR 79.9; 88.0); 76% women). The patients underwent a structured baseline interview during the initial 48 hours of the hospital stay, including explanatory variables: the self-reported New Mobility Score (NMS) (158) to assess functional independency (in retrospect two weeks before admission and in retrospect over the day of admission); the Charlson Index (159) as a measure of co-morbid conditions on admission; the Mini Mental State Examination (MMSE) (160) to assess cognitive function on admission; and the Verbal Ranking Scale (VRS) (161) as a measure of pain. The mobility level during hospitalization was assessed by two wireless accelerometers (Augmentec Inc., Pittsburgh, Pennsylvania, USA). An algorithm-identification of lying, sitting, and standing/walking was developed based on pilot data. The algorithm was cross-validated on six older medical patients, not included in the primary study, who wore the accelerometers under supervision, following pre-defined behaviors. Basic mobility was assessed by the Cumulated Ambulation Score (CAS) (6,162) within 48 hours of admission, and repeated daily throughout hospitalization.

Table 3. Overview of main outcome measures.

OUTCOME	STUDY	METHODS	PROCEDURE	DATA REDUCTION
Mobility				
24h mobility	I+III★	I: Patient-worn accelerometers 24h/d during hospitalization. III: Patient-worn accelerometers 24h/d during hospitalization and for 1 week following the three follow-up assessments*.	I: Two wireless monitors (Augmentech Inc., Pittsburgh, PA) attached 15 cm above the patella and 15 cm above the ankle joint, respectively, anteriorly on the patient's right leg. III: One activPAL3^{TM} wireless monitor attached to the patient's right thigh.	I: Hours per day spent lying, sitting and standing/walking. III: Hours per day spent lying, sitting/standing and walking.
Basic mobility	I	The Cumulated Ambulation Score. Evaluated on admission and daily throughout hospitalization.	Investigator administered score sheet followed. Quantification of ability to get in and out of bed, sit-to-stand from a chair, and walk.	Total score in points (0-6).
Assessor observed mobility	III★	The de Morton Mobility Index. Evaluated at all four assessments**.	Investigator administered score sheet followed. Quantification of ability to perform 15 hierarchical mobility challenges.	Total score in points (0-100).
Feasibility				
Feasibility of the STAND progression model	II	Sit-to-stand strength training exercise tested in the hospital and at home.	Standard chair 45 cm. Aim to perform 1-3 sets at 8-12 RM following the model.	Level of exercise (STAND), number of sets performed, and repetitions in each set.
Pain	II	The Verbal Ranking Scale. Evaluated before, during, and 10 minutes after the exercise.	Investigator administered score sheet. Quantification of pain.	Score in points (0-5) for 8 different body regions.
Perceived exertion	II	The Borg Scale. Evaluated after each set of the exercise.	Investigator administered score sheet. Quantification of exertion.	Total score in points (6-20).
Functional perf.				
Isometric knee-extension strength	III★	Externally fixated handheld dynamometer. Evaluated at all four assessments**	Standard chair 45 cm. Right leg.Four maximal contractions.	Highest value (Nm/kg).
Handgrip strength	III★	Handheld dynamometer. Evaluated at all four assessments**	Standard chair 45 cm with armrests. Dominant hand. Between three and five maximal contractions.	Highest value (kg).
Lower body strength	III★	30-second chair stand test. Evaluated at all four assessments** Alternative: Modified 30-second chair stand test.	Standard chair 45 cm. Arms folded across chest. One stand for familiarization. Repetitive chair stands in 30 seconds. If unable to stand with arms folded over chest then use of armrests. Repetitive stands in 30 seconds.	Number of full stands (no).
Habitual gait speed	III★+IV	4-meter gait speed test. III: Evaluated at all four assessments** IV: Evaluated at baseline.	Habitual speed with or without habitual walking-aid on a 4-meter course. Start from standing position. Two trials.	Fastest (sec) of two trials.
Curved path walking	IV	The Figure of 8 Walk. Evaluated at baseline.	Walk in a figure of 8 around two markers at habitual speed. Start from standing position in the middle between the markers.	Time to complete the figure of 8 walk (sec).
Lower extremity performance	IV	The Short Physical Performance Battery. Evaluated at baseline.	Composed of three tests: • Timed balance: side-by-side stand; semi-tandem stand; full tandem stand • Habitual gait speed on 4-meter course. • Five repeated chair stands preceded by one test stand.	Total score (0-12).
Self-reported perf.				
Activities of Daily Living	III★	Barthel 20 index. Evaluated at all four assessments**.	Investigator administered questionnaire. Quantification of ability to perform 10 activities of daily living.	Total score (0-20).
Self-reported activity limitation	IV	The Late Life Function and Disability Index – the Basic Lower Extremity subdomain (BLE) and the Advanced Lower Extremity (ALE) subdomain. Evaluated at baseline.	Investigator administered questionnaire. Quantification of ability to perform pre-defined activities.	Total BLE score (0-100) and total ALE score (0-100).

★Data collection for Study III is still ongoing. Hence, data reduction has not yet been performed; *discharge, 4 weeks after discharge and 6 months after discharge; **admission, discharge, 4 weeks after discharge and 6 months after discharge.

4.2.2 Study II

Twenty-four patients (mean age 77 (SD 7); 50% women) were included in this prospective cohort study to test the feasibility of a model for progressive sit-to-stand training in the hospital and in the patients' own homes. The patients were assessed within 48 hours of admission to the hospital and in their own homes shortly following discharge. On admission the patients underwent a structured baseline interview including functional independence (measured by the NMS in retrospect 2 weeks before admission and in retrospect over the day of admission) and explanatory variables: the Short Orientation-Memory-Concentration test (OMC) as a measure of cognition (163,164); and the de Morton Mobility Index (DEMMI) (165) to quantify the patient's mobility level before performing the exercise. The DEMMI was also assessed at the home visit. A progression model for sit-to-stand as a strength training exercise (STAND) was developed (Figure 2). At two time points the patients were tested for their ability to perform the exercise for 1-3 sets at a relative load of 8-12 repetition maximum (RM) for 8-12 repetitions: in the hospital within 48 hours of admission, and shortly following discharge in their own homes. The exercise was considered feasible if three criteria were met: 1) 75 % of the assessed patients could perform the exercise at a relative load of 8-12 RM at both time points (1 set in the hospital; 2 sets at home); 2) no ceiling or floor effect was seen; 3) no adverse events were observed. For each set of training at both time points the level of the model, the extra load added (kg), the number of repetitions performed, and perceived exertion using the Borg Scale (166) were recorded. Pain was assessed with VRS (167) before and after the DEMMI test and before, during, and 10 minutes after the exercise.

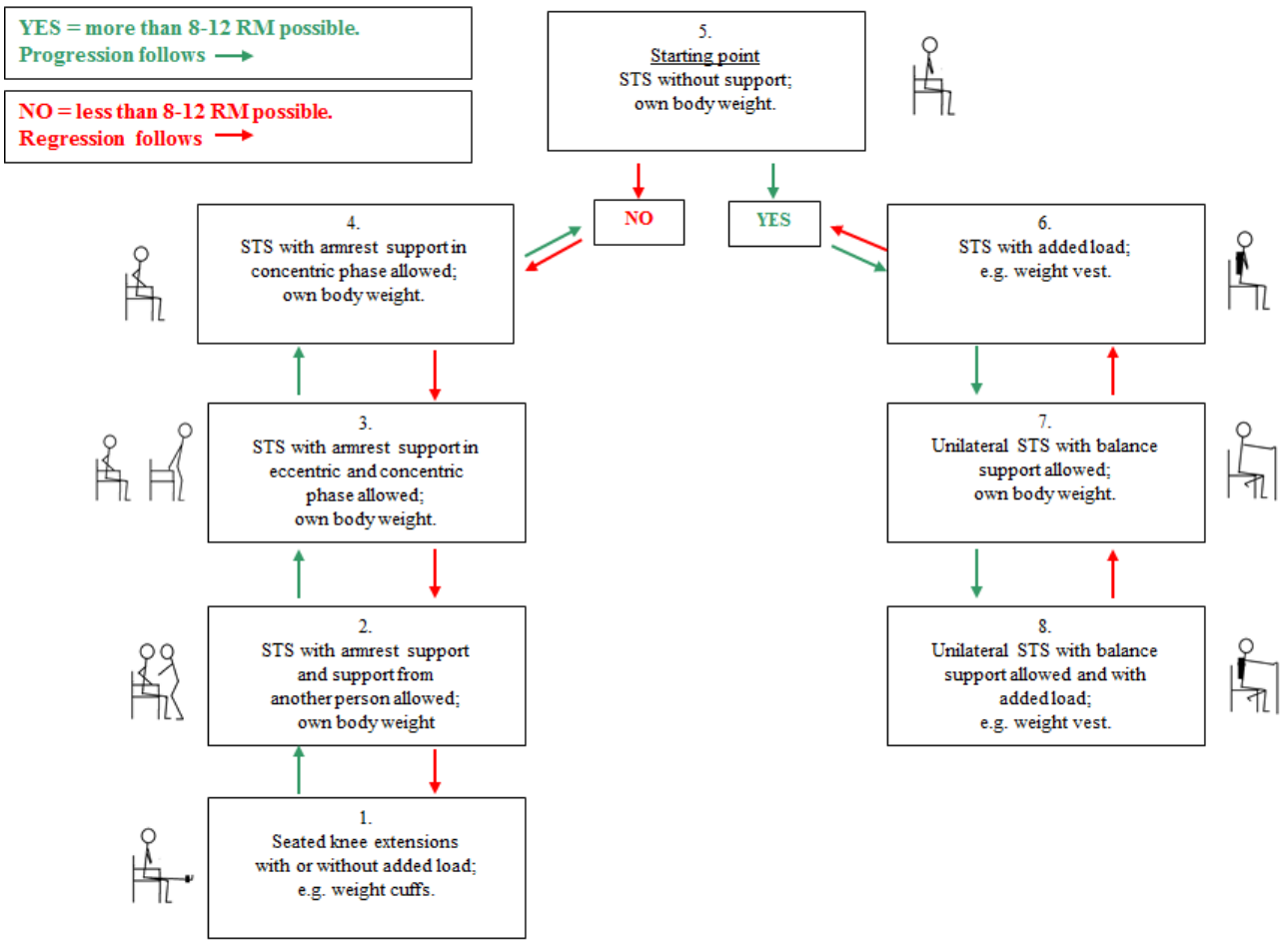


Figure 2. Progression model for loaded sit-to-stand exercise (STAND).

STS: Sit-to-stand; 8-12 RM: 8-12 repetitions maximum (a zone in which muscular fatigue should be reached.)

4.2.3 Study III

In total, 80 patients (≥65 yrs) will be included in this ongoing randomized, controlled, investigator blinded trial to investigate the effect of a simple, low technology, supervised strength training program for the lower extremities, combined with post-training protein supplementation, during hospitalization and 4 weeks after discharge. Patients are randomly allocated to one of two groups: 1) strength training during hospitalization (training every day), and for 4 weeks after discharge (3 training sessions per week); 2) usual care. Prior to study start, physiotherapists in the hospital and in the involved municipalities have been trained in the intervention, and all training sessions are supervised on a 1:1 basis. Each training session starts with a 5-min warm up program. After the warm-up the patients are asked to perform two strength training exercises (sit-to-stand and heel-raise) for 3 set of 8-12 repetitions at 8-12 RM following models of progression based on the STAND model (see Study II). Training loads are adjusted for each set to reach the aimed relative load (RM). The total duration of each training session is approximately 10-15 minutes. Protein is

considered an integrated part of strength training why the patient is asked to consume an oral protein supplement (Nutridrink Compact Protein from Nutricia A/S), containing 18 g milk-based protein and 300 kcal, immediately after each training session. During each training session the supervising physiotherapist completes an exercise diary containing information on level and load of the exercise, the number of sets performed, experienced pain, and the amount of protein consumed. Trained investigators, blinded to the randomization, perform structured interviews and assessments in the hospital within the first 48 hours of admission (baseline), and at three time points in the patient's own home: shortly after discharge, 4 weeks after discharge (primary end point), and 6 months after discharge. The same investigator performs all assessments of the same patient whenever logistically possible.

The primary outcome is change in the DEMMI score from baseline to 4 weeks after discharge (end of intervention, primary end point) (165). The secondary outcomes are 24-hour mobility measured by an *activ*PAL3^{TM} activity monitor (PAL Technologies Ltd, Glascow, UK), isometric knee extension strength (IKE) in the dominant leg using a handheld dynamometer (Power Track II Commander; JTech Medical, Utah, USA) (168,169), the 30-sec sit-to-stand test using a standard arm chair with a seat height of 45 cm (170), habitual gait speed (HG) on a 4-meter course (37,38), hand-grip strength (HGS) in the dominant hand using a handheld dynamometer (Digi-II; Saehan) (171), and the Barthel Index 20 (BI) (172). In addition, a range of possible confounders and modifiers are assessed, including cognitive function, depression, health status, nutritional status, physical activity level, pain, use of medication, and history of training.

Validation of the ActivPal activity monitor

For Study III we chose to change from the accelerometers used in Study I (Augmentec.com) to the ActivPal activity monitors (PAL Technologies Ltd., Glasgow, UK). This was chosen since the ActivPal monitors can record activity continuously for 7 days as opposed to 2 days for the Augmentec monitors. The aim in Study III was to monitor the patients for one week periods after discharge to get a picture of post-discharge activity. Seven days were chosen since 7 days has been shown to provide a good measure of usual physical activity in community dwelling older adults (173). Because of possible limitations using the ActivPal monitors (which will be elaborated in the discussion) we chose to perform a validation study on the ActivPal monitors, which are delivered with an inbuilt algorithm for distinguishing between lying/sitting, standing, and walking. Six healthy adults (28-48 yrs) were included in the study to examine the precision of the ActivPAL

activity monitor in measuring step counts and gait at different gait speeds. The participants were asked to walk on a threadmill at 7 different speeds in a random order of 2 minute intervals wearing an ActivPAL™ on the upper right thigh (0.28 m/s; 0.45 m/s; 0.50 m/s; 0.56 m/s; 0.61 m/s; 0.67 m/s and 0.89 m/s). During each 2 minute interval, steps were counted via direct observation. Data from the ActivPal monitors were compared with direct observations for agreement.

4.2.4 Study IV

Four hundred and thirty community-dwelling primary care patients (mean age 76.6 (SD 7); 58% women) were included in this cross-sectional study investigating the association between MCI and mobility based on baseline data from the Boston Rehabilitative Impairment Study in the Elderly (Boston RISE). The patients underwent a structured baseline interview including neuropsychological testing, physical performance testing and questionnaires on functional ability. Neuropsychological tests were used to characterize patients with MCI, and further sub-classify these patient according to their impaired cognitive domain in amnestic MCI (aMCI; memory impairment), non-amnestic MCI (naMCI; non-memory impairment), and multiple domain MCI (mdMCI; memory and non-memory impairment). The cognitive tests included were: 1) the Trail Making Test (TMT), consisting of two sub-tests (Trails A and Trails B) (174,175), 2) the Digit Symbol Substitution Test (DSST) (174,176), 3) and the Hopkins Verbal Learning Test, revised (HVLT-R), consisting of three subtests (total recall, delayed recall, and recognition discrimination) (177,178). MCI was defined as impairment on two sub-tests within the neuropsychological test battery (179). All patients were identified as either cognitively intact (No-MCI) or as having cognitive impairment (MCI). The subtest scores of the HVLT-R were used to define memory impairment, whereas the subtest scores of the TMT and the DSST were used to define non-memory impairment. Performance-based and self-reported mobility was assessed by habitual gait speed (HGS) on a 4-meter straight course (37,38), the Figure-of-8-Walk (F8W) around two cones 1.5 m apart (180), the Short Physical Performance Battery (SPPB) (37,38), and the sub-domains of basic lower extremity function (BLE) and advanced lower extremity function (ALE) of the Late Life Function and Disability Index (LLFDI) (181). Both self-report and performance-based mobility measures were used to investigate the association between MCI domains and mobility.

4.3 Statistical analyses

The main statistical analyses are presented below (for further details, please see Papers I-II+IV and Manuscript III). For all studies descriptive data are presented as means with standard deviations, medians with inter-quartile ranges, or frequencies with percentages depending on variable type. Comparisons between groups (Studies I, III (to be performed), and IV) were analyzed with the χ^2 test for categorical variables, the Student's t-test for normally distributed continuous variables, and the Mann-Whitney U-test for non-normally distributed continuous variables. To compare change in performance measures from pre-admission to admission (Study I) and from admission to at home (Study II) the Wilcoxon Signed Rank test or the paired t-test were used depending on variable type. All data for Studies I-II were double entered and validated in EpiData Entry, version 3.1 (The EpiData Association, Odense, Denmark). For Study IV all data were collected using electronic data collection forms coded with ID numbers, and validated in a technical review by a research team member before being transferred to a master file. For all studies the level of significance was set at $P \leq 0.05$, and all tests were two-tailed. All statistical tests were performed using the Statistical Analysis System (SAS) version 9.2 (Studies I and IV), and version 9.3 (Study II), SAS Institute, Gary, NC, USA.

4.3.1 Study I

To compare hours spent lying, sitting, and standing/walking between days with an independent CAS score (CAS = 6) and a dependent CAS score (0-5), both an unadjusted and an adjusted (adjusted for individual levels of CAS) linear regression were used. Also, a Kruskal-Wallis test was used for associations with potential explanatory variables.

4.3.2 Study II

Linear regression analyses were used to evaluate if the level of STAND depended on mobility (DEMMI) and cognition (OMC), respectively.

4.3.3 Study III

In this randomized controlled trial the estimated sample size for the primary outcome is based on previous research from our hospital (182), where a random sample of 25 older medical patients had a mean change in the DEMMI score of 1.8 from baseline to 30-days follow-up, and a standard deviation of 12.8. In order to detect a minimal clinically important difference of 10 points (183) in

the between-group change in the DEMMI score at the four week assessment (primary end point), a sample size of 27 patients per study arm is needed with 80% power and a type I error rate of 5%. A maximum of 80 patients are expected to be included.

4.3.4 Study IV

An analysis of variance (ANOVA) and an analysis of co-variance (ANCOVA) were used to determine associations between each mobility measure and cognitive status comparing MCI vs. No-MCI. First, we adjusted for gender, race and education. Then, cognitive status was entered into the adjusted model as a categorical variable (aMCI, mdMCI, naMCI, and No-MCI) to calculate estimates for differences in mobility measures between all MCI sub-types. In a post hoc analysis further adjustment was made for current health status and chronic conditions. Also, an additional analysis included baseline MMSE status as a categorical variable to explore whether MMSE <24 modified the association between the respective MCI subtypes and mobility.

5. Results

A summary of the main results are listed below. For further details please consult Papers I-II+IV. Since Manuscript III is a trial protocol no results from the study will be reported in this section. However, a status concerning the ongoing inclusion will be given.

5.1 Study I

24-hour mobility during hospitalization in older medical patients.

Sixty-eight patients met the inclusion criteria, 49 of whom agreed to wear accelerometers during their hospitalization. Forty-three patients were able to walk independently (ambulatory patients), and six patients were unable to walk independently (non-ambulatory patients). One of the ambulatory patients was excluded due to lack of accelerometer data. The patients wore the accelerometers for 4.4 days on average. The ambulatory patients were lying in bed 17.0 hours (IQR: 14.4-19.1), sitting 5.1 hours (IQR: 2.9-7.1), and standing/walking for 1.1 hours (IQR: 0.6-1.7) per day. They were significantly more active than the non-ambulatory patients ($p<0.001$) (Figure 3). On days with a CAS score of 6 (independence in basic mobility), the ambulatory patients were lying 4.1 hours less compared to days with a CAS score of 0-5 (dependency in basic mobility) (15.4 versus 19.5 hours; $p<0.001$), they were sitting 2.4 hours more (6.0 versus 3.6 hours; $p<0.001$), and standing/walking 0.9 hours more (1.6 versus 0.7 hours; $p<0.001$).

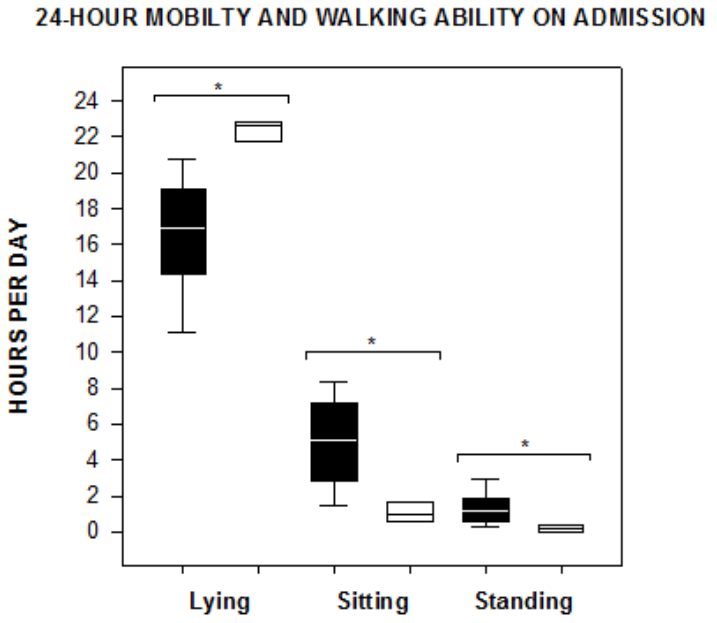


Figure 3. Hours per day spent lying, sitting and standing/walking during hospitalization.

= ambulatory patients

= non-ambulatory patient

Data are given as median (IQR) and 5/95 percentiles.

** denotes statistically significant between-group differences.*

The in-hospital mobility level was independent of pre-admission and admission NMS, co-morbidities and pain. However, patients with a MMSE score >24 were standing/walking significantly more hours during a day than patients scoring <24 (p=0.02). When cross-validating the algorithm based on data from six older medical patients, the algorithm classified time spent lying, sitting, and standing and/or walking with <9.2%, <4.7% and <10.4%, respectively.

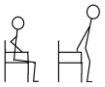
5.2 Study II

Feasibility of progressive sit-to-stand training among older hospitalized patients.

Twenty-four patients consented to participate in the study. A total of 5 patients (20.8%) dropped out of the study; one patient dropped out during the initial examination, leaving 23 patients to be tested at the hospital, and four patients dropped out before the home test, leaving 19 patients to be tested at home. A statistically significant decline in NMS was seen from two weeks prior to hospitalization to admission (from 9 (IQR 5.5;9) to 3 (IQR 2;9); p=0.03); at the home visit the median NMS score was 6.5 (IQR 3;9), but this numerical difference was not statistically significant.

Twenty patients (83%) were able to perform at least one set of 8-12 RM at a given level of STAND in the hospital, and 15 patients (79%) were able to perform two sets of 8-12 RM at home. Half of these could perform three sets of 8-12 RM. The mean Borg score when performing the highest level possible was 14.2 (±1.9) in the hospital and 14.1 (±1.6) at home. Table 4 shows the distribution of patients on the different levels of STAND in the hospital and at home, respectively.

Table 4. Overview over the distribution of patients on the 8 levels of STAND according to the highest level performed in the hospital and at home, respectively.

Level in STAND	Description of level	Illustration	In hospital (n)	At home (n)
1	Seated knee extensions with or without added load, e.g. weight cuffs.		2	0
2	STS with armrest support and support from another person allowed; own body weight.		0	0
3	STS with armrest support in eccentric and concentric phase allowed; own body weight.		2	3
4	STS with armrest support in concentric phase allowed; own body weight.		2	1
5 Starting point	STS without support; own body weight.		6	4
6	STS with added load; e.g. weight vest.		6	4
7	Unilateral STS with balance support allowed; own body weight		1	1
8	Unilateral STS with balance support allowed and added load; e.g. weight vest.		1	2

STS: sit-to-stand

For all patients progression or regression of the exercise was possible, indicating no floor or ceiling effect. Also, no patients reported an increase in pain during or after performing the exercise.

Those scoring higher on the DEMMI performed the exercise at the most challenging levels of STAND (on admission, β=0.10(CI:0.07;0.13), P<0.0001; at home, β=0.07(CI:0.03;0.12), P=0.004), whereas the level of STAND did not depend significantly on OMC (on admission: 0.07(-0.12;0.26), P=0.45; at home: -0.01(-0.42;0.41), P=0.96) (Figure 4).

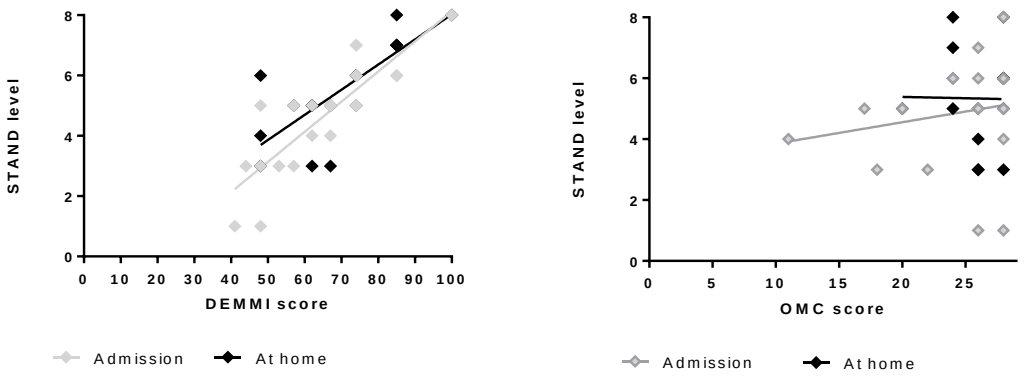


Figure 4. The association between STAND and DEMMI score (Panel A) and OMC score (Panel B), respectively.

STAND level: indicates the level of the model (1 to 8); DEMMI score: score on the de Morton Mobility Index (0-100); OMC score: score on the Short Orientation-Memory-Concentration test (0-28). The higher the score the more difficult level of STAND, the better mobility (DEMMI) and the better cognition (OMC), respectively.

5.3 Study III

Supervised progressive in-hospital and post-discharge strength training compared with usual care in older medical patients: study protocol for a randomized controlled trial (the STAND-Cph trial).

By the time of writing this thesis, inclusion of patients for Study III is still ongoing (December 2015). Seventy-six patients have been included in the study. Of these, 20 have dropped out (26%) – 12 before the discharge assessment, eight before the 4-week assessment, and 1 before the 6 month assessment. Also, five have been excluded from the study (7%) – one was discharged to a rehabilitation unit, two were hospitalized due to apoplexia cerebri at the time of assessment, one was diagnosed with an aortic aneurysm and was to avoid high intensity exercise, and one was enrolled in a pilot project including sit-to-stand training in the municipality at discharge. Thus, 51 patients are enrolled in the study of which 35 have completed all assessments (except for one missing out on the discharge assessment), 13 have completed all but the 6-month assessment, and three have completed the admission and discharge assessments. Due to a higher attrition rate than expected (33% vs. 25%) patients are still being enrolled to ensure a sample size matching the sample size calculation of 54 patients with 4-week assessments (primary endpoint).

Validation of the ActivPal activity monitor

The ActivPAL categorized walked time on gait speeds of 0.56-0.89 m/s with <0.1% error. For speeds of 0.28 m/s, 49.6% of the time was categorized as walking, and for 0.45 m/s and 0.50 m/s, respectively, 88.8% and 86.7% of the time walked was categorized as walking. The ActivPal counted steps with <1% error for gait speeds of 0.61-0.89 m/s. For 0.28 m/s, 43.6% of the steps were registered, for 0.45 m/s, 90.5% of the steps were registered, and 0.50 m/s, 97.2% of the steps were registered by the ActivPal.

5.4 Study IV

Mild Cognitive Impairment Status and Mobility Performance: An Analysis from the Boston RISE Study

In total, 430 participants were included in the study. Of these, 42% were classified as having MCI; 15.8% had aMCI, 22.7% had mdMCI and 3.5% had naMCI. MCI participants performed significantly worse in tests of mobility performance and self-reported functional performance than participants without MCI (e.g. HGS: β=-0.13, $p<0.01$; SPPB: β=-1.39, $p<0.01$) even when adjusting for sex, race and education ($p<0.01$) (Table 5).

Table 5. Mean difference given as betas, 95%-confidence intervals and p-values from multiple regression models demonstrating the difference in mobility between those with MCI and without MCI among Boston RISE participants.

	Unadjusted model; β(CI); p-value		Adjusted model 1*; β(CI), p-value	
HGS (m/s)	-0.13 (-0.17;-0.10)	<0.001	-0.12 (-0.16;-0.07)	<0.001
F8W (sec)**	1.19 (1.13;1.27)	<0.001	1.19 (1.13;1.27)	<0.001
SPPB (4-12)	-1.39 (-1.80;-0.98)	<0.001	-1.35 (-1.80;-0.90)	<0.001
BLE	-4.55(-6.84;-2.25)	<0.001	-4.06(-6.48;-1.65)	0.001
ALE	-5.97(-8.74;-3.20)	<0.001	-5.57(-8.43;-2.71)	<0.001

*MCI: mild cognitive impairment; CI: 95% confidence interval; HGS: Habitual gait speed; F8W: Figure of 8 walk; SPPB: Short Physical Performance Battery; BLE: basic lower extremity function; ALE: advanced lower extremity function. * Adjusted for sex, race, and education; **F8W was log2-transformed. Results are given as 2^{β}–coefficients.*

All MCI subtypes performed significantly worse than No-MCI on all mobility measures in the adjusted analysis ($p<0.05$), except for aMCI versus No-MCI on F8W and BLE. Moreover, naMCI patients performed more poorly on a number of mobility tests than aMCI (e.g. SPPB ($p=0.01$) and BLE ($p=0.04$)) (Figure 5). Similarly, patients with mdMCI performed worse on F8W ($2^{\beta}=1.21$; $p<0.001$) and SPPB ($\beta=1.07$, $p<0.01$) than aMCI (for further details see Paper IV). Adjustment for current health status, chronic conditions and MMSE, respectively, did materially alter the findings.

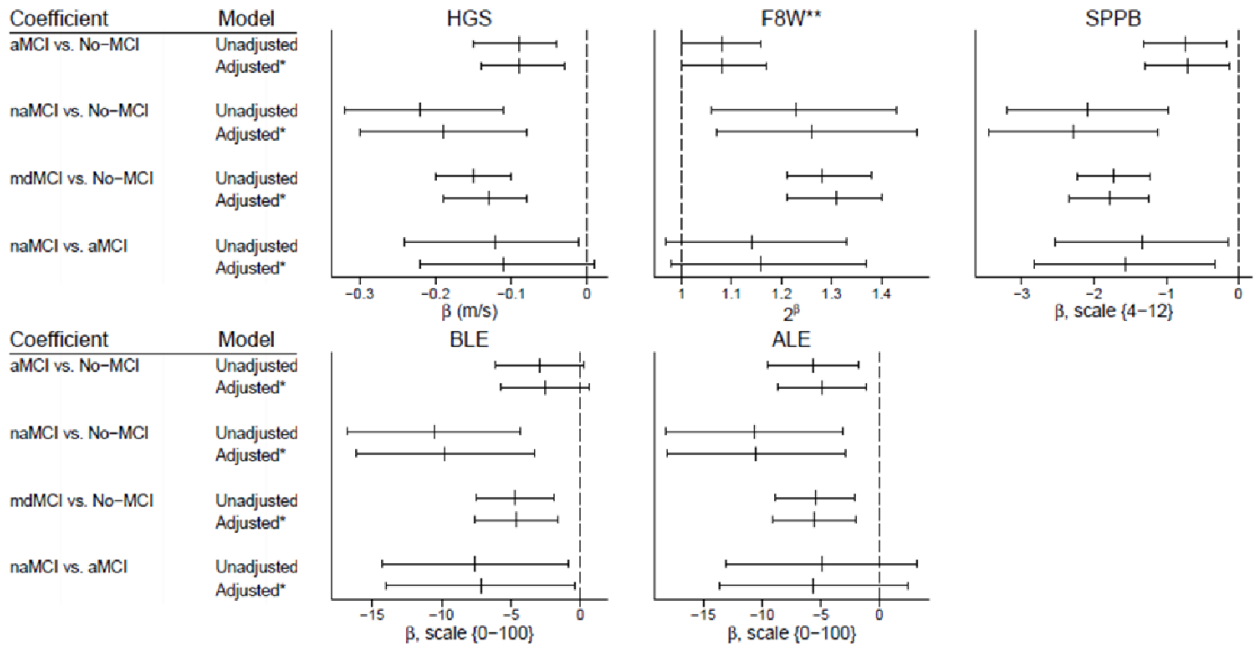


Figure 5. Mean difference given as betas and 95%-confidence intervals from multiple regression models demonstrating the difference in mobility between MCI- subtypes and No-MCI for 5 performance measures among Boston RISE participants. Confidence intervals not crossing the vertical dotted line represent statistically significant values.

*MCI: mild cognitive impairment; No-MCI: No MCI; aMCI: amnestic MCI; mdMCI: multiple domain MCI; naMCI: non-amnestic MCI; HGS: habitual gait speed; F8W: Figure-of-8 walk; SPPB: Short Physical Performance Battery. *adjusted for sex, race, and education;**F8W was log2-transformed. Results are given as 2^{β}–coefficients.*

6. Discussion

This thesis has evaluated 24-hour mobility during hospitalization (Study I), and the feasibility of a progression model for sit-to-stand based strength training (STAND) in the hospital and at home (Study II) in acutely admitted older medical patients. This model is currently being tested in a confirmatory randomized controlled study, for which the study protocol has been submitted for publication and outlined as Study III. Also, the association between different types of MCI and mobility was evaluated in community-dwelling primary care patients (Study IV).

6.1 Key Findings

The key findings of this thesis are:

- A cohort of acutely admitted older medical patients, who were able to walk on admission, were assessed with accelerometers throughout their hospitalization and were found to spend a median of 17.0 hours per day in bed, 5.1 hours per day sitting, and 1.1 hours per day standing or walking. Also, their in-hospital mobility level seemed to depend on their basic mobility (ability to independently get in and out of bed, rise from a chair, and walk), and on cognition.
- An algorithm to measure mobility level in older medical patients was developed and validated for two accelerometers (Augmentec.com) placed on the thigh and lower leg, respectively. The algorithm could discriminate between time spent lying, sitting and standing and/or walking, with a misclassification of 4.7-10.4% of the seconds measured.
- A simple progression model (STAND) for loaded sit-to-stand exercise was found feasible in acutely admitted older medical patients in the hospital- and home setting. STAND could be used to reach a strength-training intensity of 8-12 repetition maximum, with no ceiling or floor effect observed, and with no reported pain as a consequence of performing the exercise. Moreover, no association was found between level of STAND and cognition.
- Among a cohort of primary care patients, performance-based and self-reported mobility was associated with MCI. Those with MCI, and different sub-types of MCI, had worse mobility than those without MCI (also when adjusting for sex, race, and education). Also, mobility appeared to be poorest among those with non-amnestic MCI.

6.2 24-hour mobility

Low levels of in-hospital mobility are commonly reported in older medical patients. In Study I, we found that the included older medical patients, who were independently walking on admission, spent most of their in-hospital time being inactive (17h/day lying). The level of in-hospital mobility corresponded well with levels seen in other studies evaluating in-hospital mobility levels based on accelerometers (95,101) and step counts (96) – i.e. Brown et al. (91) found older medical patients (45 men; age 74±6.5 yrs; mean stay 5.1 days) to spend an average of 20 hours per day in bed, 3.1 hours sitting and 0.9 hours standing or walking; Villumsen et al. (95) found a cohort of geriatric patients (100 patients; 84±6.3 yrs; median stay 13.5 days) to spend 83 minutes per day standing and walking; and Fisher et al. (96) found a cohort of geriatric patients (239 patients; 76±6 yrs; average stay 4.9 days) to spend 57 minutes per day walking, taking 739 steps, and the remaining time being non-mobile. Similar levels of daily steps have been reported by Ostir et al. (97), who found an association between the number of steps taken in the last 24 hours of hospitalization and risk of death within 2 years (for each 100-step increase the hazard ratio decreased by 3%). Likewise, low in-hospital mobility levels have been shown to be associated with increased risk of decline in ADL, new institutionalization and death (92,94), and in older adults with mobility limitations, an association between sedentary behavior and higher odds of metabolic syndrome has been found (184). To the author's knowledge, no studies have evaluated post discharge mobility on a 24-hour basis or the association between in-hospital mobility and post discharge mobility, so whether post discharge levels correspond with those seen in community-dwelling older adults (185) is unknown. This knowledge, however, will be obtained from Study III in which 24-hour mobility will be assessed by accelerometers three times for one week after discharge (at discharge, 4 weeks and 6 months). Nevertheless, the levels of activity seen in hospitalized older adults call for attention in order to avoid the negative consequences seen with low in-hospital mobility levels (e.g. decline in ADL, risk of institutionalization and death) (92–94,97). Study I provides new knowledge about the association between 24-hour mobility and basic mobility (ability to get in and out of bed, sit and stand from a chair and walk), which was assessed daily throughout hospitalization. Independence in basic mobility was found to correlate with daily levels of 24-hour mobility. Thus, it seems that working on solutions to better basic mobility may be one way of improving in-hospital mobility levels. One way of achieving this goal will be evaluated in Study III.

6.3 Assessing 24-hour mobility

Due to the previously mentioned negative effects of low in-hospital mobility, gaining knowledge about in-hospital mobility levels and the characteristics of those with low mobility levels is important. By the time of conducting Study I, only one study had used accelerometers in assessing mobility levels in older medical patients continuously throughout hospitalization (91). Accelerometers can provide an uninterrupted measure of activity as opposed to nurse reports (92), mobility index' (93) and hallway observations (98), and can overcome issues of over- or underreporting by clinicians (92,186), as well as lack of ability to cover every hour of the day (98).

Consistent with Dr. Brown and colleagues (101), in Study I, we found the accelerometers used (Augmentec Inc., Pittsburgh, Pennsylvania, USA) valid in assessing time spent lying, sitting, and standing/walking using a two-accelerometer approach. Our study added to this validation by using a two-axis solution with measurements every second as opposed to a one axis solution with measurements every 20 seconds (101). Nevertheless, consistent with Brown and colleagues we were unable to differentiate between standing and walking. Thus, despite the ability to measure continuously on a 24-hour basis obstacles were encountered in obtaining an image of all activity performed. Moreover, the accelerometers used could measure a maximum of 24 hours before re-charging was necessary, making it logistically difficult to use the accelerometers in the home setting.

Different types of accelerometers for measuring mobility exist. Therefore, in Study III the ActivPal accelerometer was chosen (PAL Technologies Ltd, Glascow, UK), since it can measure continuously for 7 days, and should be able to distinguish standing from walking. However, this differentiation has shown to be difficult at very slow walking speed, why underestimation of time spent walking might occur. When discriminating between standing and walking, previous studies in healthy adults have found a percentage error of <1% for speeds from 0.67–1.56 m/s (187) and 3.7% for 0.45 m/s (188). Our validation study showed similar results for faster walking speeds, but higher percentage errors for lower walking speeds - the ActivPAL categorized walked time on walking speeds of 0.56-0.89 m/s with <0.1% error, 0.28 m/s with a 50.4% error, and 0.45 m/s and 0.50 m/s, respectively, with an 11.2% and 13.3% error. This limit of the ActivPal in assessing time spent walking is worth considering, since it is likely to underestimate time spent walking in older hospitalized patients. In older hospitalized adults (≥65 yrs) mean walking speeds of 0.43 m/s have been reported (189), and in a study from Hvidovre Hospital in 317 older medical patients, 46% walked at a speed below 0.67 m/s, and 34% at a speed below 0.56 m/s (182). Thus, measurements

of one third of older medical patients are likely to underestimate time spent walking. However, underestimation is probably less critical than overestimation as slow gait speed (self-selected) has been shown to be associated with daily ambulatory activity, with slow walkers being less ambulatory than faster walkers (190). This calls for particular attention on slow walkers, since gait speed has been shown to be a predictor of adverse events (e.g. disability, cognitive impairment, institutionalization, falls, and/or mortality) (191).

6.4 Functional decline before and during hospitalization

Decline in ADL function is commonly reported by older medical patients both before hospitalization (in retrospect) and during hospitalization (92,93,102–105), and studies have found that around 40 % are discharged with worse ADL function than two weeks before admission (102,104,108,110). Consistent with previous studies, patients in Study I declined in functional independence from two weeks before hospitalization to admission, estimated by the NMS (in retrospect). Similarly, in Study II a decline in the NMS was seen from two weeks before hospitalization to admission (from 9 (IQR 5.5;9) to 3 (IQR 2;9); p=0.03). However, in a subsample of 33 patients (149) from Study I, with functional assessments of muscle strength (hand-grip strength, knee-extension strength) and functional performance (Timed Up and Go) on admission, discharge and 1 month after discharge, functional decline during hospitalization, as previously reported in studies using self-report measures (102,104,108,110), could not be found. Instead, an improvement was seen in the Timed Up and Go test during hospitalization (149). In-hospital improvement in functional performance measures, i.e. walking speed, grip strength (150) and SPPB (192), has also been reported in other studies, while de Buyser et al. (150) did not find a significant change in ADL scores. However, both data from the Study I subsample and from de Buyser et al. showed the patients to have poor performance at discharge – knee extension strength (149) was at the threshold level for independent ability to perform ADL (84) and increased risk of future mobility limitations (87), and hand grip strength and walking speed (150) were at levels indicating mobility limitations (16). Thus, a discrepancy between self-report measures commonly used to describe functional changes and performance-based functional measures seems present and are well in line with studies reporting that performance based and self-reported measures of physical function assess different, partially overlapping, aspects of physical functioning (193,194). Also, community-dwelling older adults have been shown to recalibrate their self-report of functional limitations based on recent health problems (195). That is, people who had experienced illness during the last week and pain or stiffness on the day of assessment had an inflated perception of

limitations, i.e. greater self-reported disability on a given level of observed function, than people without these problems. However, when a performance test was administered before self-report assessments, associations between self-report and performance based measures improved (195). Thus, psychosocial and health factors seem to influence self-report measures of disability (193,195), suggesting that both self-report and performance based measures should be used in evaluating populations over time (195). This has been done in Study III, but the associations are yet to be analyzed.

The lack of decline seen in functional performance measures during hospitalization (149,150) is speculated to be due to suppressed performance on admission as a consequence of the acute illness, with stabilization of the medical illness during hospitalization overshadowing the possible negative consequences of in-hospital inactivity (149). This argument is in accordance with the results of a study in older adults admitted for diagnostic investigation, who declined significantly in functional capacity, i.e. upper extremity muscle strength, and 6-min walk test, during 5 days of hospitalization (107). The change in 6-min walk test was beyond a minimal important difference reported in patients with arterial hypertension (196). Another reason for the lack of decline seen in functional performance measures could be that further decrease is difficult to identify during hospitalization, due to an already low functional level on admission. However, despite the lack of change in functional performance seen in the Study I subsample, the low levels of functional performance at discharge are worthy of concern, since functional performance has been linked with future risk of falls and functional decline (197), mobility- and ADL disability (35–37), hospital readmissions (119) as well as death (38,39,197). Furthermore, the need for help in ADL's before admission has been shown to correlate with low ADL scores after discharge (105). Also, a study in older medical patients (≥65 yrs) showed that those who improved or remained stable in self-reported ADL function during hospitalization had lower risk of death in the months following discharge than those who declined (198). This underlines the importance of counteracting functional decline during hospitalization, especially since older adults consider mobility as vital to health and as an indicator of independence, well-being and freedom allowing them to participate in life as they know it, thus not only affecting the physical aspects of life (199). Also, this risk of functional decline associated with hospitalization was the reason for conducting Studies II and III.

6.5 Barriers to mobility and exercise

An association between basic mobility and 24-hour mobility was found in Study I. However, factors other than dependence in basic mobility may foster in-hospital inactivity. Acute illness and inflammation have been linked with lower fatigue resistance as well as poor muscle strength and functional performance in geriatric patients and community-dwelling older adults (200–203), and may affect the urge for being active. Indeed, in one study in older medical patients (≥75 yrs), weakness, need for assistance, potential risk of falling, lack of interest from staff, and structural barriers were mentioned as reasons for being inactive (204). Similarly, the number of steps taken during hospitalization has been found to be associated with a history of falls, age 75 or older, and preadmission mobility impairment (96).

Older medical patients that may benefit from physical rehabilitation during and after hospitalization may have barriers preventing participation. In a study in acutely admitted older medical patients, those declining to participate expressed that they did not feel like exercising or did not believe they could (129). A study in community-dwelling older adults with a history of falls or self-reported mobility disability, found exercise at home, an improvement in the ability to undertake daily tasks, and no need to use transportation to be the three most important attributes for engaging in physical activity among participants 66 years or older (139). In Denmark, physical rehabilitation after discharge is undertaken by the municipalities, and most often rehabilitation takes place in rehabilitation centers, thus requiring transportation to and from the center, and most likely extra time waiting for transportation before and after the rehabilitation session. This can be a barrier for some older adults (139) and may affect compliance with rehabilitation. Also, for older adults discharged with a rehabilitation plan, initiation of rehabilitation is most likely to be between two and four weeks after discharge, thus creating a treatment gap between hospitalization and rehabilitation. Besides, acutely hospitalized older adults may prefer for exercise to be initiated in the hospital or shortly after discharge (129,138). Therefore, initiating exercise training during hospitalization and continuing the exercise training in the patients' own homes after discharge (Study II and III), seems rational.

6.6 Feasibility

To try to overcome the previously reported lack of knowledge regarding the optimal nature and dose of exercise in older adults (123,145,146), we chose a minimal time-consuming treatment approach taking implementation in a busy care setting into account. According to a recent review

(205) low intensities are often the first choice among physiotherapists, as this is perceived to be safer. Low intensities, though, may be inadequate to achieve optimal effects on functional performance (148), why we wanted to investigate if higher intensities could be performed by older medical patients without inducing adverse events. Since we found few studies investigating the effect of a cross-continuum program initiated during hospitalization and continued after discharge (129,135), and due to problems with compliance in these studies (129,135), we chose a program with full supervision from trained staff.

Study II was conducted as a feasibility study to evaluate important parameters of the full-scale study (Study III) (206), i.e. if the progression model could be used to ensure proper loading (8-12 RM) without inducing adverse events, before using it in Study III. We wanted to ensure, that the exercise could be understood and performed, and that proper loading could be achieved. Study II showed that the progression model could be used in hospitalized older adults, both in those with high and low mobility, as measured by the DEMMI, and in those with and without signs of cognitive impairment. However, the ability to perform strength training following the model was only tested once in the hospital and once in the patients' own homes, leaving us without knowledge about the possible use of the model over time. The lack of observed ceiling and floor effect, though, is a promising finding in this regard.

6.7 Cognition

Older adults with cognitive impairment have been reported to be at greater risk of functional decline before admission (94), during hospitalization (109,113,114) and after discharge (113) and less likely to recover from ADL disability during hospitalization and after hospitalization than non-impaired (113). In Study I, patients with cognitive impairment (MMSE≤24) were found to be standing or walking significantly less than those without cognitive impairment, possibly inducing a greater risk of functional decline during hospitalization. In this regard, it is promising that Study II showed the STAND model to be feasible, and thus a potential means of exercise, for both patients with and without cognitive impairment. The ability of both cognitively impaired and non-impaired hospitalized older adults to perform a strength training program including the STAND model, and the effect of the program, though, are yet to be illuminated (Study III).

Cognitive impairment and mobility limitations have also been found to influence the ability of independent living in community-dwelling older adults (57–59). In Study IV, the association

between cognition and mobility performance was evaluated in community-dwelling primary care patients, and those with MCI were found to have worse mobility performance than those without MCI. In addition, those with impairments in non-amnestic cognitive domains, e.g. processing speed and executive function, performed the worst. These findings are consistent with previous studies also linking executive dysfunction with disability (56,207–209). Furthermore, co-existence of cognitive impairment and mobility limitations has been shown to affect the ability of community-dwelling older adults to remain at home (59). Altogether, older adults with cognitive impairment and functional disability, or one of the two, are prone to experience adverse events and need particular attention. There is reason to believe, though, that both cognitively impaired and non-impaired can benefit from training interventions. Results from a meta-analysis on training interventions in cognitively impaired and cognitively intact older adults, showed that cognitively impaired can benefit similarly to non-impaired in strength- and endurance outcomes from both strength- and endurance training (210). Moreover, a recent systematic review found that in older adults with MCI, physical exercise can be beneficial on several cognitive domains including executive function (211). Thus, there is reason to believe that the strength training program to be evaluated in Study III can improve mobility in cognitively impaired as well as cognitively non-impaired.

6.8 Training interventions

Previous studies evaluating strength training during (127) and after hospitalization (128), and in community-dwelling older adults (130) have used 10 week programs, using both weight training machines (127,128), and elastic bands for resistance (130), with programs consisting of 3-5 lower extremity exercises (128,130) or only one exercise (127). Common to these studies is a positive effect seen on leg muscle strength and functional performance. However, problems recruiting acutely admitted older medical patients for in-hospital and post discharge training have also been encountered (129), why the feasibility and effect of cross-continuum training programs remains to be fully elucidated. Study III is based on two lower extremity exercises performed daily during hospitalization and three times per week for four weeks after discharge, and thus providing the participants with a lower volume of strength training than in the studies mentioned above. Since data collection in Study III is still ongoing, it is unclear whether four weeks of strength training after discharge is sufficient to induce effects similar to those seen after 10 weeks. However, four weeks were chosen since it has previously been reported, that recovering function within the first month after discharge is of importance for long term outcomes (102). A previous study in older

hospitalized adults has shown positive effects of exercise therapy performed during the first four weeks after discharge (135), leading us to believe, that four weeks might be sufficient in inducing an effect, even though the exercise program in Study III is of a smaller volume (but higher intensity). Also, a study in older home care clients found that structured exercise programs are not the preferred activity of these older adults (212), why a four week program may be more acceptable than a program of longer duration. Siebens et al. (135) evaluated the effect of an exercise program of 12 minimally challenging exercises for flexibility and strength (three exercises for the lower extremities) combined with a walking program, in older medical and surgical patients (≥70 yrs). The exercises were performed twice daily during hospitalization (once with supervision), and three times per week (non-supervised) at home after discharge for one month (28% performed the home program), and an amelioration in iADL was found one month after discharge. Although the program used is not similar to the one used in Study III, it bodes well for an ability to induce a positive effect, even using programs of shorter duration. However, a recent meta-analysis evaluating strength training programs of 8 to 52 weeks of duration on strength gains in adults over the age of 55, found that programs of longer duration were superior to shorter duration (213), which questions the sufficiency of four weeks of training.

Both resistance training and amino acids can stimulate an anabolic response (156), and combining the two has been shown to enhance the muscular response to exercise in healthy older adults (153–155). Therefore, protein was chosen as an integrated part of strength training in Study III. Nevertheless, although the protein supplementation provided in Study III was intended to boost anabolism, it is unclear whether it will merely reduce an existing protein deficit. According to the recommendations of an international study group (214), older adults need a greater amount of daily protein than young adults to maintain muscle mass, and older adults with acute or chronic diseases or marked malnutrition, need even more. In Study II, 79.2% of the patients were considered to be at nutritional risk (based on a low body mass index, decreased appetite, weight loss within the last three months, and severity of disease), which is in line with previously reported lack of adequate nutritional intake among older hospitalized adults (215). Thus, despite provision of protein in connection with strength training, some of the patients might still be undernourished.

6.9 Methodological considerations

The studies have some limitations worth considering, some of which have been mentioned previously. In Study I we were unable to distinguish between standing and walking with the accelerometers used. We attempted to overcome this lack of specificity in the assessment of 24-hour mobility by introducing a novel type of accelerometer in Study III. Nevertheless, similar obstacles were encountered, namely an inability of the accelerometer to correctly assess time spent walking at slow walking speeds – speeds that are commonly seen in older medical patients. Thus, regardless of the accelerometers used, we are likely to underreport the time spent walking, although an assessment of upright time can be obtained.

In Study II, 90% of the patients were either excluded (80%) or declined to participate (10%) in the study, leaving us with a very select group of older medical patients. Similar or lower consent rates, however, have been reported in previous studies in older medical patients (129,135,216), underlining the difficulty of recruiting patients in the acute setting and limiting the generalizability of the results. Similar inclusion rates have been encountered in Study III, in which the main reasons for not wishing to participate have been consistent with reasons found by Dr. Brown and colleagues, namely feeling too ill to participate, feeling incapable of exercising during the hospital stay (129), as well as not feeling a need for exercise.

Study IV was cross-sectional and therefore does not add information about a possible causal association between cognitive impairment and mobility limitations. However, associations were found between cognition and mobility. In Study III, we have included cognitive assessments similar to the ones used in Study IV, and we will therefore be able to extend the investigations from Study IV to older medical patients.

7. Conclusions

In two prospective cohort studies, we found that the included acutely admitted older medical patients (+65 yrs) spent a median of 17 hours per day of their in-hospital time in bed. The level of in-hospital mobility seemed to depend on the patients' levels of basic mobility, i.e. their ability to independently get in and out of bed, rise from a chair, and walk, and on their cognitive level. Accelerometers used in measuring in-hospital mobility could validly assess time spent lying, sitting, and standing and/or walking in these patients. Also, based on a pre-defined criteria for feasibility, we found that a simple progression model for loaded sit-to-stands (STAND) was feasible in acutely admitted older medical patients in the hospital- and home setting, in obtaining a strength-training intensity of 8-12 repetition maximum for 8-12 repetitions with no indication of ceiling or floor effect for load, and no report of adverse events. Moreover, the level of STAND performed did not depend on cognition. The effect of a cross-continuum strength training program is currently being evaluated in a randomized controlled trial, and data are still to be analyzed. Also, in a cross-sectional study in older community-dwelling primary care patients, performance on a range of performance-based and self-reported mobility measures was associated with MCI status. Performance was worse among those with MCI, and appeared to be poorest among those with non-amnestic MCI.

8. Perspectives

The findings presented in this thesis are of relevance for clinicians and researchers encountering mixed populations of older adults, by confirming previously reported concerns regarding in-hospital inactivity in older medical patients and in having proposed a simple model for high intensity strength training as a possible method of training for older medical patients with and without mobility limitations and cognitive impairment.

The low levels of in-hospital mobility and muscle strength (Study I and Study I subsample) and require attention. In order to avoid in-hospital in-activity and the associated negative effects it seems relevant to focus on regaining independence in basic mobility (Study I). In conducting Studies II and III we have proposed a minimally time consuming solution. The fact that the older medical patients were able to perform the sit-to-stand exercise as proposed, both in the hospital and in their own homes, is an important finding. Due to continuous economical cuts in the health care sector in Denmark, we wanted to investigate the effect of a program that could realistically be implemented in a busy care setting and continued after discharge, using only little time and equipment and thus, demanding few resources. The final proof of feasibility of the entire intervention will not be established until data from Study III have been analyzed. Thus, whether our program including the sit-to-stand exercise provides a feasible suggestion for a way of overcoming in-hospital inactivity, loss of muscle strength and function, remains unanswered at the moment.

When outlining suggestions for activity and rehabilitation in older medical patients it is crucial to take possible barriers towards physical activity into account – both in the hospital and in the home setting – and combining this knowledge with what is considered to be important for older adults (e.g. strength training). In most hospital wards in Denmark, patients spend most of their time in their bed room (eating, watching television etc.). Thus, the structure of the hospital wards does not encourage activity. Re-introducing dining rooms, encouraging staff and relatives to facilitate out of bed activity etc., may be other ways of avoiding a negative circle of inactivity. Also, a simple daily walking program seems like a good suggestion for a simplistic in-hospital approach (217), and corresponds well with an activity preferred by older adults (212). Also, it may be that training as proposed in Study III should only be targeted patients at risk of developing mobility limitations and that this differentiation could be made on admission. Bodilsen et al. (182) found that physical performance measures (gait speed, hand grip strength, chair stand, basic mobility) - particularly chair-stand and gait speed - assessed on admission, could identify mobility limitations in acutely

admitted older medical patients 30 days after hospital discharge. So, an admission evaluation could potentially be conducted to screen for those who are at risk of developing mobility limitations and thus at need for extra attention during hospitalization. This thesis brings forward a suggestion for a program meeting the requirements of avoiding in-activity and promoting independence in basic mobility during and after hospitalization. However, the effect of the program is still unknown.

9. Summary

Mobility in older acutely admitted and primary care patients – in-hospital physical activity and simple strength training

Older medical patients (≥65 yrs) constitute more than half of the patients seen in Danish medical wards, and low levels of mobility are common during hospitalization and associated with adverse events. Besides, older hospitalized adults display poor muscle strength and functional performance, and risk losing independence as a consequence of their hospitalization. Patients with cognitive impairments seem especially vulnerable. Only few studies have assessed in-hospital mobility and basic mobility continuously throughout hospitalization in older adults, and few studies have examined the feasibility and effect of cross-continuum strength training. Therefore, the main objectives of the studies included in this thesis were to evaluate 24-hour mobility and basic mobility during hospitalization in acutely admitted older medical patients and validate the accelerometers used (Study I), to test the feasibility of a model for progressive sit-to-stand training in the hospital- and home setting (Study II) and the effect of simple, supervised, cross continuum strength training (Study III) in acutely admitted older medical patients, and to describe the association between mobility performance and mild cognitive impairment in older community-dwelling primary care patients (Study IV).

Study I

Forty-three ambulatory older medical patients (≥65 yrs) were included. Cognition was assessed on admission by The Mini Mental State Examination (MMSE), and 24-hour mobility was assessed throughout hospitalization by two wireless accelerometers. An algorithm for identification of time spent lying, sitting, and standing/walking using the accelerometers, was cross-validated on six older medical patients. The Cumulated Ambulation Score was used to assess basic mobility every day throughout hospitalization. The patients were assessed for 4.4 days and were lying in bed 17.0 hours, sitting 5.1 hours, and standing/walking for 1.1 hours per day. On days with independence in basic mobility, the patients were significantly more active that on days with dependence in basic mobility ($p<0.001$). Patients with a MMSE score >24 were standing/walking significantly more per day than patients scoring <24 ($p=0.02$). The algorithm could classify time spent lying, sitting, and standing/walking with a 4.7-10.4% error.

Study II

Twenty-four older medical patients were included. Cognition was assessed on admission by the Short Orientation-Memory-Concentration test. A progression model for sit-to-stand as a strength training exercise (STAND) was developed. The model was considered feasible if 75% of the patients could perform the exercise at 8-12 repetitions maximum for 8-12 repetitions at a given level of the model in the hospital and in their own homes after discharge, if no ceiling or floor effect were seen, and if no adverse events were observed. Pain was assessed before, during and after performing the exercise. Twenty-three patients were tested in the hospital, and 19 of these were also tested at home. Twenty patients (83%) were able to perform the exercise following STAND in the hospital, and 15 patients (79%) at home. No floor or ceiling effects were found, and no patients reported an increase in pain during or after performing the exercise. Thus, STAND was considered feasible. The level of STAND did not depend significantly on cognition ($P \geq 0.45$).

Study III

To date, 76 patients have been included in this randomized controlled study. Inclusion is still ongoing, why data are still to be analyzed.

Study IV

Four hundred and thirty community-dwelling primary care patients were included. A battery of neuropsychological tests was used to characterize patients with mild cognitive impairment (MCI) and further sub-classify these patients in amnestic MCI, non-amnestic MCI, and multiple-domain MCI. All patients were classified as either cognitively intact or as having MCI. Performance-based and self-reported mobility were assessed by habitual gait speed, the Figure-of-8-Walk, the Short Physical Performance Battery, and the Late Life Function and Disability Index. Forty-two percent of the patients had MCI. MCI participants as well as MCI subtypes performed significantly worse in tests of mobility than patients without MCI. Moreover, patients with non-amnestic MCI performed most poorly.

Conclusions

In conclusion, this thesis showed that the included acutely admitted older medical patients (+65 yrs) spent a median of 17 hours per day of their in-hospital time in bed, and their mobility level seemed to depend on their basic mobility. Accelerometers could be used to measure time spent lying, sitting, and standing and/or walking in these patients and a model for progressive sit-to-stand

training was found feasible to be used in the hospital- and home setting, irrespective of cognitive level of the patients. The effect of simple, supervised, cross continuum strength training is still to be analyzed since the study is ongoing. Also, in the older community-dwelling primary care patients assessed performance-based and self-reported mobility was associated with MCI status, with the poorest performance seen among those with non-amnestic MCI.

10. Resumé (Summary in Danish)

Mobilitet blandt akut indlagte og hjemmeboende ældre patienter – fysisk aktivitet under indlæggelse samt simpel styrketræning

Ældre medicinske patienter (≥ 65 år) udgør mere end halvdelen af de patienter, der behandles på medicinske afdelinger i Danmark, og et lavt aktivitetsniveau er almindeligt under indlæggelse og forbundet med uønskede hændelser. Indlagte ældre fremstår desuden med lav muskelstyrke og dårlig funktionsevne og er i risiko for at miste uafhængighed som følge af deres indlæggelse - patienter med kognitive problemer synes særligt sårbare. Kun få studier har målt aktivitetsniveau og basismobilitet løbende under indlæggelse blandt ældre og få undersøgelser har undersøgt gennemførlighed og effekt af styrketræning gennemført på tværs af sektorer. Derfor var formålene med studierne i denne afhandling, at måle 24-timers aktivitetsniveau og basismobilitet løbende under indlæggelse blandt akut indlagt ældre medicinske patienter og validere de anvendte aktivitetsmålere (Studie I), at teste brugbarheden af en model for progressiv rejse-sætte-sig træning under indlæggelse og i eget hjem efter udskrivelse (Studie II) samt effekten af simpel, superviseret, tværsektoriel styrketræning blandt akut indlagte ældre medicinske patienter (Studie III), og at beskrive sammenhængen mellem mobilitet og mild kognitiv svækkelse blandt hjemmeboende ældre patienter (Studie IV).

Studie I

Treogfyrre ældre medicinske patienter (≥ 65 år) blev inkluderet. Kognition blev vurderet ved indlæggelse via Mini Mental State Examination (MMSE), og 24-timers aktivitetsniveau blev målt under hele indlæggelsen ved hjælp af to trådløse aktivitetsmålere. En algoritme til identifikation af tid brugt henholdsvis liggende, siddende og stående/gående målt med aktivitetsmålerne, blev krydsvalideret på seks ældre medicinske patienter. Cumulated Ambulation Score blev anvendt til at vurdere basismobilitet hver dag under hele indlæggelsen. Patienterne blev mål i gennemsnitligt 4,4 dage og dagligt lå de 17 timer i sengen, sad 5,1 timer, og stod/gik 1,1 time. Patienterne var signifikant mere aktive på dage, hvor de var uafhængige i basismobilitet end på dage med en grad af afhængighed ($p < 0{,}001$). Patienter med en MMSE score >24 stod/gik signifikant flere timer om dagen, end patienter med en score på <24 ($p = 0{,}02$). Algoritmen kunne klassificere tid brugt liggende, siddende og stående/gående med en fejlprocent på 4,7-10,4.

Studie II

Fireogtyve ældre medicinske patienter blev inkluderet. Kognition blev vurderet ved indlæggelse via Short Orientation-Memory-Concentration test. En progressionsmodel for rejse-sætte-sig som styrketræning (STAND) blev udviklet. Modellen blev anset for brugbar, hvis 75 % af patienterne kunne lave 8-12 gentagelser til udtrætning på hospitalet og i eget hjem efter udskrivelse på et givent niveau af modellen, hvis der ikke sås gulv- eller lofteffekt, og hvis ingen uønskede hændelser blev observeret. Smerte blev vurderet før, under og efter udførelse af øvelsen. Treogtyve patienter blev testet på hospitalet, og 19 af disse blev også testet i eget hjem. Tyve patienter (83 %) var i stand til at udføre øvelsen efter STAND-modellen på hospitalet, og 15 patienter (79 %) i eget hjem, der sås ikke loft- eller gulveffekt, og ingen patienter rapporterede om smerter under eller efter udførelse af øvelsen. Således blev STAND anset for brugbar. Desuden var det gennemførte niveau af STAND uafhængigt af den enkeltes kognitive niveau ($P \geq 0.45$).

Studie III

Til dato er 76 patienter blevet inkluderet i dette randomiserede, kontrollerede studie. Da studiet er igangværende, er data endnu ikke blevet analyseret.

Studie IV

Fire hundrede og tredive hjemmeboende patienter blev inkluderet. Et batteri af neuropsykologiske tests blev anvendt til at karakterisere patienter med mild kognitiv svækkelse (MCI), og yderligere sub-klassificere disse patienter i amnestisk MCI, ikke-amnestisk MCI og flerdomæne MCI. Alle patienter blev klassificeret som enten kognitivt intakte eller som havende MCI. Funktionsbaseret og selvrapporteret mobilitet blev vurderet ved habituel ganghastighed, Figure-of-8-Walk, Short Physical Performance Battery og Late Life Function and Disability Index. Toogfyrre procent af patienterne havde MCI. Patienter med MCI og sub-typer af MCI havde signifikant dårligere mobilitet end patienter uden MCI. Patienter med ikke-amnestisk MCI havde dårligst mobilitet.

Konklusion

Denne afhandling har vist, at de inkluderede akut indlagte ældre medicinske patienter (+65 år) brugte 17 timer om dagen i sengen under indlæggelse, og at deres aktivitetsniveau syntes at afhænge af deres basismobilitet. Aktivitetsmålere kunne anvendes til at måle tid brugt liggende, siddende, stående/gående blandt disse patienter, og en model for rejse-sætte-sig træning blev fundet anvendelig på hospitalet så vel som i patienternes eget hjem, uanset kognitivt niveau. Effekten af simpel, superviseret, tværsektoriel styrketræning kendes endnu ikke, da studiet er igangværende.

Blandt hjemmeboende ældre var funktionsbaseret og selvrapporteret mobilitet associeret med mildt kognitivt besvær, og patienter med non-amnestisk mildt kognitivt besvær klarede sig dårligst.

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PAPERS
AND
MANUSCRIPTS

Paper I

Twenty-Four-Hour Mobility During Acute Hospitalization in Older Medical Patients

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Twenty-Four-Hour Mobility During Acute Hospitalization in Older Medical Patients

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Background. Inactivity during hospitalization in older medical patients may lead to functional decline. This study quantified 24-hour mobility, validated the accelerometers used, and assessed the daily level of basic mobility in acutely admitted older medical patients during their hospitalization.

Methods. This is a prospective cohort study in older medical patients able to walk independently (ambulatory patients) and those not able to walk independently (nonambulatory patients) on admission. The 24-hour mobility level during hospitalization was assessed by measuring the time in lying, sitting, and standing and/or walking, by two accelerometers. Basic mobility was quantified within 48 hours of admission and repeated daily throughout hospitalization.

Results. Forty-three ambulatory patients and six nonambulatory patients were included. The ambulatory patients tended to be hospitalized for fewer days than the nonambulatory patients (7 vs 16, p = .13). The ambulatory patients were lying median 17 hours, (interquartile range [IQR]: 14.4–19.1), sitting 5.1 hours (IQR: 2.9–7.1), and standing and/or walking 1.1 hours (IQR: 0.6–1.7) per day. On days with independency in basic mobility, the ambulatory patients were lying 4.1 hours less compared with days with dependency in basic mobility ($p < .0001$), sitting 2.4 hours more ($p = .0004$), and standing 0.9 hours more ($p < .0001$). The algorithm identification for lying, sitting, and standing and/or walking of the accelerometers, corresponded by 89%–100% with positions performed by older medical patients.

Conclusions. Older acutely hospitalized medical patients with walking ability spent 17 h/d of their in-hospital time in bed, and the level of in-hospital mobility seemed to depend on the patients' level of basic mobility. The accelerometers were valid in assessing mobility in older medical patients.

Key Words: 24-hour mobility—Hospitalization—Older—Basic mobility.

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IN 2009, older medical patients (aged 65 years and older) accounted for 53% of all hospital admissions and 66% of all in-patient days in Danish medical wards (1). The older medical patient was hospitalized for 6.3 days on average (2), which is costly and may lead to a decline in an already low preadmission level of functional performance, due to inactivity during hospitalization (3–5).

Restricted activity and bed rest in healthy older adults have been found to be associated with reduced muscle mass and strength, functional decline, and new disability in activities of daily living (6–11). Moreover, functional decline is common during hospitalization in older adults (3–5,12). This may be caused by inactivity, because the in-hospital frequency of ambulation is low, regardless whether the patients are able to walk independently or not (13,14). Moreover, complete bed-rest episodes are common in hospitalized older adults (3,13–15). Low mobility during hospitalization is associated with new institutionalization, death (3), and declining function in activities of daily living at discharge and at 1-month follow-up (3,5), which induces a risk of staying dependent in activities of daily living (16). Furthermore, the odds of functional decline are higher for low in-hospital mobility compared with high in-hospital mobility (5). Hence, physical inactivity during hospitalization in older medical patients could potentially reduce their level of functional performance.

Previous studies have assessed mobility levels of medical patients during hospitalization by accelerometry (17), step counts (14), nurse reports (3), direct observation (13), and interviews (5). Similarly, functional level before, during,

and after hospitalization has been assessed subjectively by self-report or care-giver observations (3,4,12,17). To our knowledge, no previous study has combined assessment of 24-hour mobility level by accelerometry and objective daily assessments of basic mobility during hospitalization in acutely hospitalized older medical patients. Basic mobility refers to the ability to get in and out of bed, stand up from a chair, and walk and may well be a core measure of both functional ability and risk of hospital-associated disability (18,19).

The primary aim of the study was to quantify 24-hour mobility during hospitalization in a group of acutely admitted older medical patients, who were able to walk independently preadmission and to assess their daily level of basic mobility. The secondary aim of the study was to develop and validate an algorithm to quantify in-hospital mobility using accelerometers.

Methods

Study Design

The study was a prospective cohort study, conducted from December 2010 to June 2011 at Copenhagen University Hospital, Hvidovre, Denmark. During hospitalization, 24-hour mobility was measured in all patients who were able to walk without personal assistance on admission and compared with a group of patients who were not able to walk on admission. All patients gave written informed consent before taking part in the study, and the local ethics committee approved the study (06072010-1631).

Participants

Older medical patients (aged 65 years and older) who were acutely admitted from their own home to the medical services of the hospital, via the acute medical admission ward, who were able to walk on admission, and who had at least one comorbidity, were included consecutively on weekdays. A maximum of two patients were included on a daily basis, due to time-wise and accelerometer limitations. If more than two patients met the abovementioned inclusion criteria, the patients to be included were randomly selected. The exclusion criteria were as follows: not able to cooperate in the measurements, not able to give informed consent to participate, isolation-room stay, chronic obstructive pulmonary disease (COPD) patients participating in a COPD rehabilitation program, terminal illness, inability to walk with or without a walking aid, and unable to speak Danish. Additionally, patients with an expected hospitalization of 2 days or less, or transferred to the intensive care unit, were excluded. Six older medical patients not able to walk on admission were included as an immobility reference. The inclusion and exclusion criteria for these patients were the same, except for the inability to walk independently on admission.

Procedures

Descriptive data.—Medical records were extracted for demographic data, length of hospital stay, comorbidity, admission diagnosis, discharge destination, and readmissions. The patients underwent a structured baseline interview during the initial 48 hours of the hospital stay, to collect information about use of walking aid, and the self-reported New Mobility Score (NMS). The interview and the collection of data throughout the study were conducted by the first and second author. NMS was used to assess functional independency (20) in retrospect 2 weeks before admission and in retrospect over the day of admission, respectively. The NMS assesses the ability to perform indoor walking, outdoor walking, and shopping and provides a score between 0 and 3 (0 = unable, 1 = with personal assistance, 2 = with an aid, and 3 = with no difficulty and no aid) for each function, resulting in a total score from 0 (no walking ability at all) to 9 (fully independent; 20). A NMS of 0–5 was used to reflect poor functional independency and a score of 6–9 to reflect good functional independency (21). The Charlson Index was used as a measure of comorbid conditions on admission (22). The Katz Index of Activities of Daily Living (KATZ) was used to assess the ability to perform activities of daily living on admission (23). The Mini-Mental State Examination (MMSE) was used to assess cognitive function on admission (24). The MMSE consists of 13 items with a total score of 0–30. Patients who scored less than 24 were considered cognitively impaired (24). On admission, the patients were asked if they felt pain and localization of the pain. Pain was scored on a 5-point Verbal Ranking scale, where 0 = no pain, 1 = light pain, 2 = moderate pain, 3 = severe pain, and 4 = intolerable pain (25).

Mobility data

Accelerometers.—The mobility level during hospitalization was assessed by accelerometers, 24 hours a day, from within 48 hours of admission to discharge. For long admissions (>10 days), recordings were stopped after 10 days. Two wireless monitors (Augmentative Inc. Pittsburgh, PA) were attached 15 cm above the patella (Xthigh) and 15 cm above the ankle joint (Xankle), respectively, anteriorly on the patient's right leg. The monitors can store data for 48 hours. Every day or every second day, the patients had the monitors replaced and their skin examined for irritation. In the data analysis, we considered a day to be from 12 AM until 12 AM, to avoid half-day measurements, as the accelerometers were normally attached in the morning. When studying the distributions of sitting, lying, and standing and/or walking during a day, only patient-days with more than 18 hours of measuring were included, to avoid skewed days in the analysis. The monitors measure horizontal position (X), vertical position (Y), and depth (Z) with respect

to gravity and were programmed to sample every second. The acceleration output for each axis due to gravity was (for the x-axis): Ax = (VOUTX − VOFF)/*S*, where VOUTX is the voltage output for the x-axis, VOFF is the offset voltage, and *S* the sensitivity of the accelerometer. *S* for the accelerometers used was 16.176 mg (26). The position of the accelerometer was calculated based on measurements from two axes by Angle = tan − 1(AX/AZ). Using these angles, we developed the following algorithm identification of lying, sitting, and standing and/or walking based on pilot data.

If $225 < X_{thigh} \leq 315$, the patient was categorized as standing; if $170 < X_{thigh} \leq 210$ or $X_{thigh} \leq 10$ or $X_{thigh} > 330$ and $210 < X_{ankle} \leq 330$ and if $210 < X_{thigh} \leq 225$ or $315 < X_{thigh} \leq 330$, the patient was categorized as sitting; and if $170 < X_{thigh} \leq 210$ or $X_{thigh} \leq 10$ or $X_{thigh} > 330$ and $X_{ankle} \leq 210$ or $X_{ankle} > 330$ and if $0 < X_{thigh} \leq 170$, the patient was categorized as lying.

To cross-validate this algorithm, we tested the accelerometers in six older medical patients, who were not included in the study. The patients wore the accelerometers under supervision, and following a schedule with predefined behaviors (henceforth, real positions). The real positions included lying in bed, transfers, sitting, standing, and walking. The positions were maintained for 1 minute, except for the walking position, which was maintained for 3 minutes. The comparison between real positions and the algorithm is presented in Table 1. The levels of correspondence for lying, sitting, and standing and/or walking were 90.8%–100%, 95.3%–98.6%, and 89.6%–96.5%, respectively. The cutoff values for lying, sitting, and standing and/or walking corresponded well with the real positions performed.

Table 1. Relationship Between Dual-Accelerometry Algorithm-Derived Positions and Observed Actual Positions

	Algorithm Position			
Real Position	Seconds measured	Lying (%)	Sitting (%)	Standing (%)
Lying in bed, elevated headrest	360	100	0	0
Lying on back in bed, legs straight	366	99.73	0.27	0
Lying on back in bed, legs bend	360	99.72	0.28	0
Lying on right side, legs bend	360	99.72	0.28	0
Lying on right side, legs straight	302	100	0	0
Lying on left side, legs bend	359	90.81	8.36	0.84
Lying on left side, legs straight	323	98.14	1.55	0.31
Transfer from lying to sitting	357	10.92	86.55	2.52
Sitting on bedside	360	0	98.61	1.39
Transfer from bed to chair	360	2.22	73.06	24.7
Sitting in chair	360	1.11	95.28	3.61
Standing	366	0	10.38	89.62
Walking	826	0.85	2.66	96.49

Note: Accelerometer data from six older medical patients, who were asked to perform different positions (*real position*) for 1 min each (the walking position was performed for 3 min). The *real position* data are compared with the algorithm positions of lying, sitting, and standing and/or walking. The table shows how the algorithm would categorize the different *real positions*.

Cumulated Ambulation Score (CAS)

The Cumulated Ambulation Score (CAS) (27) was obtained within 48 hours of admission and repeated daily throughout hospitalization. It was used as an objective measure of basic mobility. It quantifies the patients' independency in three basic activities (getting in and out of bed, sit to stand from a chair, and walking). Each activity is scored on a 3-point ordinal scale from 0 to 2 (0 = unable, 1 = with guidance/support, and 2 = independently), resulting in a total CAS score between 0 and 6. The CAS has been found to have high intertester reliability and to be a valid predictor of length of hospitalization, time-to-discharge status, 30-day mortality, and postoperative medical complications in older patients with hip fracture (27,28).

Statistical Analysis

Descriptive data are given in medians with interquartile ranges (IQRs) or percentages, depending on variable type. Comparisons between the two groups of patients were analyzed with the χ^2 test for categorical variables, and the Kruskal–Wallis test for continuous variables. The NMS before admission and on admission was compared with a Wilcoxon test. Hours per day spent lying, sitting, and standing and/or walking are presented as medians with IQRs and as 5th and 95th percentiles. A linear regression was used to compare hours spent lying, sitting, and standing and/or walking between days with an independent CAS score (CAS = 6), and a dependent CAS score (0–5). This analysis was also adjusted for patients' individual levels of mobility. Secondary exploratory associations of time spent lying, sitting, and standing and/or walking with potential explanatory variables were analyzed with the Kruskal–Wallis test. All statistical tests were performed using the SAS version 9.2; p values ≤ .05 were considered statistically significant.

Results

Sixty-eight older medical patients met the inclusion criteria. Of those, 49 agreed to wear accelerometers during their hospital stay. Forty-three patients were able to walk independently (henceforth, ambulatory patients), and six patients were unable to walk independently (henceforth, nonambulatory patients). One patient was excluded due to lack of accelerometer data, one had a 3-day pause wearing accelerometers due to an episode of acute psychosis, and two wanted the accelerometers removed after 3 and 4 days, respectively. Data from the latter three patients were included in the analysis.

Descriptive Data

The ambulatory patients had a nonsignificant tendency of being hospitalized for fewer days than the nonambulatory patients (7 vs 16, $p = .13$; Table 2). The ambulatory patients had significantly higher NMS (5 vs 0, $p < .001$),

Table 2. Comparison of Baseline Characteristics of Ambulatory and Nonambulatory Patients

	N	Ambulatory Patients (*N* = 42)	Nonambulatory Patients (*N* = 6)	*p* Value
Sex; number (%)	48			
Men		23 (55%)	2 (33%)	.41*
Women		19 (45%)	4 (67%)	
Age; median (interquartile range; IQR)	48	84.7 (78.6; 87.2)	82.8 (79.9; 88.0)	.71**
Days in hospital; median (IQR)	48	7.0 (5.0; 11.0)	16.0 (6.0; 29.0)	.13**
New Mobility Score (NMS); median (IQR)				
Fourteen days prior to admission	48	6.0 (5.0; 9.0)	1.5 (0; 9.0)	.10**
Admission	47	5.0 (3.0; 6.0)	0 (0; 1.0)	<.001**
Charlton Index on admission; number (%)	48			
0		26 (62%)	3 (50%)	.58*
1		12 (28%)	2 (33%)	
2		2 (5%)	1 (17%)	
3		2 (5%)	0 (0%)	
Katz Index of Independency in Activities of Daily Living; median (IQR)	44	6.0 (5.0; 6.0)	1.0 (1.0; 1.0)	<.001**
Cumulated Ambulation Score (CAS) baseline; median (IQR)	48	6.0 (6.0; 6.0)	1.5 (0; 3.0)	<.001**
Out of bed		2.0 (2.0;2.0)	1.0 (0;1.0)	<.001**
Sit to stand		2.0 (2.0;2.0)	0.5 (0;1.0)	<.001**
Walking		2.0 (2.0;2.0)	0 (0;1.0)	<.001**
Mini-Mental State Examination (MMSE) test on admission; median (IQR)	39	26 (22;28)		
Pain measured by the Verbal Ranking scale				
Yes	37	15 (39.5%)	NA	

Notes: Used statistics: *Fisher's exact test; **Kruskal–Wallis test. Significant values are given for differences between the two groups of patients.

KATZ score (6 vs 1, $p < .001$), and CAS score on admission (6 vs 1.5, $p < .001$), compared with the nonambulatory patients. The average CAS score during hospitalization was 5.5 for the ambulatory patients and 1.6 for the nonambulatory patients. The ambulatory patients had a significantly higher NMS 2 weeks before hospital admission compared with the day of admission (6 vs 5, $p = .001$).

Mobility Data

The cumulated in-hospital time was 352 days. The patients wore the accelerometers 57% of the time, with a minimum of 11% and a maximum of 99%; the patients wore the accelerometers 4.4 days on average. The ambulatory patients were lying in bed less hours per day than the nonambulatory patients, 17.0 hours (IQR: 14.4–19.1) versus 22.6 hours (IQR: 22.3–22.8; $p = .0002$), sitting more hours, 5.1 hours (IQR: 2.9–7.1) versus 1.0 hours (IQR: 0.6–1.4; $p = .0006$), and standing and/or walking for more hours per day, 1.1 hours (IQR: 0.6–1.7) versus 0.2 hours (IQR: 0.03–0.4; $p = .0008$; Figure 1A).

In the ambulatory patients, the CAS was scored for a total of 121 days; 33 days with a score between 0 and 5, corresponding to some level of dependency, and 88 days with score of 6, corresponding to being independent in basic mobility. On days with a CAS score of 6, the patients were lying 4.1 hours less compared with days with a CAS score of 0–5 (15.4 vs 19.5 hours; $p < .0001$), they were sitting 2.4 hours more (6.0 vs 3.6 hours; $p = .0004$) and standing and/or walking 0.9 hours more (1.6 vs 0.7 hours; $p < .0001$; Figure 1B).

When adjusting for patients and examining individual changes, the differences in time spent lying, sitting, and standing and/or walking were smaller between days with a CAS score of 6 and days with a CAS score of 0–5. On days with a CAS score of 6, a patient would tend to spend 1.5 hours less lying ($p = .09$) and spend 0.5 hours more sitting ($p = .05$) compared with the same patient on a day with a score of 0–5.

Table 3 shows the association of mobility level with explanatory variables in ambulatory patients. The in-hospital mobility level was independent of preadmission and admission NMS. Patients with a preadmission NMS of 0–5 did not differ in in-hospital mobility level, compared with patients with a score of 6–9 ($p = .48$) nor did patients with an admission NMS score of 0–5 differ in in-hospital mobility level compared with patients with a score of 6–9 ($p = .30$). The mobility level was independent of comorbidities and pain. Patients with a MMSE score of more than 24 were standing and/or walking significantly more hours during a day than patients scoring less than 24 ($p = .02$).

Discussion

This study showed that acutely admitted older medical patients, who were able to walk on admission, on average spent 17 h/d of their hospital stay in bed, 5.1 h/d sitting, and 1.1 h/d standing and/or walking. Two accelerometers used simultaneously were found valid in discriminating between lying, sitting, and standing and/or walking in older medical patients and in discriminating between in-hospital activity and in-hospital inactivity.

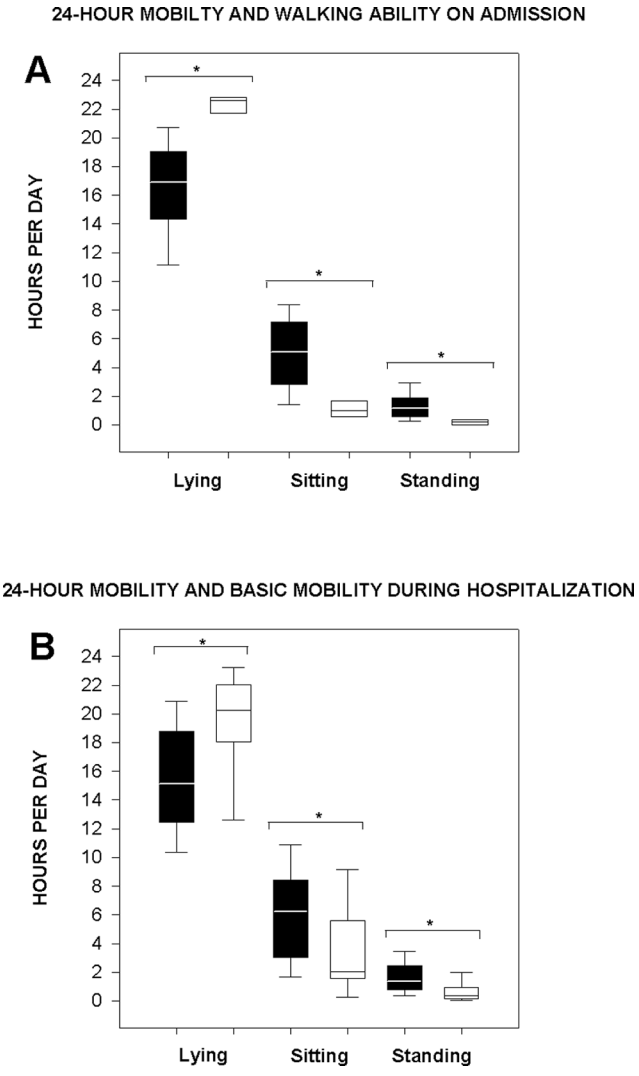

Figure 1. **(A)** Hours per day spent lying, sitting, and standing and/or walking during hospitalization. Black bars = ambulatory patients, open bars = nonambulatory patients. Data are given in median (IQR) and 5th and 95th percentiles. **(B)** CAS score compared with hours spent lying, sitting, and standing and/or walking for ambulatory patients ($N = 42$). Black bars = days with a CAS score of 6, open bars = days with a CAS score of 0–5. Data are given in median (IQR) and 5th and 95th percentiles. *—denotes statistically significant between-group (A) or between-CAS category differences (B).

The mentioned levels of in-hospital mobility correspond with levels seen in previous studies. Brown and colleagues (15) investigated the in-hospital mobility in a group of older medical patients with an average hospital stay of 5.3 days and found the patients to be lying 73.7%, sitting 22.6%, and standing 3.7% of the time. Likewise, Callen and colleagues (13) monitored older medical patients for an average of 56.4 hours and found the patients to be lying 83.3%, sitting 12.9%, and standing or walking 3.8% of the time. In the present study, the time spent lying, sitting, and standing and/or walking differed, depending on the overall level of basic mobility. Patients being independent in basic mobility spent less time lying and more time sitting and standing and/or walking, than patients who were dependent to some degree in basic mobility. This stresses the relevance of focusing on enabling patients to get out of bed and up from a chair in addition to walking independently. Indeed, Callen and colleagues (13) found that the frequency of hallway ambulation among older patients was equally low for patients who were able and not able to walk independently.

Factors other than dependency in basic mobility may cause patients to be inactive during hospitalization. One factor might be the presence of acute illness, which may affect physical performance. Also, patients presenting generalized inflammation may be weaker and less fatigue resistant—despite no difference in estimated muscle mass—than patients without inflammation (29). Moreover, we found neither the patients' functional independency on admission (NMS) nor pain to correlate with the level of in-hospital mobility, suggesting that factors other than those regarding the physical function of a patient may influence a patient's mobility level during hospitalization. These factors may not only be structural barriers, but also be conflicting views on mobility and lack of mobility between health care professionals and patients (30). The patients in the present study needed assistance to get out of bed more often than to rise from a chair or walk, calling for increased attention to this point from the ward personnel.

In the present study, the patients had a decline in functional independency from 2 weeks before admission to admission, measured by the NMS. Inactivity during hospitalization might deteriorate a declining functional level even further, as the odds of functional decline is higher for low in-hospital mobility compared with high in-hospital mobility (5). Considering the effects of low mobility during hospitalization, it is of great importance to work on solutions for a physically active hospitalization and for preventing in-hospital functional decline. Focus should be on obtaining a general awareness about the importance of being physically active during hospitalization and on ensuring availability of walking aids, allowing staff and relatives to ambulate patients. In this study, the patients' functional independency on admission did not correlate with the in-hospital mobility level, suggesting that supervised activity or training might be possible for the patients to carry out and might be necessary.

Strengths and Limitations

The strengths of the study include using two accelerometers combined with a daily score of basic mobility. We found the accelerometers valid in assessing time spent lying, sitting, and standing and/or walking, and in discriminating between in-hospital activity and in-hospital inactivity. The two accelerometer approach has previously been used to quantify mobility in older individuals (15,31) and has been found to provide valid data in hospitalized older patients using an algorithm based on a one-axis solution with measurements every 20 seconds (15). Our study adds to this validation,

Table 3. Association of Mobility Level With Possible Explanatory Variables

		Lying (h/d)		Sitting (h/d)		Standing (h/d)	
	N	Median (IQR)	*p* Value	Median (IQR)	*p* Value	Median (IQR)	*p* Value
New Mobility Score (NMS); preadmission	41						
0–5		16.7 (14.8;19.0)		5.1 (3.9;7.3)		1.2 (0.7;2.1)	
6–9		17.9 (14.4;19.2)	.96	4.1 (2.8;7.1)	.49	0.9 (0.6;1.7)	.77
NMS; admission	40						
0–5		17.4 (15.0;18.9)		5.1 (3.8;7.1)		0.9 (0.5;1.7)	
6–9		15.4 (11.3;19)	.71	4.8 (2.5;7.4)	.76	1.5 (0.8;2.2)	.31
Mini-Mental State Examination (MMSE)	38						
0–24		18.1 (14.4;18.9)		5.1 (2.9;8.1)		0.6 (0.3;1.5)	
>24		15.9 (14.3;18.7)	.43	5.1 (3.3;7.1)	.75	1.5 (0.8;2.2)	.02*
Charlson Index	41						
0		17.9 (14.9;19.2)		4.0 (2.5;7.1)		1.0 (0.6;2.2)	
1+		15.6 (13.5;18.3)	.18	6.1 (3.8;7.3)	.13	1.4 (0.7;1.7)	.56
Pain	36						
No		15.4 (14.3;18.9)		7.0 (2.9;7.4)		1.5 (0.6;2.2)	
Yes		18.1 (15.9;19.1)	.14	4.0 (3.1;5.1)	.07	0.8 (0.6;1.4)	.4

Notes: Mobility patterns compared with the New Mobility Score, the Mini-Mental State Examination, the Charlson Index of Comorbidities, and pain. Data are noted as median (IQR). *significant values at the 5% level.

using an algorithm based on a two-axis solution with measurements every second. We included data until the 10th day to assure that data from each patient was equally weighted and to focus on a period corresponding to an average admission period. Moreover, 10 days were considered an adequate period of time to describe a patient's mobility habits, as 7 days has been shown to provide a good measure of usual physical activity in community-dwelling older people (32).

Our study had some limitations. As in previous work using Augmentec accelerometers, we were unable to differentiate standing and walking (15). However, to ensure accuracy of our cutoff limits between the different positions, we tested the cutoff values of our algorithm against real positions, performed by six older medical patients and found a good level of correspondence. We were not able to measure all patients throughout hospitalization. The reasons for lack of measurements were of a structural character, including postponement of a planned discharge after removal of accelerometers, removal of accelerometers by patients or staff, or patients going through examinations not allowing accelerometers to be worn. We measured patients as many days as logistically possible, and in the analysis of the data, we only included patient-days with more than 18 hours of measuring to assure both night and day measurements and to avoid skewed days in the analysis.

Conclusions

This study showed that older acutely hospitalized medical patients spent 17 h/d of their in-hospital time in bed. Accelerometers, used in measuring the level of in-hospital mobility, were found valid in assessing the time spent lying, sitting, and standing and/or walking in these patients. The level of in-hospital mobility seemed to depend on the patients' level of basic mobility, that is, their ability to independently get in and out of bed, rise from a chair, and walk.

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Paper II

Feasibility of progressive sit-to-stand training among older hospitalized patients

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Feasibility of progressive sit-to-stand training among older hospitalized patients

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ABSTRACT

Background. In older patients, hospitalization is associated with a decline in functional performance and loss of muscle strength. Loss of muscle strength and functional performance can be prevented by systematic strength training, but details are lacking regarding the optimal exercise program and dose for older patients. Therefore, our aim was to test the feasibility of a progression model for loaded sit-to-stand training among older hospitalized patients.

Methods. This is a prospective cohort study conducted as a feasibility study prior to a full-scale trial. We included twenty-four older patients (≥65 yrs) acutely admitted from their own home to the medical services of the hospital. We developed an 8-level progression model for loaded sit-to-stands, which we named STAND. We used STAND as a model to describe how to perform the sit-to-stand exercise as a strength training exercise aimed at reaching a relative load of 8–12 repetitions maximum (RM) for 8–12 repetitions. Weight could be added by the use of a weight vest when needed. The ability of the patients to reach the intended relative load (8–12 RM), while performing sit-to-stands following the STAND model, was tested once during hospitalization and once following discharge in their own homes. A structured interview including assessment of possible modifiers (cognitive status by the Short Orientation Memory test and mobility by the De Morton Mobility Index) was administered both on admission to the hospital and in the home setting. The STAND model was considered feasible if: (1) 75% of the assessed patients could perform the exercise at a given level of the model reaching 8–12 repetitions at a relative load of 8–12 RM for one set of exercise in the hospital and two sets of exercise at home; (2) no ceiling or floor effect was seen; (3) no indication of adverse events were observed.

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The outcomes assessed were: level of STAND attained, the number of sets performed, perceived exertion (the Borg scale), and pain (the Verbal Ranking Scale).
Results. Twenty-four patients consented to participate. Twenty-three of the patients were tested in the hospital and 19 patients were also tested in their home. All three criteria for feasibility were met: (1) in the hospital, 83% could perform the exercise at a given level of STAND, reaching 8–12 repetitions at 8–12 RM for one set, and 79% could do so for two sets in the home setting; (2) for all assessed patients, a possibility of progression or regression was possible—no ceiling or floor effect was observed; (3) no indication of adverse events (pain) was observed. Also, those that scored higher on the De Morton Mobility Index performed the exercise at higher levels of STAND, whereas performance was independent of cognitive status.
Conclusions. We found a simple progression model for loaded sit-to-stands (STAND) feasible in acutely admitted older medical patients (≥65 yrs), based on our pre-specified criteria for feasibility.

Subjects Clinical Trials, Geriatrics, Kinesiology
Keywords Older medical patients, Strength training, Cross continuum, Supervision, Physical therapy

INTRODUCTION

In older hospitalized medical patients, self-reported decline in functional skills is common before and during hospitalization (*Covinsky et al., 2003*; *Brown, Friedkin & Inouye, 2004*; *Boyd et al., 2008*; *Mudge, O'Rourke & Denaro, 2010*; *Oakland & Farber, 2014*; *Zisberg et al., 2015*) and associated with low in-hospital mobility (*Brown, Friedkin & Inouye, 2004*; *Zisberg et al., 2015*); 30–35% experience a decline in the ability to perform Activities of Daily Living (ADL) from admission to discharge (*Covinsky et al., 2003*; *Boyd et al., 2008*) and barely one third of these patients return to their preadmission level within the first year after discharge (*Boyd et al., 2008*).

In healthy older adults, even a few days of experimental immobilization or periods of bed rest can reduce muscle strength and functional performance (*Kortebein et al., 2007*; *Hvid et al., 2010*; *Hvid et al., 2014*; *Coker et al., 2014*). Also, older adults are more sensitive to bed rest inactivity and have an impaired ability to fully recover compared to younger adults (*Kortebein, 2009*; *Hvid et al., 2010*; *Hvid et al., 2014*). Lower activity levels are common among hospitalized older adults (*Pedersen et al., 2012*; *Villumsen et al., 2014*), and are linked to a decline in functional performance and associated with new institutionalization and death (*Brown, Friedkin & Inouye, 2004*; *Zisberg et al., 2015*). Moreover, hospitalization is associated with a subsequent loss of muscle strength (*Alley et al., 2010*), putting hospitalized older adults at a higher risk of losing independence as a consequence of their hospitalization. Maintaining independence is considered the most important health outcome by many older adults (*Fried et al., 2011*). Therefore, preventing inactivity and loss of muscle strength and functional performance during hospitalization may well be a way of preventing loss of independence.

According to recent systematic reviews, loss of muscle strength and functional performance can be prevented by systematic strength training in both healthy and ill older adults (*De Morton, Keating & Jeffs, 2007*; *Kraemer & Ratamess, 2004*; *Liu & Latham, 2009*; *Koopman & van Loon, 2009*; *Stewart, Saunders & Greig, 2014*). Also, strength training initiated during hospitalization can prevent decline in strength and functional performance associated with hospitalization (*Sullivan et al., 2001*; *Suetta et al., 2007*). In addition, beneficial effects of strength training on functional performance are reported among newly discharged older adults and among frail community-dwelling older adults (*Chandler et al., 1998*; *Courtney et al., 2012*). In general, exercise programmes for older hospitalized or community-dwelling adults consist of a range of exercises (*Chandler et al., 1998*; *Siebens et al., 2000*; *Alexander et al., 2001*; *Bean et al., 2004*; *Brown et al., 2006*; *Nolan & Thomas, 2008*; *Courtney et al., 2012*; *Tibaek et al., 2013*; *Abrahin et al., 2014*). Few studies have examined the effect of a cross-continuum program initiated during hospitalization and continued after discharge (*Siebens et al., 2000*; *Brown et al., 2006*). Moreover, these previous studies have experienced problems with compliance (*Siebens et al., 2000*; *Brown et al., 2006*) necessitating the importance of ongoing supervision from trained staff even within the home setting (*Siebens et al., 2000*; *Brown et al., 2006*; *Wall, Dirks & van Loon, 2013*). Additionally, details are lacking regarding the optimal nature and dose of exercise (*De Morton, Keating & Jeffs, 2007*; *Liu & Latham, 2009*; *Steib, Schoene & Pfeifer, 2010*). It appears, though, that higher intensities are superior to lower intensities in older adults (*Nicola & Catherine, 2011*; *Raymond et al., 2013*; *White et al., 2015*).

The ideal exercise program for a hospitalized patient should be feasible to perform within a busy care setting. It should be relatively simple requiring minimal equipment and also address the impairments (poor limb strength) and functional deficits (poor mobility skills) common to hospitalized patients (*Bodilsen et al., 2013*; *De Buyser et al., 2014*). Therefore, we focused upon repeated sit-to-stand exercises, since it meets all of these criteria. Our aim was to test the feasibility of a model for progressive sit-to-stand training among older hospitalized patients. Specifically, we wanted to investigate if the progression model would enable the patients to reach a strength training intensity of 8–12 repetitions maximum (RM) for 8–12 repetitions during hospitalization and shortly following discharge, with no indications of ceiling or floor effects for loading, no indications of adverse events and with acceptable exercise adherence.

METHODS

Study design

The study is a prospective cohort study conducted as a feasibility study (*Bowen et al., 2009*; *Arain et al., 2010*; *Abbott, 2014*) to indicate the feasibility of a progression model for loaded sit-to-stands when used as a simple strength training exercise. The study was performed from December 2012 to July 2013. Participants were included to test their ability to perform the progressive sit-to-stand exercise once in the hospital and once in their own homes within the first two weeks following discharge. Inclusion took place at Copenhagen University Hospital, Hvidovre, Denmark. The feasibility study was performed prior to

a full-scale randomized controlled trial (ClinicalTrials.gov-identifier: NCT01964482). All participants were informed about the study verbally and in writing before providing written informed consent. The local ethics committee approved the study (H-2-2012-115). The reporting of the study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies (*Von Elm et al., 2014*), and the description of the intervention follows the Template for Intervention Description and Replication (TIDieR) checklist (*Hoffmann et al., 2014*). When we designed the present study, endorsement of registration of all trials was not as prevalent as today, which is why it was not registered. All criteria related to feasibility, however, were pre-specified.

Subjects

Older medical patients (≥65 yrs) acutely admitted from their own home to the medical services of the hospital, via the emergency department, were included by random sampling. The exclusion criteria were: (1) inability to rise from a chair with help; (2) inability to cooperate in measurements; (3) inability to give informed consent to participate; (4) diagnosis of Chronic Obstructive Pulmonary Disease (COPD) and participation in a COPD rehabilitation program; (5) terminal illness or being in cancer treatment; (6) inability to speak or understand Danish; (7) isolation-room stay; (8) transferral to the intensive care unit; (9) an expected hospitalization of one day or less.

Procedures

All assessments were performed by two skilled physiotherapists—one with 15 years of experience (the primary investigator, MMP), and one with two years of experience (HGJ). The same physiotherapist performed all assessments for a given patient. Before initiation of the study, HGJ was trained in all assessments and the progression model and assisted MMP in assessing the first two patients to ensure standardization.

Descriptive data

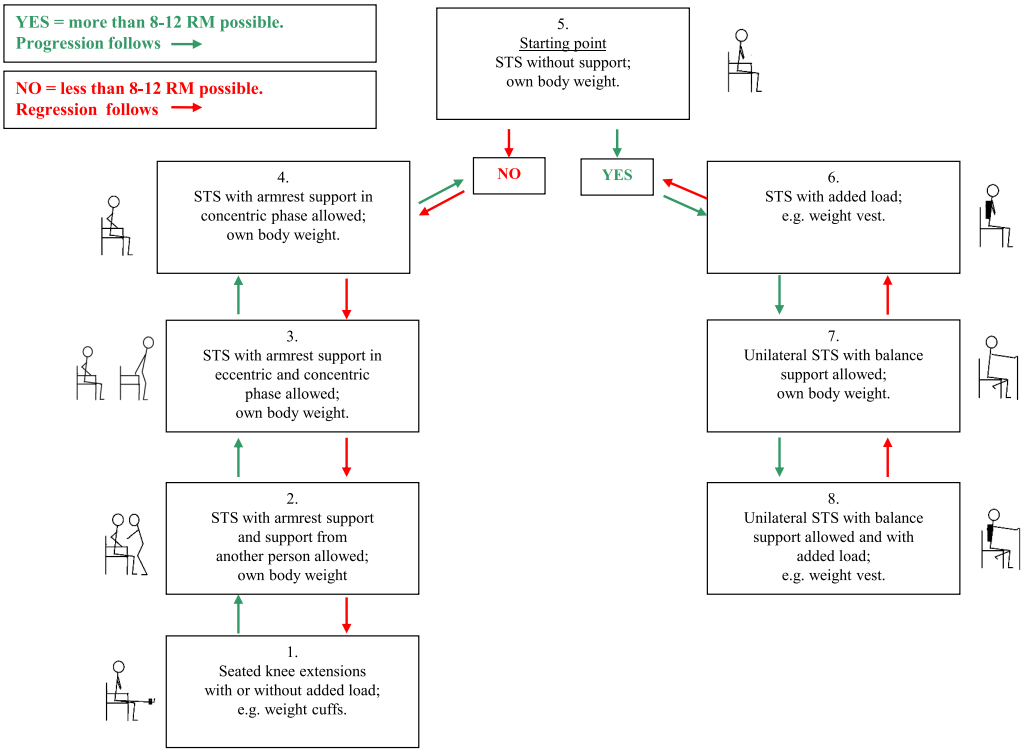
Medical records were extracted for demographic data, co-morbidities, length of hospital stay, admission diagnosis, and discharge destination. The patients underwent a structured baseline interview within the initial 48 h of the hospital stay, to collect information about marital status, residence before hospitalization, recent weight loss, basic mobility, functional independence, physical activity level 2 weeks prior to admission, health status, nutritional status, cognitive status, and mobility: the Cumulated Ambulation Score (CAS) was used as an objective measure of basic mobility. It quantifies the patients' independence in three basic activities: getting in and out of bed, sit-to-stand from a chair, and walking (*Foss, Kristensen & Kehlet, 2006*); the New Mobility Score (NMS) was used to assess functional independence in retrospect 2 weeks before admission and in retrospect over the day of admission, respectively (*Parker & Palmer, 1993*); the level of self-reported physical activity was assessed by a questionnaire modified by Schnohr (*Saltin & Grimby, 1968*; *Schnohr, Scharling & Jensen, 2003*) categorizing physical activity of the patient in level 1: low physical activity, level 2: moderate physical activity, and levels 3 + 4: high physical activity; The EQ-VAS of the EQ-5D was used to assess health status (*Rabin & de Charro, 2001*); and

Nutritional Risk Screening (NRS) was used to screen for nutritional risk (*Kondrup, 2003*). In addition, two possible modifiers were assessed both on admission and in the patients' own homes: (1) the De Morton Mobility Index (DEMMI) (score 0–100) to quantify the patient's mobility level before performing the exercise (*De Morton, Davidson & Keating, 2008*). A level of <62 is below normative values for community-dwelling older adults and thus considered to reflect limited mobility (*Macri et al., 2012*); (2) The Short Orientation-Memory-Concentration test (OMC) to assess cognitive status (*Katzman et al., 1983*). A score of 0 reflects the worst cognitive status and a score of 28 reflects the best cognitive status. A score ≤22 was considered to reflect impaired cognition (*Wade & Vergis, 1999*).

The progression model for loaded sit-to-stands (STAND)

We developed a progression model for loaded sit-to-stands as a strength training exercise and named the model STAND (Fig. 1). STAND was intended to be suitable for older medical patients in the hospital and in their own homes and to ensure training to muscular fatigue in both settings. While developing STAND several meetings were held with physiotherapists from the municipality of Copenhagen to include their ideas on the contents of the different levels of the model. Within 48 h of admission, the patients were contacted at the ward by one of the two physiotherapist to test their ability to perform a sit-to-stand strength training exercise for the lower extremities (acute-phase feasibility). On day one or two after discharge from the hospital, the patients were contacted again by telephone to arrange a re-test of the ability to perform the strength training exercise in their own homes (stable-phase feasibility). The difficulty of the exercise was predefined by STAND ensuring exercise to muscular fatigue in every exercise set (Fig. 1). The easiest level of STAND (level 1) was seated knee-extensions with or without a weight-cuff, which simulates some of the muscle actions required to go from sit-to-stand. Weight cuffs of 0.5 kg, 1 kg, 1.5 kg, 2 kg, 3 kg, 4 kg and 5 kg were used. The most difficult level (level 8) was squat on one leg with added extra weight in the form of a weight vest (Titan Box, 30 kg). The vest had 30 pockets, 15 on the front and 15 on the back, each of which could contain a 1 kg weight—the maximal load of the vest being 30 kg.

The patient was seated on a standard chair with armrests, and a seat height of approximately 45 cm. As a warm-up exercise, the patient was asked to perform five unloaded knee extensions for each limb. The starting point in STAND was level 5 (Fig. 1): sit-to-stand with arms crossed over the chest. From at seated position, the patient was asked to rise to a fully extended position and to sit down in a constant pace. The patient was verbally encouraged to perform as many repetitions as possible maintaining the same pace to ensure training to muscular fatigue (*Tan, 1999*). All exercises were performed at a moderate velocity with both the concentric (raising) and the eccentric (lowering) component being performed over two seconds, separated by a one-second isometric pause after the concentric and eccentric phases, respectively (*Kraemer & Ratamess, 2004*). Both sessions (in-hospital and at home) aimed at three sets of 8–12 repetitions maximum (henceforth: 8–12 RM) corresponding to training at 60–70% of 1 RM (*Tan, 1999*; *Kraemer et al., 2002*; *Kraemer & Ratamess, 2004*). In each set, the aim was to reach fatigue at 8–12



STS: Sit-to-stand; 8-12 RM: 8-12 repetitions maximum (a zone in which muscular fatigue should be reached)

Figure 1 Progression model for loaded sit-to-stand exercise (STAND). bis. Description of model-procedure.

Notes.

Preparation

Seated on a standard chair with armrests, and a seat height of approximately 45 cm, the individual should perform 5 unloaded knee extensions for each limb as a warm-up.

Procedure

- Perform all exercises at a moderate velocity with both the concentric (raising) and the eccentric (lowering) component being performed over 2 s, separated by a 1-second quasi-isometric pause after the concentric and eccentric phases, respectively.
- Perform as many repetitions as possible maintaining the same pace to ensure training to muscular fatigue.
- If muscular fatigue is reached within 8–12 repetitions, stay at the same level.
- If muscular fatigue is reached before 8 repetitions, perform the exercise at a lower level.
- If muscular fatigue is reached after more than 12 repetitions, perform the exercise at a higher level.
- Aim at 3 sets of 8–12 repetitions to muscular fatigue (3 × 8–12 RM).
- Allow minimal extra support after 6 non-compensatory repetitions to attain muscular fatigue—if a proper technique is maintained.
- Allow increased speed in the last two repetitions if necessary to ensure training at the highest possible level.
- Adjust loads/levels on a set-by-set basis.
- Ensure a 1-minute pause between sets.

(Continued on next page)

(Continued...)

Levels—the starting point is level 5:

All levels are started from a seated position.

Level 1: Attach an appropriate weight cuff (≥0.5 kg) around the ankle. Fully extend the knee and bend it reaching 90° flexion.

Level 2: From a seated position, rise to a fully extended position and sit down using the armrests as support and with additional support from the physiotherapist.

Level 3: From a seated position, rise to a fully extended position and sit down using the armrests as support.

Level 4: From a seated position, rise to a fully extended position using the armrests as support. Sit down with the arms crossed over the chest.

Level 5: From a seated position with arm crossed over the chest, rise to a fully extended position and sit down.

Level 6: From a seated position with arm crossed over the chest and wearing a weight vest (1–30 kg), rise to a fully extended position and sit down.

Level 7: From a seated position (hands on chair in front of you for balance support), rise to a fully extended position on one leg and sit down (shift legs after each set, aiming at 3 sets per leg).

Level 8: From a seated position wearing a weight vest (1–30 kg) (hands on chair in front of you for balance support), rise to a fully extended position on one leg and sit down (shift legs after each set, aiming at 3 sets per leg).

RM (*Kraemer & Ratamess, 2004*), and the correct level of STAND was chosen accordingly (Fig. 1). A two-minute pause was held between sets (*Kraemer & Ratamess, 2004*). In order to ensure that an appropriate training load was achieved, a given level of training was accepted if the patient could perform six non-compensatory repetitions and needed extra support performing the last repetitions (e.g., minimal use of armrests) as long as a proper technique could be maintained. Moreover, increased speed in the concentric phase was allowed in the last two repetitions to optimize limb power output, as leg power has been shown to be associated with physical performance in mobility-limited older adults (*Bassey et al., 1992*; *Bean et al., 2002*). The same skilled physiotherapist supervised all exercise sessions and assessed the level of each patient throughout the sets. The duration of each exercise session was 10–15 min.

Outcomes measures

Criteria for feasibility

STAND was considered feasible if three criteria were fulfilled: (1) 75% of the assessed acute-phase patients and stable-phase patients, respectively, could perform the exercise at a given level of the model without session failure. In the hospital, a session failure was defined as inability to perform at least one set of 8–12 RM, and at home a session failure was defined as inability to perform at least two sets of 8–12 RM. One to three sets are recommended for improving muscular strength in older adults (*Kraemer & Ratamess, 2004*) and both one set and multiple sets have been shown to be efficient in improving physical performance and muscle strength in older women (*Abrahin et al., 2014*). Thus, a smaller training volume was accepted in the acute-phase. All causes of session failure were recorded; (2) no clustering of patients at the lowest level (level 1) or the highest level (level 8) was seen—no ceiling or floor effect; (3) no indication of adverse events were observed, e.g., no persistent increase in pain.

Training level and -load

For each set in the two sessions (in-hospital and at home), the level in STAND, the extra load added (kg), and the number of repetitions were noted.

The Borg scale

The Borg Scale was administered immediately after each set of the exercise as a measure of perceived exertion (*Borg, 1970*). In healthy older adults, a Borg score of 14–16 has been shown to correspond to 70–90% of 1 RM (*Row, Knutzen & Skogsberg, 2012*) and the Borg score was used as an indicator of whether the perceived effort corresponded with the RM level.

The Verbal Ranking Scale (VRS)

Before and after assessment of the DEMMI and before, during, and 10 min after the exercise, the patients were asked if they felt pain and wherefrom by the use of the VRS (*Melzack, 1975*). The absence of pain was not a feasibility criterium, but information on pain was collected to gain knowledge about potential adverse events.

Statistical analysis

No formal sample size calculation was performed due to the descriptive character of the study and as no efficacy testing was to be performed (*Arain et al., 2010*; *Abbott, 2014*). However, a sample size of 24 was decided to be sufficient to obtain a proper variability in the functional level of the patients and thereby be able to evaluate the feasibility of the model in older medical patients. The feasibility results are presented as descriptive data given as means with standard deviations, medians with inter-quartile ranges or percentages, depending on variable type. To evaluate if the level of STAND depended on mobility and cognition, linear regression analyses were used to regress the level of STAND on DEMMI and OMC, respectively. Change in performance measures from admission to at home was tested using Wilcoxon Signed Rank test and the paired *t*-test depending on variable type. All data were double entered in the programme 'Epidata Software' (version 3.1) and all data management and analyses were performed using the SAS version 9.3.

RESULTS

Patient characteristics

A total of 248 patients were assessed for eligibility and fulfilled the inclusion criteria. Of these, 200 were excluded based on our exclusion criteria: six were unable to rise from a chair with help; 65 were not able to participate (e.g., due to dementia or confusion); one was participating in a COPD rehabilitation program; 15 were in cancer treatment or terminally ill; four were unable to speak or understand Danish; three were transferred to an isolation room; and 106 were discharged within the first 24 h (Fig. 2). Forty-eight were asked to participate in the study. Of these, 24 patients consented to participate in interviews and tests and 24 declined to participate. The patients were included over a period of 13 weeks with an average inclusion of 1.8 patients per week. One patient dropped out during the initial examination, leaving 23 patients to be tested at the hospital. Two patients did not

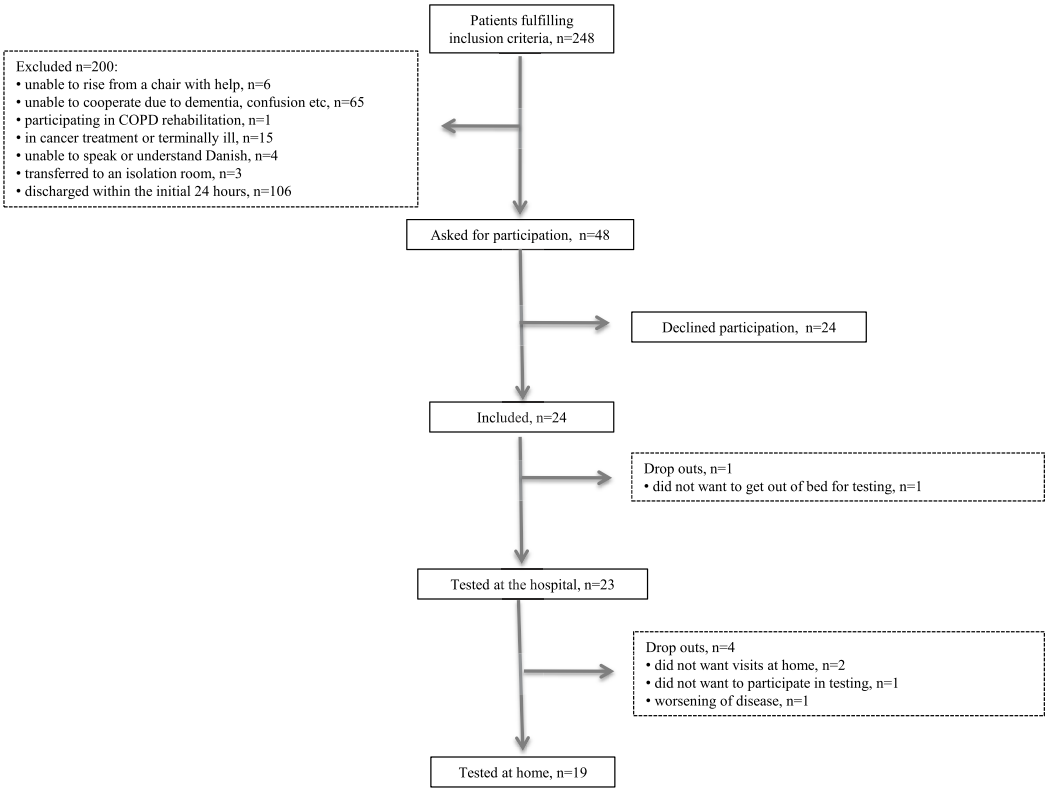


Figure 2 **Flowchart.**

want the following home visit, one patient declined to participate in testing at home, and one patient was unable to participate due to worsening of disease, leaving 19 patients to be tested at home. Thus, a total of 20.8% dropped out of the study. Patient characteristics are presented in Table 1. No patients changed in CAS from admission to follow-up. Also, no significant change was seen in NMS and DEMMI whereas self-rated health improved significantly (Table 2).

Feasibility

Sets and loading

At the hospital, 20 of the 23 patients (83%) were able to perform at least one set of 8–12 RM at a given level of STAND—the remaining three patients stopped after 6–7 repetitions; one due to dyspnea, one due to muscular fatigue, and one due to back pain that was present before performing the exercise. All three patients were subsequently able to perform several sets of 8–12 RM in their own home.

At home, 15 of the 19 patients (79%) were able to perform two sets of 8–12 RM, and 8 of these were able to perform three sets of 8–12 RM. Reasons for not attaining the goal of two sets of 8–12 RM were: one patient could perform seven repetitions in set one and 10 repetitions in set two; one patient stopped after one set due to knee pain—this pain did not persist after ending the exercise; one patient wanted to stop after one set due to a

Table 1 **Patient characteristics on admission.**

	N	
Age; mean (SD)	24	77 ± 7
Gender, female; *n* (%)	24	12 (50%)
Living alone, yes; *n* (%)	24	13 (54%)
Use of gait devices, yes; *n* (%)	24	9 (37.5%)
Reason for admission; *n* (%)	24	
Pneumonia		10 (41.7%)
COPD exacerbation		2 (8.3%)
Dyspnea		1 (4.2%)
Urinary tract infection		3 (12.5%)
Gastroenteritis		1 (4.2%)
Pulmonary embolism		2 (8.3%)
Atrial fibrillation		3 (12.5%)
Anemia		2 (8.3%)
Physical activity level (PA); *n* (%)	23	
Low PA		5 (21.7%)
Moderate PA		5 (21.7%)
High PA		13 (56.6%)
Comorbidities; *n* (IQR)	24	5 (3.5;5.5)
Medications; *n* (IQR)	24	6 (2.5;7.5)
Length of stay; median (IQR)	24	4.5 (3;7)
Follow-up—number of days after discharge; median (IQR)	19	9 (6;13)
Nutritional risk screening	24	
At risk; *n* (%)		19 (79.2%)
OMC; median (IQR)/*n* (%)	24	26 (22;28)
CAS; median (IQR)	24	6 (6;6)
NMS, 14 days prior to admission; median (IQR)	24	9 (5.5;9)
NMS at admission; median (IQR)	24	3 (2;9)
DEMMI; mean (SD)	23	66.1 ± 15.18

Notes.

OMC, The Short Orientation-Memory-Concentration test; CAS, The Cumulated Ambulation Score; NMS, The New Mobility Score; DEMMI, The De Morton Mobility Index.

Table 2 **Performance measures on admission and at home.**

Performance measure	*N*	Admission	*N*	Home-visit	*P*-value
CAS; median (IQR)	24	6 (6;6)	20	6 (6;6)	NA[a]
NMS admission; median (IQR)	24	3 (2;9)	20	6.5 (3;9)	0.13
DEMMI; mean (SD)	23	66.1 (15.18)	19	70.6 (14.7)	0.12
EQ-VAS; mean (SD)	24	56.6 (24.3)	20	67.4 (23.8)	0.01

Notes.

[a] No participants changed in CAS.

sensation of muscular fatigue during the first set; one patient wanted to stop in set two due to a sensation of muscular fatigue.

The 20 patients completing one set at the hospital were distributed in STAND as follows: two seated knee extensions, two sit-to-stand using the arm rests when standing and sitting down, two sit-to-stand using the arm rests when sitting down, six sit-to-stand with the arms crossed over the chest, six sit-to-stand with extra load, one unilateral sit-to-stand, and one unilateral sit-to-stand with extra load. The 15 patients completing two sets at home were distributed in STAND as follows: three sit-to-stand using the arm rests when standing up and sitting down, one sit-to-stand using the arm rests when sitting down, four sit-to-stand with the arms crossed over the chest, four sit-to-stand with extra load, one unilateral sit-to-stand, and two unilateral sit-to-stand with extra load (Table 3). The mean Borg score when performing the highest level possible was 14.2 ($\pm$1.9) on admission and 14.1 ($\pm$1.6) at follow-up.

Indicators of floor/ceiling effect

Two patients were at the lowest level of STAND at the hospital (knee-extensions with three and six kg, respectively). For both patients, further regression was possible by using less weight (they both performed the exercise at level 3 at home). One patient was at the highest level of STAND at the hospital and two were at the highest level at home (unilateral sit-to-stand with six kg and four kg, respectively)—for both patients, further progression was possible by adding more weight.

Pain

Four patients and two patients, respectively, reported an increase in pain after the DEMMI test at the hospital and at home. None of these patients reported any pain before the exercise.

Four patients reported light to moderate pain in the shoulder, leg and chest, respectively, before performing the exercise at the hospital. The pain remained unchanged during and after the exercise for three of the patients and one patient reported no pain after ended exercise. Three patients reported light leg pain during the exercise but no pain before and after the exercise. Four patients reported light to moderate pain in the shoulder, back, leg and head, respectively, before performing the exercise at home. The pain remained unchanged during and after the exercise for three of the patients and one patient reported less pain after ended exercise. Two patients reported light back pain during the exercise but no pain before and after the exercise.

Mobility and cognition

As shown in Fig. 3 those that scored higher on the DEMMI performed the exercise at the most challenging levels of STAND (on admission, $\beta = 0.10$ (CI [0.07–0.13]), $P < 0.0001$; at home, $\beta = 0.07$ (CI [0.03–0.12]), $P = 0.004$), whereas the level of STAND did not depend significantly on OMC (on admission: $0.07(-0.12;0.26)$, $P = 0.45$; at home: $-0.01(-0.42;0.41)$, $P = 0.96$).

Table 3 **Overview over the 8 levels of the STAND model and the distribution of patients on the 8 levels according to the highest level performed in the hospital and at home, respectively.**

Level in STAND	Description of level	Illustration	In hospital (*n*)	At home (*n*)
1	Seated knee extensions with or without added load, e.g., weight cuffs.		2	0
2	STS with armrest support and support from another person allowed; own body weight.		0	0
3	STS with armrest support in eccentric and concentric phase allowed; own body weight.		2	3
4	STS with armrest support in concentric phase allowed; own body weight.		2	1
5 Starting point	STS without support; own body weight.		6	4
6	STS with added load; e.g., weight vest.		6	4
7	Unilateral STS with balance support allowed; own body weight.		1	1
8	Unilateral STS with balance support allowed and with added load; e.g., weight vest.		1	2

Notes.
STS, sit-to-stand.

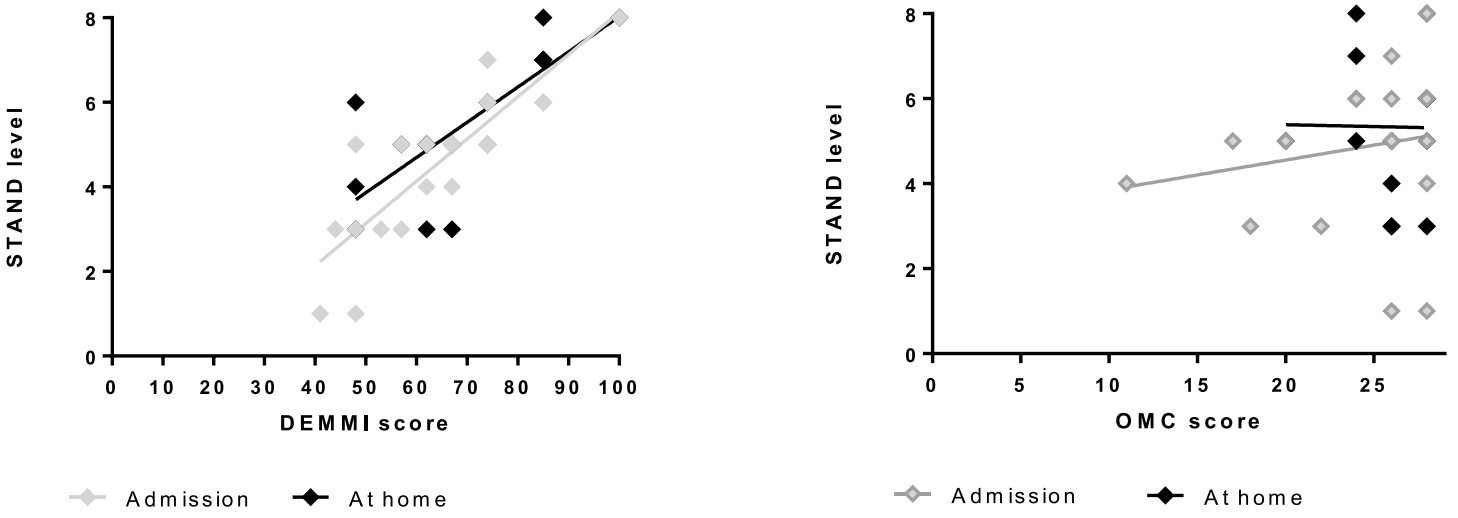


Figure 3 The association between DEMMI score (A) and OMC score (B), respectively, and performed level of STAND on admission and at home. DEMMI score: score on the De Morton Mobility Index (0–100). The higher the score the better mobility. OMC score: score on the Short Orientation-Memory-Concentration test (0–28). The higher the score the better cognition. STAND level: 1 indicates lowest level of the model (seated knee-extensions) and 8 indicates highest level of the model (unilateral sit-to-stand with added load).

DISCUSSION

The major finding of our feasibility study was that our exercise model of progressive sit-to-stands (STAND) was feasible among hospitalized older adults and demonstrated potential for being used in a future study appropriately powered to evaluate the effect of the exercise on mobility, physical activity, functional performance and independence in this population. Specifically, we found that more than 75% of the patients assessed during hospitalization and shortly following discharge in their own home were able to perform the sit-to-stand exercise at a given level of STAND reaching an intensity of 8–12 RM for 8–12 repetitions. No clustering of patients at the highest or lowest level of STAND was seen, suggesting no ceiling or floor effect, and for all patients assessed a possibility of either progression or regression was possible. Finally, no adverse events were reported.

Consistent with this study, previous studies have found resistance training to be feasible in older hospitalized patients (*Siebens et al., 2000*; *Mallery et al., 2003*). However, these studies have used either low intensity exercises; due to a concern of potential risks of exercising older hospitalized patients (*Siebens et al., 2000*); or exercises performed lying in bed (*Mallery et al., 2003*). Our study shows that a performance-based, higher-intensity exercise is feasible both in hospitalized older adults with high and low mobility (*Macri et al., 2012*) (a DEMMI score of 44–80) and with and without mild cognitive impairment (*Katzman et al., 1983*) (an OMC score of 18–28). Moreover, we found a strong association between the level of STAND and DEMMI which indicates that the achieved level of STAND reflected the mobility level of the patients. Additionally, the level of STAND was not associated with cognition, which implies that STAND can be used independent of cognitive level. It has previously been shown that high intensity resistance training is superior to low intensity in frail older adults (*Seynnes et al., 2004*), which is why STAND may be a good

choice in older hospitalized adults. We were able to provide optimal resistances with the exercise as more than 75% of the assessed patients were able to perform the exercise with a loading of 8–12 RM for 8–12 repetitions for the intended number of sets. Of those not able to reach the intended loading/number of sets two thirds stopped after 6–7 repetitions or due to muscular fatigue. This may indicate that they were able to perform the exercise but needed better adjustment of the load or needed better information regarding the management of muscular fatigue when performing strength training. The mean Borg score when performing the highest level possible was 14, corresponding to a 75% effort (*Avers & Brown, 2009*). Thus, this subjectively perceived effort corresponds well with 8–12 RM (*Kraemer & Ratamess, 2004*) and indicates that the patients have exercised at the intended level. Also, no adverse events were seen. Therefore, this mode of progressive exercise seems appropriate as a simple strength training exercise in acutely admitted older medical patients.

Limitations and strengths

A limitation of the study is that the assessed patients represent a select group of acutely admitted older medical patients as 90% of the patients fulfilling the inclusion criteria were either excluded (80%) or declined to participate (10%). The proportion of patients consenting to participate, however, is equal to (*Mallery et al., 2003*) or higher (*Siebens et al., 2000*; *Brown et al., 2006*) than seen in previous exercise studies in older hospitalized adults, which underlines the difficulty of including patients in the acute setting and limits the generalizability to acutely admitted older patients equivalent to our sample. In addition, we consider our exclusion criteria reasonable as the majority of those excluded either would probably not have been able to perform the exercise with the intended quality (e.g., due to dementia or confusion; 32.5%), or would not benefit from a program including the exercise (e.g., due to being in cancer treatment or terminally ill; 7.5%) or had a very short hospital stay (discharged within the first 24 h; 53%). However, patients excluded due to inability to rise from a chair might benefit from exercise based on the STAND model (level 1) or other interventions based on less demanding exercises equivalent with the ones used by Mallery and co-workers (*2003*). Another limitation of our study is that the feasibility of STAND has only been tested for one session in each setting (hospital and home) and therefore, we are not able to evaluate whether the patients can comply with the exercise over time or whether STAND is sufficient in ensuring the right load over time, e.g., a training period of 4 weeks. We do believe, though, that the model can be used for a longer training period, as progression and regression was possible for all levels of the model and neither floor nor ceiling effect was seen.

A major strength of our study is that the exercise, following STAND, is well-described, simple and low in cost making it possible to implement both in an acute hospital ward as well as in the patients' homes. A study by *Sullivan et al. (2001)* in hospitalized frail elderly showed that 10 weeks of resistance training consisting of three sets of eight leg presses in a leg press chair increased strength and lowered sit-to-stand time. The sit-to-stand exercise (level 2–8 of STAND) corresponds well with the leg press exercise, requiring the

use of similar muscle-synergies. However, in the hospital and especially in the home setting weight-lifting equipment like a leg press chair is not often available why it is promising that using a weight vest and the sit-to-stand exercise patients can be loaded to the same extend enabling low technology resistance training both in the hospital and at home. Additionally, as expressed in several recent reviews it is very important to use exercise programs that are detailed with regard to technique, dosage and progression of the exercise. Our program complies with the recommendation (*De Morton, Keating & Jeffs, 2007*; *Liu & Latham, 2009*; *Steib, Schoene & Pfeifer, 2010*; *Kosse et al., 2013*; *Giné-Garriga et al., 2014*; *Timmer, Unsworth & Taylor, 2014*; *White et al., 2015*). Moreover, the inclusion of physiotherapist supervision ensures optimal dosage and technique and may also enhance compliance. This design element was included to overcome challenges within previous studies that used unsupervised training in the home setting (*Siebens et al., 2000*; *Buhl et al., 2015*).

Perspective

We are now conducting a randomized controlled trial to test a cross-continuum strength training intervention in older medical patients (NCT01964482). The goal of the trial is to investigate the effect of a simple, supervised strength training program consisting of two lower-extremity strength training exercises. The exercises are based on STAND and performed during hospitalization and the first four weeks after discharge at home.

CONCLUSIONS

Based on our pre-defined criteria for feasibility we found that a simple progression model for loaded sit-to-stands (STAND) was feasible in acutely admitted older medical patients (+65 yrs) in the hospital- and home setting. Following the progression model, a strength-training intensity of 8–12 RM for 8–12 repetitions was reached for two thirds of the assessed patients with no indication of ceiling or floor effect for load, and no report of adverse events.

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Competing Interests

The authors declare there are no competing interests.

Author Contributions

- Mette Merete Pedersen conceived and designed the experiments, performed the experiments, analyzed the data, wrote the paper, prepared figures and/or tables, reviewed drafts of the paper, interpreted analyzed data.
- Janne Petersen conceived and designed the experiments, analyzed the data, contributed reagents/materials/analysis tools, reviewed drafts of the paper, interpreted analyzed data.
- Jonathan F. Bean reviewed drafts of the paper, interpreted analyzed data.
- Lars Damkjaer conceived and designed the experiments, reviewed drafts of the paper.
- Helle Gybel Juul-Larsen performed the experiments, reviewed drafts of the paper.
- Ove Andersen contributed reagents/materials/analysis tools, reviewed drafts of the paper, interpreted analyzed data.
- Nina Beyer and Thomas Bandholm conceived and designed the experiments, reviewed drafts of the paper, interpreted analyzed data.

Human Ethics

The following information was supplied relating to ethical approvals (i.e., approving body and any reference numbers):

The Ethics Committee of the Capital Region of Copenhagen (H-2-2012-115).

Data Availability

The following information was supplied regarding data availability:

Raw data can be found in the Supplemental Information.

Supplemental Information

Supplemental information for this article can be found online at http://dx.doi.org/10.7717/peerj.1500#supplemental-information.

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Manuscript III

Supervised progressive cross-continuum strength training compared with usual care in older medical patients: study protocol for a randomized controlled trial (the STAND-Cph trial).

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Title page

Title

Supervised progressive cross-continuum strength training compared with usual care in older medical patients: study protocol for a randomized controlled trial (the STAND-Cph trial).

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Protocol version

Version 3 updated 25.11.2015. The protocol follows the SPIRIT 2013 checklist: Standard Protocol Items: Recommendations for Interventional Trials [1].

Trial registration

Clinicaltrials.gov: NCT01964482 (October 14th 2013).

Key Words

Older medical patients; Hospitalization; Progressive strength training; Supervision; Mobility; Cross-continuum

Abstract

Background

Hospitalization in older adults is characterized by physical inactivity and a risk of losing function and independence. Systematic strength training can improve muscle strength and functional performance in older adults. Few studies have examined the effect of a program initiated during hospitalization and continued after discharge. We conducted a feasibility study prior to this trial and found a progression model for loaded sit-to-stands feasible in older medical patients. This study aims to determine if a simple supervised strength training program for the lower extremities (based on the model) combined with post-training protein supplementation initiated during hospitalization and continued at home for 4 weeks is superior to usual care on change in mobility 4 weeks after discharge in older medical patients.

Methods

Eighty older medical patients (≥65 yrs) acutely admitted from their own home will be included in this randomized, controlled, investigator-blinded study. After baseline assessments patients will be randomized to 1) Intervention: progressive strength training during hospitalization and after discharge (home-based) or 2) Control: usual care. Shortly after discharge, four weeks after discharge (primary end point) and 6 month after discharge patients will be assessed in their own homes. The intervention encompasses strength training consisting of two lower extremity exercises (sit-to-stand and heel-raise) daily during hospitalization and 3 times per week for 4 weeks after discharge. Both exercises follow pre-defined models for progression and will be performed for 3 sets of 8-12 repetitions maximum in each training session. Hereafter, the patient will be asked to consume an oral protein supplement containing 18 g milk-based protein. The primary outcome will be change in the de Morton Mobility Index score from baseline to 4 weeks after discharge. Secondary outcomes will be 24-hour mobility level, isometric knee extension strength, the 30-sec sit-to-stand test, habitual gait speed, hand-grip strength, and Activities of Daily Living.

Discussion

We chose to investigate the effect of a minimal time-consuming treatment approach, i.e. two well-performed strength training exercises combined with protein supplementation, to facilitate implementation in a busy clinical care setting, given a positive trial outcome.

Introduction

Background and rationale

Ageing is associated with a decline in muscle strength and functional performance which is why older adults (+65 years) do not possess the same reserve capacity as younger adults [4–8]. In general, older hospitalized adults display poor muscle strength and functional performance indicative of poor mobility [9, 10] and are at risk of becoming dependent after acute illness and hospitalization [11–13]. Moreover, hospitalization is associated with a subsequent loss of muscle strength [14], putting hospitalized older adults at a higher risk of losing independence as a consequence of their hospitalization.

During hospitalization, older adults spend most of their time being physically inactive and lying in bed [16–20]. This can lead to a decline in observed and self-reported ability to perform activities of daily living (ADL) at discharge and at one month follow-up [18, 21], inducing a risk of dependency [22], and increasing the risk of institutionalization and death [18]. Older adults are more sensitive to bed rest inactivity compared to younger adults [23–26], and have an impaired ability to fully recover [24, 25]. In healthy older adults, restricted activity and bed rest are associated with reduced protein synthesis and reduced muscle mass and strength [25, 27, 28], and new disability in ADL [29, 30]. Likewise, a study by Boyd et al [12] has shown that new disability in ADL is experienced by one third of older medical patients from hospital admission to discharge, and only 30 % of these return to their preadmission level within the first year after discharge [12]. Self-reported decline is seen even after short hospital stays [31]. Thus, reducing physical inactivity during hospitalization and maintaining independency, is considered the most important health outcome by many older adults [15]. Regaining function within the first month after discharge seems especially important as one month status is indicative of functional status one year after discharge [12].

Systematic strength training can improve muscle strength and functional performance in healthy older adults [32–35], and this has also been reported in patients with chronic diseases [36]. Both strength training initiated during hospitalization in older geriatric patients [37] as well as post discharge training [38, 39] and training of functionally impaired community-dwelling older adults [40] have shown positive effects on strength and functional performance. Most exercise programs for older hospitalized [39, 41–43] or community-dwelling [39, 40, 44–46] adults cover a range of exercises including upper- and lower body strength training, balance- and walking exercises and stretching exercises and few have examined the effect of a program initiated during hospitalization

and continued after discharge [39, 43, 47]. These studies, however, have experienced problems with compliance [39, 43, 47]. A recent systematic review suggests that "the recovery of patients could further benefit from a community based or an in-home intervention program which build on in-hospital programs" [48]. In addition, acutely hospitalized older adults express that initiating exercise in the hospital or shortly after discharge is a good idea [47, 49]. Further, supervision can benefit adherence to training [48, 50], and participation is more likely if recommended by a physiotherapist [51]. This emphasizes the importance of supervision from trained staff both in the hospital and in the home setting [43, 47, 52].

Regarding the content of an exercise program, recent reviews suggest that information is lacking about the appropriate dose of strength training in different settings for older adults as well as detailed descriptions of exercises and dosage [2, 32, 53], although it seems that higher intensities are superior to lower intensities [2, 54].

As the lower extremities are especially sensitive to bed rest [27, 55] and lower extremity strength is associated with functional performance (e.g. mobility and the ability to perform ADL) [56–59], it seems reasonable to focus on counteracting loss of strength and functional performance in the lower extremities. Moreover, combing strength training with protein supplementation may be even more beneficial as it may stimulate muscle protein synthesis and thus increase the exercise response on muscle mass and strength as seen in healthy older adults [60–62].

Therefore, the aim of this study is to determine in a randomized, investigator-blinded controlled trial if a simple, low technology, supervised strength training program for the lower extremities, combined with post-training protein supplementation initiated during hospitalization and continued at home for 4 weeks after discharge is superior to usual care on change in mobility 4 weeks after discharge in older medical patients.

Methods

Study design

The study, which is called the Cross-Continuum Progressive Strength Training in Older Medical Patients – Copenhagen (STAND-Cph) trial, is a randomized, controlled, parallel-group (2 groups), investigator-blinded, superiority trial being conducted in the Copenhagen area, Denmark. The trial investigates the effect of a simple, low technology, supervised strength training program

commenced during hospitalization and continued for 4 weeks after discharge (ClinicalTrials.gov-identifier: NCT01964482). The study is conducted as a full-scale trial following a feasibility study that has tested the feasibility of a progression model for loaded sit-to-stands when used as a simple strength training exercise in older medical patients [63]. Participants will be randomized to either progressive strength training or usual care, and the primary endpoint will be 4 weeks after discharge (end of exercise period). In addition, the participants will be followed up after 6 months. Table 1 provides an overview of the trial characteristics.

Table 1. Trial registration data

Data category	Information
Primary registry and trial identification number	ClinicalTrials.gov: NCT01964482
Data of registration in primary registry	October 14th 2013
Secondary identifying numbers	The Ethics Committee of the Capital Region of Denmark: H-2-2012-115 The Danish Data Protection Agency: 2007-58-0015
Source(s) of monetary or material support	Danish Regions/The Danish Health Confederation, The Lundbeck Foundation (UCSF) (grant numbers FP 07/2012, FP 48/2012 and FP 61/2013), the Research Foundation of Hvidovre Hospital, the Capital Region of Copenhagen, and The Danish Foundation for Research in Physiotherapy
Primary sponsor	Danish Regions/The Danish Health Confederation
Secondary sponsor(s)	The Lundbeck Foundation (UCSF), the Research Foundation of Hvidovre Hospital, the Capital Region of Copenhagen, and The Danish Foundation for Research in Physiotherapy
Contact for public queries	MMP, TB [mette.merete.pedersen@regionh.dk]
Contact for scientific queries	MMP, TB. Clinical Research Centre, Hvidovre Hospital, University of Copenhagen, Denmark
Public title	In-hospital and post discharge training of older medical patients
Scientific title	Supervised progressive cross-continuum strength training compared with usual care in older medical patients: study protocol for a randomized controlled trial (the STAND-Cph trial)
Country of recruitment	Denmark
Health condition(s) or problem(s) studied	Progressive strength training in older medical patients
Intervention(s)	Intervention: Strength training daily during hospitalization and 3 times per week for 4 weeks after discharge
	Control: usual care
Key inclusion and exclusion criteria	Inclusion criteria: Age ≥65 yrs; acutely admitted from own home to the Emergency Department at Hvidovre Hospital, Denmark
	Exclusion criteria: Terminal illness; in treatment for diagnosed cancer; diagnosis of Chronic Obstructive Pulmonary Disease (COPD) and participation in a COPD rehabilitation program; living outside the municipalities of Copenhagen and Broendby; inability to speak or understand Danish; inability to cooperate in tests/exercises; an expected hospitalization >24 hours; assigned to physical rehabilitation in the community; a Cummulated Ambulation Score (CAS) of 0 in the sit-to-stand item
Study type	Interventional
	Allocation: randomized
	Blinding: Investigator blind
Date of first enrolment	Sept 2013
Target sample size	72
Recruitment status	Recruiting
Primary outcome(s)	The de Morton Mobility Index
	Timeframe: Change from baseline to 4 weeks after discharge (end of intervention)
Key secondary outcomes	24-hour mobility measured by *activ*PAL3™ ; Isometric knee extension strength in the dominant leg; the 30-sec sit-to-stand test; habitual gait speed; hand-grip strength in dominant hand; the Barthel Index 20

Study setting

The study will be conducted at Hvidovre Hospital, University of Copenhagen, Denmark and in the participants' own homes in the municipalities of Copenhagen, and Broendby. Hvidovre Hospital has a 552-bed capacity. Recruitment will take place in the 20-bed Emergency Department (ED) through which the majority of older medical patients (≥65 yrs) are admitted. There are approximately 4000 admissions of older medical patients to the ED every year, and around 50% are discharged within the first 24 hours. In Denmark, the healthcare system is public and provides feeless, tax-paid primary medical care, hospital treatment, and homecare services uniformly for all citizens.

Study sample and recruitment procedure

Older medical patients (≥65 yrs) acutely admitted from their own home to the medical services of the hospital will be included by random sampling within 24 hours of admission. Each day (Monday to Friday) the primary investigator or one of three assistant investigators will receive a computer generated list of all newly admitted older medical patients (≥65 yrs). The investigator will check the medical records of all the listed patients to determine their eligibility according to the inclusion- and exclusion criteria as listed below:

Inclusion criteria

- Age ≥65 yrs
- Admitted from own home

Exclusion criteria

- Terminal illness
- In treatment for diagnosed cancer
- Diagnosis of Chronic Obstructive Pulmonary Disease (COPD) and participation in a COPD rehabilitation program
- Living outside the municipalities of Copenhagen and Broendby
- Inability to speak or understand Danish
- Inability to cooperate in tests/exercises
- Transferred to the intensive care unit or isolation-room stay
- An expected hospitalization <24 hours
- Assigned to physical rehabilitation in the municipality
- A Cummulated Ambulation Score (CAS) of 0 in the sit-to-stand item

Eligible patients will be visited at the ward by one of four investigator where they will be given a written description of the study to read and will be informed about the study verbally. The investigators will ensure that all questions are answered before the patient is asked to participate in the study. The Ethics Committee of the Capital Region has granted an exemption for the 24 hour consent time, which is normal practice when including patients for medical research in Denmark. The exemption was granted to be able to follow the patients through their entire hospitalization and assess their functional level before an effect of medical treatment is seen. Patients who accept to participate will be asked to sign an informed consent form to be included in the study. The patient will keep the original document and two copies will be archived.

After inclusion, baseline assessments will be performed where after the patients will be randomized to either: 1) Intervention: progressive strength training during hospitalization and the first month after discharge (home-based) or 2) Control: usual care. Four weeks (primary end point) and 6 month (follow up) after discharge the patients will be assessed in their own homes. Figure 1 shows the study flow.

Randomization

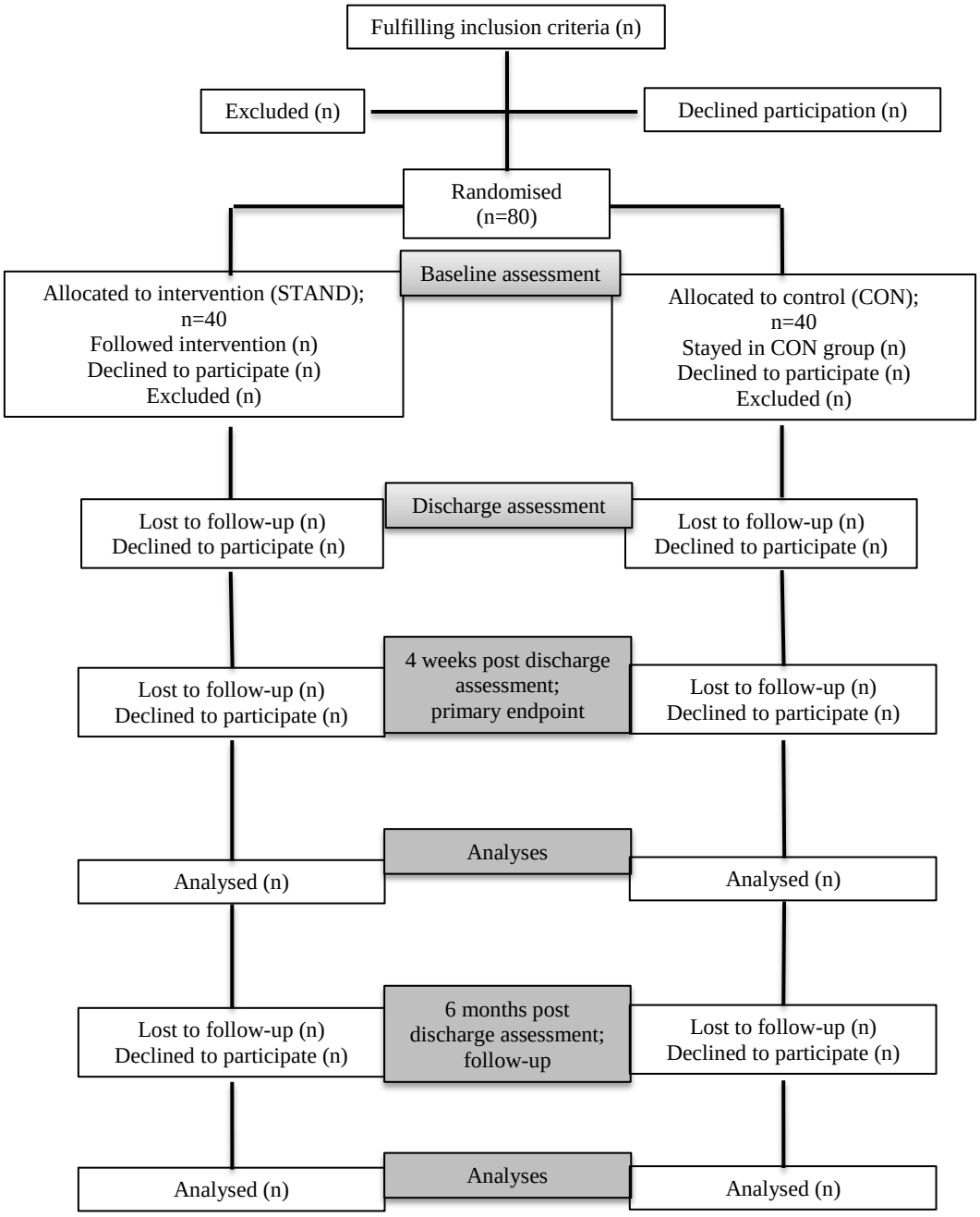
Patients who consent to participate will be randomly allocated to either of the two groups. Randomization will follow a computer generated block randomization list produced by the study coordinator (JP). Randomization is stratified within the two participating municipalities. The recruitment will follow a 2:1 allocation in one of the municipalities (A) and a 1:2 allocation in the other municipality (B). This randomization procedure is followed to comply with the capacity of the municipalities.

Blinding

To ensure concealment of allocation, a study nurse will be in charge of the randomization procedure following the randomization list and the investigators will be blinded to allocation. Moreover, the study nurse will inform the investigators when patients are ready for 4 week follow-up tests. Patients will be asked not to reveal to the investigators to which group they belong. The discharge test in the patient's home will be conducted before the first post-discharge training session to avoid that the investigator sees the exercise equipment in the home. Additionally, all contacts with physiotherapists in the hospital and in the municipalities will be undertaken by the study nurse to

ensure blinding of the investigators. In the case of a possible adverse event and non-presence of one of the co-authors to evaluate the severity of the event, the allocation of a patient can be revealed to the investigators in order to assure proper treatment of the patient.

Figure 1. Expected flow of patients



Sample size

Based on data from an unpublished cohort study performed at Hvidovre Hospital, 25 consecutively included older medical patients had a mean change in the de Morton Mobility Index [64] score of 1.8 and a standard deviation of 12.8 from admission to one month after discharge. A change of 10 points in the DEMMI score is considered a minimal clinically important difference [64]. To be able to detect a 10 point difference in the between-group change in the DEMMI score at the four week assessment (primary end point), we will need a sample size of 27 patients per study arm to obtain a type I error rate of 5% and a power of 80% for a 2-sample t-test of a normal mean difference with at 2-sided significance level. We will continue to recruit patients until 54 patients have been assessed for the primary end point (4 weeks). We expect a maximum of 80 patients to be included in the study.

Study principles

The protocol follows the SPIRIT 2013 (Standard Protocol Items: Recommendations for Interventional Trials) check list [1] and the description of the intervention follows the Template for Intervention Description and Replication (TIDieR) checklist [65]. The reporting of the study once completed will follow the CONSORT (Consolidated Standards of Reporting Trials) Statement, using the extension for non-pharmacological trials [66].

Study groups

Control group

Patients in the control group will receive routine care during hospitalization and after discharge. No efforts will be made to change this care during the study period. Routine care will be used as a comparator to reflect the current care for these patients.

According to the Danish Healthcare Quality Programme (DDKM) [67], the functional level and nutritional status of hospitalized patients must be described within 24-48 hours after admission [68] and treatment planned accordingly. No standard involves in-hospital training [68], but patients needing recovery (e.g. rehabilitation) should be identified [69], and rehabilitation (including exercise) should be planned to target the patient's impairment and limitations. Often rehabilitation starts during hospitalization, and if it continues after discharge a rehabilitation plan must be prepared by the hospital. At Hvidovre Hospital around 5% of older medical patients are discharged

with a rehabilitation plan (personal communication with Geriatric Team in the ED, Oct. 30th 2015) involving exercise therapy supervised by physiotherapists.

Intervention group

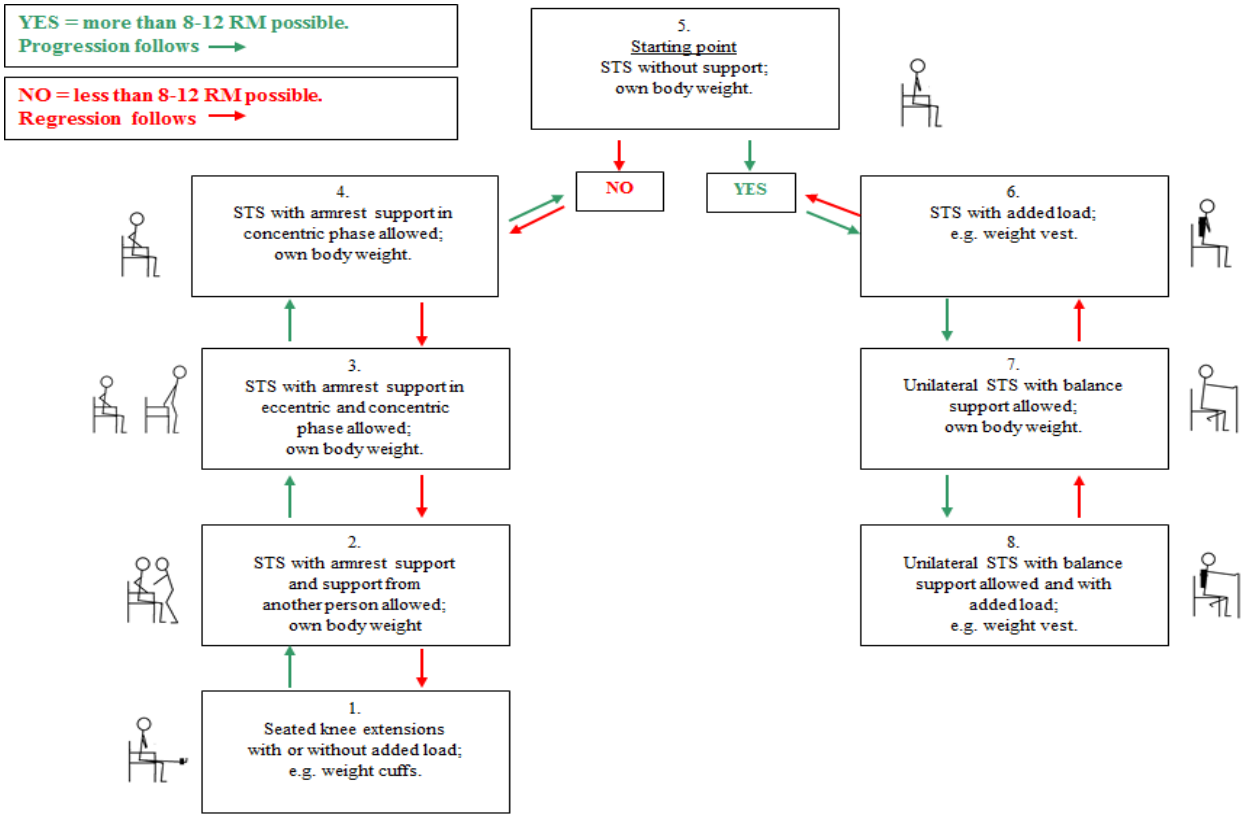
Patients in the intervention group will receive 1:1 supervised progressive strength training daily on week days during hospitalization and 3 times per week for 4 weeks (12 training sessions, 1:1 supervised) after discharge. To account for possible cancellations, i.e. due to illness or other obstacles for training completion, it will be allowed to distribute the 12 in-home training sessions over a maximum of 5 weeks. The training will take place in the patient's bedroom during hospitalization and in the patient's own home after discharge.

Training intervention

All training sessions will be supervised by a skilled physiotherapist. Two physiotherapists with 3 years of experience will supervise the in-hospital training sessions and 5 physiotherapists with 4-15 years of experience will supervise the at-home sessions. In every training session, the patient will be asked to perform a warm up program consisting of seated exercises for the lower extremities (hip flexions, knee-extensions, heel-raises, hip abductions/adductions). The patient will be asked to perform each exercise for 20 repetitions. The warm up program has a duration of 5 minutes.

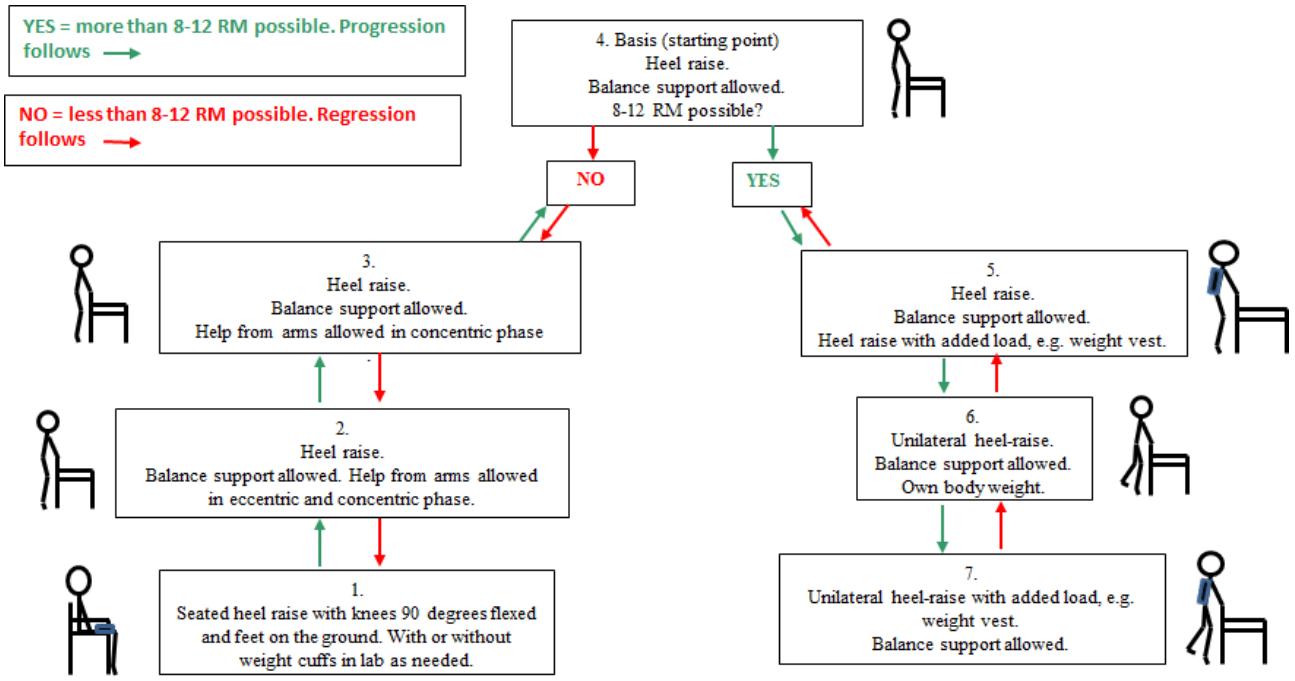
After warm up, the patient will be asked to perform a progressive strength training program for the lower extremities, based on a minimum treatment approach, consisting of a sit-to-stand exercise (Figure 2) and a heel raise exercise (Figure 3) as outlined in detail below. For both exercises, the progression will follow predefined models based on the STAND model (Figure 2), which we have tested and found feasible in older medical patients [63]. In each exercise, the progression model allows for performing the exercise from a seated position (level 1) to performing the exercise unilaterally with extra load added (level 7/level 8). The patient will be asked to perform 3 sets of 12 repetitions maximum (RM) of each exercise. This will correspond to 60–70% of 1 RM [33, 70, 71]. The aim will be to reach contraction failure (muscular fatigue) at a relative load zone of 8-12 RM in each set [33]. A 2-minute pause will be held between sets [33]. The correct level of each exercise will be chosen according to the progression models by the supervising physiotherapist. The patient will be asked to work at moderate velocity using 2 seconds in the concentric (raising) phase and 2 seconds in the eccentric (lowering) phase of the exercise. An isometric pause of 1-second will be held after both the concentric and the eccentric phase [33]. If a patient can perform 6 non-compensatory repetitions and needs a little support performing the last repetitions (e.g. minimal use

Figure 2. Progression model for loaded sit-to-stand exercise (STAND)



STS: Sit-to-stand; 8-12 RM: 8-12 repetitions maximum (a zone in which muscular fatigue should be reached)

Figure 3. Progression model for loaded heel-raise



of armrests/minimal balance support), and if a proper technique is maintained, training at the given level will be accepted to enable the patients to reach fatigue in every set. Moreover, increased speed will be allowed in the last two repetitions of each set to optimize leg power, which has been shown to be associated with physical performance in mobility-limited older adults [56, 72]. Each set of each exercise is considered unique and determines whether the patient will stay on the same level or either progress or regress. The total duration of each exercise session will be approximately 10-15 minutes.

STAND

Each training session will begin with the sit-to-stand exercise. The patient will be asked to sit in a standard chair with armrests with a seat height of approximately 45 cm. The chair is placed so that is cannot slide during the exercise. The patient is to keep the feet on the floor at shoulder-width and cross the arms at the wrist with the hands placed on the opposite shoulder. The starting point in STAND is level 5 (Figure 2). The patient will be asked to rise to a fully extended position and to sit down in a constant pace and will be verbally encouraged by the supervising physiotherapist to perform as many repetitions as possible maintaining the same pace to ensure training to contraction failure [70]. If the patient is able to perform more than 12 repetitions he/she will progress to the next level (level 6), performing the exercise wearing a weight vest (Titan Box, 1-30 kg) containing the amount of kilos required to reach 8-12 RM, and so forth. If the patient is not able to perform 8 repetitions in level 5, regression is possible (level 4) allowing the patient to use the armrests in the concentric phase, and so on.

Heel-raise

The progression of the heel-raise exercise will follow the progression model for heel-raise (Figure 3). The patient will be asked to stand behind a standard chair keeping the hands lightly on the back of the chair for balance support. The patient is to keep the feet on the floor at shoulder-width. The starting point in the progression model is level 4 (Figure 3). The patient will be asked to lift both heels to stand on the forefoot and to lower the heels to a standing position at a constant pace. The patient will be verbally encouraged, by the physiotherapist, to perform as many repetitions as possible maintaining the same pace to ensure training to contraction failure [70]. If the patient is able to perform more than 12 repetitions he/she will progress to the next level (level 5), performing the exercise wearing a weight vest (Titan Box, 1-30 kg) containing the amount of kilos required to reach 8-12 RM, and so forth. If the patient is not able to perform 8 repetitions in level 4, regression

is possible (level 3) allowing the patient to support herself/himself on the back of the chair in the concentric phase, and so forth.

Protein supplement

We consider protein as an integrated part of strength training to optimize the anabolic response after training. Therefore, immediately after each training session, the patient will be asked to consume an oral protein supplement (Nutridrink Compact Protein from Nutricia A/S) containing 18 g milk-based protein and 300 kcal.

Standardization of intervention

The primary investigator will perform pre-intervention meetings with all involved physiotherapists to ensure standardization of the intervention. At the meetings, the physiotherapists will be introduced to the warm up program and the strength training protocol. At the meeting, the strength training exercises will be performed by all involved physiotherapists to ensure common knowledge about the requirements at each level of the program. A laminated version of the warm up program as well as the progression models for both strength training exercises will be provided to all involved physiotherapists. During the study period, the physiotherapists will be able to contact the primary investigator or a study nurse at all times, should any questions arise. If a physiotherapist leaves the project, e.g. in the case of leave of absence or ended employment, the primary investigator will ensure that the physiotherapist taking over will be introduced to the protocol in the same manner as already involved physiotherapists.

Outcome measures

Outcomes measures will be assessed on admission (baseline), shortly after discharge, approximately 4 weeks after discharge (primary endpoint) and 6 months after discharge. All outcomes to be assessed are presented in Table 2.

Primary Outcome Measure

The primary outcome will be change in the DEMMI score from baseline to 4 weeks after discharge (end of intervention, primary end point). The DEMMI is a valid and reliable measure of mobility in both acute and subacute older medical patients and community-dwelling older adults [64, 73–75], why it can be used to accurately monitor mobility in older adults [73]. It includes observations ranging from mobility to dynamic balance and is scored on a scale from 0 to 100 with 100

representing the highest level of mobility [73, 74], and with a minimal clinically important difference of 10 points.

Table 2. Variables to be assessed

Variable	Baseline	Discharge	4 weeks	6 months
Primary outcome				
The de Morton Mobility Index (DEMMI)	+	+	+	+
Secondary outcomes				
24-hour mobility (ActivPal monitors; 1 week assessments)	+	+	+	+
Isometric knee-extension strength	+	+	+	+
30-sec sit-to-stand test	+	+	+	+
Habitual gait speed (HGS)	+	+	+	+
Hand grip strength (HG)	+	+	+	+
Activities of Daily Living (Barthel 20)	+	+	+	+
Descriptive variables				
Age	+			
Gender	+			
Weight	+	+	+	+
Educational level	+			
Living status	+	+	+	+
History of smoking	+			
Use of ambulatory devices	+	+	+	+
Use of municipal help	+	+	+	+
History of falls during the last year	+	+	+	+
The Falls Efficacy Scale	+	+	+	+
The Nutritional Risk Screening (NRS)	+	+	+	+
The New Mobility Score (NMS)	+	+	+	+
The Cumulated Ambulation Score (CAS)	+	+	+	+
Days per week out on the street	+	+	+	+
Hospitalization within last 4 weeks			+	
Hospitalization within last 6 months	+			+
Possible confounders and modifiers				
Age	+			
Gender	+			
Cognition				
Short Orientation-Memory-Concentration test (OMC)	+			
Mini Mental State Examination (MMSE)		+	+	+
The Trail Making Test (Trails)				
Digit Symbol Substitution Test (DSST)		+	+	+
Hopkins Verbal Learning Test (HVLT)		+	+	+
The Geriatric depression scale (GDS)		+	+	+
Health status (EQ-5D)	+	+	+	+
Self-rated health (EQ-5D)	+	+	+	+
The Mini Nutritional Assessment (MNA)	+	+	+	+
Self-reported physical activity	+	+	+	+
The Verbal Ranking Scale (VRS)	+	+	+	+
Medications	+	+	+	+
History of training before hospitalization	+			
History of training in the municipality after discharge		+	+	+

Secondary Outcome Measures

The secondary outcomes will be the following six: 1) 24-hour mobility measured by an *activ*PAL3^{TM} activity monitor (PAL Technologies Ltd, Glascow, UK). The patient will be asked to wear an *activ*PAL3^{TM} on the thigh during hospitalization, the first week after discharge, the first week after the 4-week assessment and the first week after the 6 month assessment. The patient will wear the *activ*PAL3 ^{TM} halfway between the spina iliaca anterior superior and the patella on the front side of the right thigh. The monitor will be covered in Tegaderm ^{TM} transparent waterproof film (3M, Minnesota, USA), attached to the patient by a PALstickie ^{TM} (dual layer hydrogel adhesive pad) and covered by Leukomed® T transparent film (BNS medical, Hamburg, Germany) to enable the patient to wear the *activ*PAL3^{TM} while showering. The patient will be asked to wear the monitor for 24 hours per day. The *activ*PAL3^{TM} can record continuously for 7 days where after the monitor will be replaced, should the hospitalization be of a longer duration. The ActivPal3^{TM} accelerometer measures time spent sitting/lying, standing and walking, the number of steps taken, cadence and the amount of sit-to-stand and stand-to-sit transitions. The ActivPal3^{TM} is a valid and reliable measure of posture and transitions in healthy young and mobility limited older adults [76–78] and of walking at speeds between 0.67 m/s and 1.56 m/s in young and older adults [79–81]. Unpublished data from Hvidovre Hospital in 317 older medical patients showed that 46% walked at walking speeds below 0.67 m/s, why time spent walking could potentially be categorized as standing for 46% of older medical patients. For this reason, if 15% of the total sample walk with walking speeds below 0.67 m/s the ActivPal data will be dichotomized into sedentary (sitting/lying) and upright time (walking/standing); 2) Isometric knee extension strength (IKE) in the dominant leg using a handheld dynamometer (Power Track II Commander; JTech Medical, Utah). The patient will be seated in a standard chair with a seat height of approximately 45 cm, with the arms crossed over the chest and 90 degrees knee flexion [82, 83]. A strap will be attached to the chair and the patient's ankle, just proximal to the malleolus. A transducer will be placed under the strap and a thin foam pad will be placed between the transducer and the leg. The distance between the lateral femoral epicondyle and the center of the transducer will be measured (the moment arm). The patient will be asked to extend the leg as forcefully as possible for 5 seconds three times with a 1 minute pause in between. Up to two additional contractions will be performed if the last contraction elicits the highest value, to ensure that maximal force is measured. Isometric knee-extension strength will be expressed as maximal force (Nm) per kilo body weight (kg); 3) the 30-sec sit-to-stand test (STS) using a standard arm chair with a seat height of 45 cm [84]. The patient will be asked to sit with the arms crossed over the chest and stand up once without using the arms. If this is performed safely, the patient will be asked to stand up fully and sit down as many times as possible in 30 seconds

with the arms across the chest. The number of full stands will be counted. If the patient is not able to rise once from the chair without using the arms, a modified 30-sec sit-to-stand test will be used, allowing the patient to use the arm rests for support; 4) Habitual gait speed (HG) on a 4-meter course [85, 86]. The patient will be asked to walk 4 meters at his/her usual pace starting from a standing position. A walking aid will be allowed if needed. The faster of two walks will be used as the outcome; 5) Hand-grip strength (HGS) in the dominant hand using a handheld dynamometer (Digi-II; Saehan). The patient will be placed in a sitting position in an armchair, with the lower arm placed on the arm rest, an elbow flexion of 90 degrees and the wrist in a neutral position. The patient will be asked to place the contralateral hand on the leg with the palm facing upwards. The dynamometer handle will be set at position 2 [87] and the investigator will reset the dynamometer before handing it to the patient and ask the patient to squeeze the handle as forcefully as possible for 5 secs. The patient will be asked to perform the test three times with a 1 minute pause in between. If the third test shows the highest value additional tests will be performed until performance of a lower value to ensure that the highest value possible is obtained. Handgrip strength will be expressed in kilograms (kg); 6) the Barthel Index 20 (BI) is used as a measure of Activities of Daily Living (ADL) [88]. The BI assesses the help needed in regard to grooming, toilet use, feeding, transfer, mobility, dressing, stair climbing and bathing, and in addition the presence or absence of urinary and fecal incontinence. A score between 0 and 20 can be obtained with higher scores indicating less disability.

Additional variables

Descriptive variables and possible confounders and modifiers for exploratory analyses will be collected. Descriptive variables will include: education, living status, history of smoking, use of ambulatory devices, use of municipal help, history of falls during the last year, the Nutritional Risk Screening (NRS) [89–91], the New Mobility Score (recall of mobility two weeks before admission and at the day of admission) [92, 93] and the Cumulated Ambulation Score [94]. Possible confounders and modifiers will be assessed: sex; age; cognition by the Short Orientation-Memory-Concentration test (OMC) [95], the Mini Mental State Examination [96], the Trail Making Test [97, 98], the Digit Symbol Substitution Test [99], and the Hopkins Verbal Learning Test, Revised [100, 101]; depression by the Geriatric Depression Scale (GDS) [102]; health status by the EuroQol instrument [103]; nutritional state by the Mini Nutritional Assessment [104]; self-reported physical activity by a four-level questionnaire [105, 106]; pain before and after training by the Verbal Ranking Scale (VRS) [107, 108]; medications, history of training before admission, and history of training in the municipality after discharge. Moreover, baseline level of DEMMI and 24-hour

mobility using assessments from the 1st week after discharge will be treated as possible confounders and modifiers. Based on the cognitive assessments, patients will be categorized as having Mild Cognitive Impairment (MCI) or not, and those with MCI will be further sub-categorized in amnestic-MCI, non-amnestic MCI or multiple-MCI [109]. These categories will be used in the analyses.

Data collection

The primary investigator and a team of three assistant investigators will perform all baseline and follow-up assessments. All four investigators are trained physiotherapists with one to 15 years of experience.

The admission assessments will be performed at the Acute Medical Admissions Ward or at an internal medicine ward at Hvidovre Hospital, University of Copenhagen, Denmark, within the first 48 hours after admission. All follow-up assessments will be performed in the patient's own home, and the same investigator will assess the same patient at all assessments whenever logistically possible, to promote patient retention.

During each training session the supervising physiotherapist will complete an exercise diary consisting of information about the level of exercise attained according to the progression models, the extra load added (kg), and the number of sets and repetitions performed at each level. Self-reported pain will be registered immediately before and after each training session by the use of the VRS. Moreover, the physiotherapist will register reasons for non-participation as well as the amount of protein consumed after each training session. The patient time line including data collection is presented in Table 3.

Compliance

High compliance with the intervention is defined as completion of 80 % of all training sessions with a minimum of two sets performed per session.

Table 3. Patient timeline

	Study period						
Time point	Admission	Baseline	Hospital intervention	Discharge assessment	Home intervention	4 week assessment	6 month assessment
		≤ 48 h after admission	Daily during hospitalization	In patient's home	3 times per week for 4 weeks in patient's home	In patient's home	In patient's home
Enrollment							
Eligibility screen	X						
Informed consent	X						
Interventions							
Strength training			X		X		
Control							
Assessments							
Baseline assessment*		X					
Primary outcomes		X		X		X	X
Secondary outcomes		X		X		X	X
Descriptive variables and possible confounders and modifiers		X		X		X	X

**see table 2 for a detailed description of assessed variables.*

Data management

All case report forms will be checked for errors and missing data before being archived in a study database and all paper-based versions will be locked in a filing cabinet to ensure confidentiality. The primary investigator will have access to the full dataset, in which no information about allocation is visible, and co-investigators will have access as needed. Data management will comply with the rules of the Danish Data Protection Agency. The full protocol will be published and public access to de-identified patient-level data will be provided, once the data have been analyzed. All data will be double entered in Epidata Entry 3.1 (Epidata Associations, Odense, Denmark), range checked for data values, checked against the paper-based assessments and exported to SAS Enterprise Guide 6.4 (SAS Institute Inc., Gary, NC, USA). Data from the *activ*PAL3^{TM} will be downloaded to a computer using the *activ*PAL^{TM} Professional software version 7.2.32. For each *activ*PAL^{TM} monitoring the investigators will note at what time and date monitoring is started, at what time and date the monitor is attached to the patient, when the monitor is removed from the patient and reasons for not wearing the monitor if it is removed prematurely.

Statistical analyses

Descriptive data

Descriptive data for the intervention and control groups will be compared using the Chi square test for categorical variables, the Student's t test for normally distributed continuous variables, and the Mann-Whitney U test for non-parametric variables. Descriptive data will be presented as means with standard deviations, medians with inter-quartile ranges or frequencies with percentages depending on the distribution of the variable.

Primary analysis for the primary outcome

The primary analysis for the primary outcome is the between-group difference in change in the DEMMI score from baseline to 4 weeks after discharge (end of intervention). The primary analysis will follow the intention-to-treat principle using multiple imputation in case of missing outcome measures and be unadjusted. A repeated measures analysis (baseline, discharge, 4 weeks, 6 months) will be performed using the SAS procedure PROC MIXED with an unstructured covariance matrix. The patient identification number will be modelled as a random variable, and both group and time will be modelled as fixed factors. The between-group difference in change in DEMMI will be estimated from the interaction between the time and group variable.

Secondary and supplementary analyses

From the primary analysis model, the effect during hospitalization and the post intervention effect (change from 4 weeks to 6 months post discharge) will be estimated. For the secondary outcomes, similar analyses will be performed. Moreover, all analyses will be using adjustments for baseline DEMMI. To account for imbalances in in-hospital time, a sub-analysis will be performed for the effect during hospitalization and the effect from baseline to end of intervention adjusted for length of stay. Additionally, the unadjusted repeated model will be carried out following the per protocol principle, comparing patients that have fulfilled the compliance criteria with the control group. All between-group differences will be expressed as the average difference in change from baseline.

The analyses outlined above will all be reported in the main trial manuscript regarding effect of the strength training program. In addition, the following secondary analyses will be published subsequently.

To investigate the possible influence of confounders and modifiers on the effect of the intervention on DEMMI, an unadjusted analysis of variance of the between-group change from baseline to 4 weeks post discharge in the DEMMI score will be performed. In addition, this model will be extended by adjusting for all and each of the potential confounders and modifiers one by one. Confounding effects will be evaluated by comparing the unadjusted effect of group with the adjusted effects. Moreover, to investigate whether or not the effect of the intervention is modified by the potential confounders and modifiers the adjusted models will be extended with an interaction term between group and the potential confounders and modifiers. Similar analysis will be performed with 24-hour mobility (average time spent standing or walking per 24h) and with those of the secondary outcomes that showed a significant between-group difference in the primary analysis. Also, a logistic regression with compliance as the outcome and each of the potential confounders and modifiers as covariates will be performed. All analyses will follow both the intention to treat and the per protocol principle.

To investigate the effect of the intervention on cognition (MCI status, MMSE, OMC, HVLT, DSST, Trails A and B) at 4 weeks the following analyses will be performed. A generalized logistic regression for MCI status and an analysis of variance for MMSE, OMC, HVLT, DSST, and Trails A and B will be used with group as the independent variable. The analyses will follow the intention-to-treat principle with multiple imputation for missing values. Moreover, these analyses will also be performed adjusting for baseline OMC, baseline DEMMI, sex and age, depression, health status,

nutritional state, self-reported physical activity, pain, medications, length of stay and 24-hour mobility using assessments from the 1st week after discharge, and possible interactions with group will be analyzed. Additionally, the models will be repeated following the per protocol principle comparing patients. All results will be expressed as estimated means differences between the intervention and control group with the corresponding 95% confidence intervals.

All models will be investigated for goodness-of-fit (linearity, variance homogeneity and normal distribution of residuals) by visual inspection of plots and necessary changes in the models will be made accordingly. All statistical tests will be performed using SAS (SAS Institute Inc., Gary, NC, USA) and p values ≤ 0.05 will be considered statistically significant. No interim analysis will be made.

Discussion

There is limited data on the effect of strength training initiated during hospitalization and continued after discharge in older medical patients, and details about the optimal nature and dose of exercise are needed [2, 32, 53]. Higher intensities seem superior to lower intensities in older adults [3, 54, 110], and supervision essential for compliance [52]. This study provides a detailed description of a simple, supervised cross-continuum strength training program, based on a minimal time-consuming treatment approach. This approach was chosen to investigate if as little as two well-performed strength training exercises per session, combined with protein supplementation, during hospitalization and four weeks after discharge, can improve mobility in older medical patients. This approach was chosen to facilitate implementation in a busy clinical care setting, given a positive trial outcome.

Ethics

The patients will be informed that participation is voluntary and that they can withdraw at any time without losing their right to treatment. The study is approved by the Ethics Committee of the Capital Region of Denmark (H-2-2012-115) and by the Danish Data Protection Agency (2007-58-0015) and is registered at Clinicaltrials.gov (NCT01964482). The Ethics Committee will be informed about important protocol modifications for approval.

Data monitoring

No data committee will be established as the intervention is considered to be low-risk. All investigators and physiotherapists will be asked to report adverse events to MMP, and the study will be stopped if the adverse event is considered to be caused by training or testing. A hotline to an ED geriatrician has been established, should an adverse event occur or should the investigators need advice regarding a patient. The authors will meet frequently during the study to discuss trial conduct.

Roles and responsibilities

The study has been designed at Optimed, Clinical Research Centre, Hvidovre Hospital, University of Copenhagen, Denmark. The trial is overseen by the group of authors.

Authors' contributions

MMP, TB and JP will ensure completion of the study. MMP is the primary investigator and project leader and responsible for patient recruitment and data management. MMP, TB, JP and NB have designed the study in collaboration with the municipalities of Copenhagen (LD) and Broendby. MMP and TB have written the first protocol draft. Here after, all authors have contributed to writing and final approval of the protocol. Authorship for trial papers will follow the recommendations of The International Committee of Medical Journal Editors (ICMJE). No professional writers will be used.

Trial sponsor

Clinical Research Centre, Hvidovre Hospital, University of Copenhagen, Denmark. Address: Kettegård Alle 30, 2650 Hvidovre, Denmark. Contact: mette.merete.pedersen@regionh.dk; phone: +45 38 62 3350.

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Publication process

MMP will ensure that the results of the study are published in due time after study termination. The reporting of study will follow the CONSORT (Consolidated Standards of Reporting Trials) extension for randomized trials of nonpharmacological treatment [66].

Declaration of interests

All authors declare no competing interests.

Study status

Recruitment of patients is ongoing at the time of submission of this protocol. Recruitment began in October 2013 and is expected to end in February 2016.

Changes to initial plan

In the statistical analysis plan, imputation for missing data was changed from "last observation carried forward" to "multiple imputation". This protocol change was made before inclusion was completed, and while the study was still blinded. The Barthel20-Index was added as a secondary outcome before inclusion of the first patient to enable comparison with previous studies evaluating ADL during and after hospitalization [12, 13, 21, 111].

From February 2014, patients have been included from an additional municipality, the municipality of Hvidovre, due to the possibility of providing in-home training for these patients as well. Randomization in this municipality follows a 2:2 allocation. From September 2014, patients assigned to physical rehabilitation in the community have no longer been excluded from the study, as rehabilitation in the community is rarely commenced until four weeks after discharge and thus after the study's primary end point. From January 2015, a medical doctor has performed the initial screening of all eligible patients and informed the patients about the study before referring them to the primary investigator for informed consent and baseline assessments to enhance enrollment.

Abbreviations

ADL	Activities of Daily Living
BI	The Barthel Index 20
CAS	Cumulated Ambulation Score
CONSORT	Consolidated Standards of Reporting Trials
COPD	Chronic Obstructive Pulmonary Disease
DDKM	Danish Healthcare Quality Programme
DEMMI	de Morton Mobility Index
DSST	Digit Symbol Substitution Test
ED	Emergency Department
GDS	Geriatric Depression Scale
HG	Habitual gait speed
HGS	Hand-grip strength
HVLT-R	Hopkins Verbal Learning Test, Revised
IKE	Isometric knee extension strength
MCI	Mild Cognitive Impairment
MMSE	Mini Mental State Examination
MNA	Mini Nutritional Assessment
NMS	New Mobility Score
NRS	Nutritional Risk Screening
OMC	Short Orientation-Memory-Concentration test
RM	Repetitions Maximum
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
STS	30-sec sit-to-stand test
TIDieR	Template for Intervention Description and Replication
Trails	Trail Making Test
VRS	Verbal Ranking Scale

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109. Mette M. Pedersen, Holt NE, Grande L, Kurlinski LA, Beauchamp MK, Kiely DK, Petersen J, Leveille S, Bean JF: **Mild Cognitive Impairment Status and Mobility Performance: An Analysis From the Boston RISE Study**. *J Gerontol Biol Sci Med Sci* .

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Paper IV

Mild Cognitive Impairment Status and Mobility Performance: An Analysis From the Boston RISE Study

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Mild Cognitive Impairment Status and Mobility Performance: An Analysis From the Boston RISE Study

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Background. The prevalence of mild cognitive impairment (MCI) and mobility limitations is high among older adults. The aim of this study was to investigate the association between MCI status and both performance-based and self-report measures of mobility in community-dwelling older adults.

Methods. An analysis was conducted on baseline data from the Boston Rehabilitative Impairment Study in the Elderly study, a cohort study of 430 primary care patients aged 65 or older. Neuropsychological tests identified participants with MCI and further subclassified those with impairment in memory domains (aMCI), nonmemory domains (naMCI), and multiple domains (mdMCI). Linear regression models were used to assess the association between MCI status and mobility performance in the Habitual Gait Speed, Figure of 8 Walk, Short Physical Performance Battery, and self-reported Late Life Function and Disability Instrument's Basic Lower Extremity and Advanced Lower Extremity function scales.

Results. Participants had a mean age of 76.6 years, and 42% were characterized with MCI. Participants with MCI performed significantly worse than participants without MCI (No-MCI) on all performance and self-report measures ($p < .01$). All MCI subtypes performed significantly worse than No-MCI on all mobility measures ($p < .05$) except for aMCI versus No-MCI on the Figure of 8 Walk ($p = .054$) and Basic Lower Extremity ($p = .11$). Moreover, compared with aMCI, mdMCI manifested worse performance on the Figure of 8 Walk and Short Physical Performance Battery, and naMCI manifested worse performance on Short Physical Performance Battery and Basic Lower Extremity.

Conclusions. Among older community-dwelling primary care patients, performance on a broad range of mobility measures was worse among those with MCI, appearing poorest among those with nonmemory MCI.

Key Words: Cognition—Functional performance—Successful aging.

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FOR community-dwelling older adults, both cognitive impairments and mobility limitations are highly prevalent and can interfere with the ability to maintain independent living (1–3). It is estimated that among adults aged 65 or older, the prevalence of mild cognitive impairment (MCI) is between 10% and 20%, and the prevalence of mobility problems is equally as high (4,5).

MCI is defined as cognitive decline greater than that expected for one's age and education level, but which does not interfere appreciably with daily function (5,6). MCI is a well-known risk factor for dementia (7,8), with an annual conversion rate from MCI to dementia around 15% (8). Moreover, people with MCI are at increased risk of mobility decline, falls, and institutionalization (2,7,9).

Studies evaluating gait parameters indicate that cognitive function and mobility are linked. In a review, Monterro-Odasso and coworkers (9) highlighted that many of the brain regions (eg, hippocampus) affected by cognitive impairment also mediate aspects of mobility. It is also recognized that altered mobility performance precedes the behavioral manifestation of MCI (10). Therefore, mobility tests may serve as assessment tools for patients who either manifest, or are at risk for, developing cognitive impairment. A wide variety of clinical tests evaluates mobility by physical performance or self-report measures. However, few studies have contrasted how performance on these different mobility tests varies with MCI status and with specific MCI subtypes. One study that evaluated differences in gait analysis findings among different subtypes of MCI found

that different gait parameters were associated with amnestic MCI compared with nonamnestic MCI (11). Also, among older adults with MCI, executive function deficits are associated with poorer mobility performance and future risk for falls (12,13). By definition, nonamnestic MCI is largely influenced by executive function impairments, which suggests that these individuals may be at a heightened risk for poor mobility status and fall risk. Lastly, recent studies suggest that specific cognitive domains may be preferentially influential to specific mobility tests (14,15). However, these findings did not account for MCI status.

MCI is considered a subclinical state, which may remain unreported or undetected for a period of time. The first clinician to address these concerns is commonly the primary care practitioner (8). If mobility tests are to be considered as screening tools for incipient cognitive impairment (eg, MCI), then it will be essential to better understand the association between cognitive status and mobility performance. Also, it will be clinically important to evaluate these associations within primary care settings. Thus, based on the current evidence and the importance of screening for MCI within primary care settings, we investigated the association between cognitive function and mobility among older primary care patients, and more specifically the association between mobility and both MCI and MCI subtypes. We hypothesized (1) that participants with cognitive impairment, consistent with a diagnosis of MCI, would manifest greater limitation in performance-based and self-report measures of mobility than participants who did not meet diagnostic criteria for MCI (ie, cognitively intact); (2) that these associations would be maintained for all MCI subtypes; and (3) lastly that participants with nonamnestic MCI would manifest worse performance than those with amnestic MCI.

Methods

Study Design and Participants

A cross-sectional analysis was conducted using baseline data collected as part of the Boston Rehabilitative Impairment Study in the Elderly (Boston RISE), a cohort study of 430 community-dwelling and independent ambulating primary care patients aged 65 or older. The Boston RISE methods have been described in detail elsewhere (16). Briefly, participants were recruited through primary care practices at Massachusetts General Hospital and Brigham and Women's Hospital, two large academic medical centers located in Boston, Massachusetts. Eligible participants were identified through a Partners HealthCare patient database and telephone screening interviews and were invited to an initial screening and assessment visit. Potential subject were subsequently invited to undergo supplementary screening tests. Inclusion criteria were community-dwelling older adults, aged 65 or older, ability to understand and communicate in English, and self-reported difficulty with walking half a mile (6 blocks) or climbing one flight of stairs (10 steps). Patients were excluded for the presence of a terminal disease, significant visual impairment, uncontrolled hypertension, amputation of a lower extremity, use of supplemental oxygen, myocardial infarction or major surgery in the previous 6 months, planned major surgery, planned move from the Boston area within 2 years, cognitive impairment of significant severity as to likely reflect dementia (defined as Mini Mental State Examination [MMSE] score <18) (17), and Short Physical Performance Battery [SPPB] score less than 4 (18). Recruitment was based upon U.S. Census data 2000, to ensure an inclusion representing the ethnic, racial, and gender distribution of older adults residing within a 10-mile radius of our center. All of the methods of the Boston RISE study were approved by the Institutional Review Board of Spaulding Rehabilitation Hospital. Participants gave written informed consent before participation, and study procedures were approved by the Spaulding Rehabilitation Hospital Institutional Review Board.

Measures

The baseline assessments included a physical examination, a medical history questionnaire, the Self-Administered Comorbidity Questionnaire that assesses 13 comorbidities and has been validated for epidemiological trials among older adults (19), demographics, neuropsychological testing, physical performance testing, and questionnaires on functional ability.

Neuropsychological tests were used to evaluate cognitive performance and to characterize participants with MCI. Moreover, MCI was further subclassified as impairment in memory domains versus nonmemory domains using the current framework on MCI (20). Both self-report and performance-based mobility measures were used to investigate the association between MCI domains and mobility.

Cognitive measures.—Trail Making test.—The Trail Making test is a well established reliable and valid assessment of executive function that measures cognitive abilities of sequencing, visual scanning, processing speed, shifting attention, and cognitive flexibility (21,22). The test is administered in two parts, A and B, in which the participant is asked to connect circled numbers and letters. Both tests are sensitive to cognitive decline (21,22). Time to complete each test was recorded, and faster completion times indicate better performance (21,22).

Digit Symbol Substitution test.—The Digit Symbol Substitution test is a subtest of the Wechsler Adult Intelligence scale (23). The test is a measure of processing speed and visual–spatial skills, has an executive function component assessing sustained attention, and has good test–retest reliability (intraclass correlation coefficient = 0.80) (21). The test consists of a series of numbers and

corresponding symbols. The participant was asked to fill in a response form with as many corresponding symbols to numbers as possible in 90 seconds. The number of correct number–symbol matches was recorded with a higher score indicating better performance.

Hopkins Verbal Learning Test, Revised.—The Hopkins Verbal Learning Test, Revised (HVLT-R) is a valid test of verbal memory and learning (24). The test includes a list of 12 words of concrete objects that are read aloud by the examiner across three learning trials (25). The scores derived from the test are (a) total recall, the total number of words correctly recalled on trials 1–3; (b) delayed recall, the number of words correctly recalled after 20–25 minutes; and (c) recognition discrimination, the number of true responses minus the number of false responses on a subsequent recognition task (25). The HVLT-R is a valid instrument for clinical and research-based neuropsychological assessment with elderly patients (24).

Mild cognitive impairment.—The identification of participants meeting the diagnostic criteria for MCI was based on performance on the neuropsychological tests. The raw scores of each test were converted into age-adjusted standardized scores (z scores) based on published normative data from healthy age matched peers (23,26–28). Use of standardized scores allowed for comparisons across cognitive measures, cognitive domains, and across age groups. Consistent with previous studies, we used a cutoff of 1.5 *SD* below the age-adjusted means to identify impaired performance on a given cognitive measure (7,29). MCI was defined as an impairment (ie, $z < -1.5$) on two subtests within the neuropsychological test battery (HVLT-R total recall, HVLT-R delayed recall, HVLT-R recognition discrimination, Digit Symbol Substitution test, Trails A, and Trails B) (30). All participants were identified as either cognitively intact (No-MCI) or as having cognitive impairment (MCI).

MCI has been classified into two subtypes, amnestic and nonamnestic MCI, and further into single or multiple domain categories (5,30,31). Amnestic MCI denotes impairment within the cognitive domain of memory but not of sufficient severity to meet the diagnostic criteria for dementia, accompanied by preserved executive function, attention, language, and visual–spatial skills. In contrast, nonamnestic MCI denotes intact performance within the domain of memory but with impairment in at least one of the other cognitive domains (5).

The subtest scores of the HVLT-R (total recall, delayed recall, recognition discrimination) were used to define memory impairment, and the subtest scores of the Trail Making test and the Digit Symbol Substitution test (Trails A, Trails B, and Digit Symbol Substitution test) were used to define nonmemory impairment. Participants identified as having MCI were classified into one of three groups as follows: (a) single domain amnestic MCI (aMCI) if at least two tests within the memory domain were impaired (ie, $z < -1.5$) and no other cognitive impairments were identified, (b) multiple domain amnestic MCI (mdMCI) if memory and nonmemory domains were impaired, or (c) nonamnestic MCI (naMCI) if two tests within the nonmemory domain were impaired (6,30).

Measures of mobility.—Habitual Gait Speed.—Habitual Gait Speed (HGS) tested straight path walking and was measured by asking participants to walk a 4-m straight walk at their usual pace starting from a standing position (18,32). HGS is a valid and reliable measure in community-dwelling older adults (33,34) and is predictive of disability and adverse outcomes (10,34–36). Clinically meaningful differences for HGS are reported as 0.03–0.05 m/s (minimal difference) and 0.08 m/s (substantial difference) (37).

Figure of 8 Walk.—The Figure of 8 Walk (F8W) tested curved path walking (38). Participants were timed while walking in a figure of 8 pattern at their usual pace around two cones 1.5 m (5 feet) apart (39). The F8W has good test–retest reliability (intraclass correlation coefficient = 0.84) and interrater reliability (intraclass correlation coefficient = 0.90) and is a valid measure of walking skills among older adults (39).

Short Physical Performance Battery.—The SPPB is a reliable and valid measure of lower extremity performance and predictive for subsequent disability, mortality, and institutionalization among community-dwelling older adults (18,32). The SPPB is a composite score of standing balance, walking speed and the ability to rise from a chair. Each test is scored between 0 to 4 points with a maximum total score of 12. Clinically meaningful differences for the SPPB have been reported as 0.3–0.8 points (minimal difference) and 0.8–1.5 points (substantial difference) (37).

Late Life Function and Disability Index.—The Late Life Function and Disability Index assesses functioning in a variety of daily activities (40) and is associated with performance-based measures of function (41). The function component of the Late Life Function and Disability Index assesses self-reported difficulty in performing 32 physical activities. Scores on the Late Life Function and Disability Index are transformed to scaled scores (0–100) with higher scores indicating better levels of functioning (40). The subdomains of basic lower extremity (BLE) function and advanced lower extremity function were used in this study. BLE consists of 14 items including the ability to walk around the home, and advanced lower extremity consists of 11 items including abilities such as hiking a few miles. The Late Life Function and Disability Index has been validated in different cohorts of older adults (40–42).

Statistics

Descriptive analyses are presented as means with standard deviations for continuous variables and as frequencies

and percentages for categorical variables. For determining differences between two groups (MCI vs No-MCI), the Student's *t* test was used for normally distributed continuous variables, the Mann–Whitney *U* test for nonnormally distributed continuous variables, and the χ^2 test for categorical variables. Associations between each mobility measure and cognitive status were examined by analysis of variance and analysis of covariance comparing MCI versus No-MCI. First, we adjusted for gender, race, and education. Second, cognitive status was entered into similar models as a categorical variable (aMCI, mdMCI, naMCI, and No-MCI), and estimates for differences in physical performance measures between all MCI categories were calculated. Goodness of fit was investigated and physical performance measures were log-transformed where necessary. The F8W was transformed, and transformation was successful in achieving a normal distribution. Coefficients from these models are given as back-transformed 2^{β}-coefficients. As part of a post hoc analysis, we also adjusted for current health status and chronic conditions. Also, in an additional analysis, we included baseline MMSE status as a categorical variable to explore whether the distribution of low MMSE (MMSE < 24) significantly modified the association between the respective MCI subtypes and mobility. An alpha value of 0.05 was used to determine statistical significance. Data were analyzed using SAS 9.2 (SAS Institute Inc., Cary, NC).

Results

Baseline Characteristics

The 430 participants had an average age of 76.6 (*SD* = 7 years), two thirds were women, 16% had aMCI, 23% had mdMCI, and 4% had naMCI. Participants with MCI did not differ from those without MCI according to age, gender, and body mass index ($p > .05$), but a significant difference was seen in race, education, and current health status, whereby MCI was associated with poorer self-rated health ($p < .01$; Table 1).

MCI Versus No-MCI

Participants with MCI performed significantly worse in tests of mobility performance than participants without MCI (eg, HGS: $\beta = -0.13$, $p < .01$; SPPB: $\beta = -1.39$, $p < .01$), and these relationships were unchanged after adjusting for sex, race, and education ($p < .01$; Table 2). Similar results were observed in the associations of MCI with self-reported functional performance. Goodness of fit was acceptable for all measures except the F8W, which was log-transformed resulting in normally, distributed residuals.

MCI Subtypes Versus No-MCI

All MCI subtypes performed significantly worse than No-MCI on all mobility measures ($p < .05$), after adjusting for gender, race, and education, except for aMCI, which did not differ from No-MCI on F8W and BLE (Table 3).

Comparisons Between MCI Subtypes

Compared with patients with amnestic MCI, those with nonamnestic MCI performed more poorly on a number of mobility tests, for example, the SPPB ($p = .01$) and BLE ($p = .04$), and borderline significance was seen in both walking tests, for HGS ($p = .08$) and F8W ($p = .08$). Similarly, compared with patients with aMCI, those with mdMCI performed 21% worse on F8W ($2^{\beta} = 1.21$; $p < .001$) and scored 1.07 points lower on SPPB ($\beta = 1.07$, $p < .01$; Table 3). No statistically significant differences were observed between mdMCI and naMCI.

All multiple models were evaluated with the addition of current health status as an adjustment variable. The major findings were not materially altered; however, the β-estimates were diminished, and the difference in BLE between aMCI and naMCI was no longer statistically significant ($\beta = 5.53$, $p = .11$; Supplementary Appendix 1). Similar findings were observed after adjusting for chronic conditions instead of health status. Also, adjustment for MMSE categories did not materially alter our findings.

Discussion

To our knowledge, this is the first investigation to compare primary care patients with and without MCI across a broad range of mobility measures. The major findings of our study are (a) patients with MCI manifested consistently worse mobility performance compared with those without MCI across both performance-based and self-report measures of mobility and (b) when evaluating patients by MCI subtypes in relation to no MCI, these same associations held, though important differences were observed with use of certain mobility outcomes and among comparisons between certain MCI subtypes.

Our findings are consistent with prior studies reporting associations between MCI and gait speed (10,11) and add to the existing literature by showing associations between MCI and a broader range of mobility measures, including both performance-based and self-report measures. The fact that these relationships held within both performance-based and self-reported mobility outcomes is important as performance-based and self-reported functional measures have been demonstrated to assess different aspects of an individual's functioning (43). Interestingly, in differentiating MCI from No-MCI (Table 2), differences in HGS (0.12 m/s) and SPPB (1.35 points) surpassed clinically meaningful thresholds (37), which emphasizes the possible suitability of these measures as supplemental screening tools in MCI. Clinically meaningful differences have not yet been defined for F8W, BLE, and advanced lower extremity.

In general, subtypes of MCI performed worse than No-MCI on most mobility measures. Moreover, consistent

Table 1. Baseline Characteristics of Boston RISE Participants Based Upon MCI Status

		MCI Subtypes			
	No-MCI; *N* = 249	aMCI; *N* = 68	mdMCI; *N* = 98	naMCI; *N* = 15	*p* Value
Demographics					
Age	76.5±6.7	77.1±6.8	76.7±8.0	74.2±6.0	.52
Gender, female % (*n*)	69.1 (172)	70.6 (48)	60.2 (59)	80 (12)	.25
BMI	29.2±5.9	30.1±5.6	29.4±7.2	31.6±5.0	.40
Race, white% (*n*)	90.8 (226)	86.8 (59)	65.3 (64)	40 (6)	<.001
Education % (*n*)					
< High school	6.8 (17)	8.8 (6)	25.5 (25)	40 (6)	<.001
High school	24.9 (62)	38.2 (26)	39.8 (39)	20 (3)	
Graduate	37.8 (94)	33.8 (23)	20.4 (20)	20 (3)	
Post graduate	30.5 (76)	19.1 (13)	14.3 (14)	20 (3)	
Current Health, % (*n*)					
Poor–fair	13.2 (33)	17.7 (12)	27.5 (27)	46.7 (7)	<.001
Good	47.4 (118)	48.5 (33)	49.0 (48)	40.0 (6)	
Very good–excellent	39.4 (98)	33.8 (23)	23.5 (23)	13.3 (2)	
Number of chronic conditions	4.0±1.9	3.5±1.7	4.2±1.8	4.9±2.1	.02
MMSE	28.2±1.6	27.8±1.6	25.5±2.9	25.9±3.1	<.001
18–23, % (*n*)	1.2 (3)	4.4 (3)	23.5 (23)	13.3 (2)	<.001
24–30, % (*n*)	98.8 (246)	95.6 (65)	76.5 (75)	86.7 (13)	
Cognitive measures					
Trail Making test, A (s)	42.4±15.2	41.5±10.7	73.3±32.1	94.4±34.4	<.001
Trail Making test, B (s)	109.2±52.7	115.5±41.8	246.6±68-9	275.4±38.1	<.001
DSST (points)	40.7±4.5	14.5±3.4	13.7±3.3	20.4±2.0	<.001
HVLT (words)					
Total recall	21.8±4.5	14.5±3.4	13.7±3.3	20.4±2.0	<.001
Delayed recall	7.4±2.4	3.3±2.0	3.0±2.2	7.1±1.7	<.001
Recognition discrimination	10.4±1.4	7.9±1.8	7.9±2.6	10.7±1.2	<.001
Self-reported mobility					
BLE (0–100)	67.9±11.4	65.0±12.6	63.2±12.8	57.4±9.6	<.001
ALE (0–100)	44.3±13.9	38.7±14.1	38.8±15.7	33.7±16.4	<.001
Performance-based mobility					
SPPB (0–12)	9.3±2.1	8.5±2.0	7.6±2.4	7.2±2.4	<.001
HGS (m/s)	0.96±0.2	0.87±0.2	0.87±0.2	0.76±0.21	<.001
F8W (s)	8.18±2.4	8.83±2.7	10.74±4.0	10.74±5.5	<.001

Notes: MCI = mild cognitive impairment; No-MCI = no MCI; aMCI = single domain amnestic MCI; mdMCI = multiple domain amnestic MCI; naMCI = non-amnestic MCI; BMI = body mass index; MMSE = Mini Mental State Examination; DSST = the Digit Symbol Substitution test; HVLT = the Hopkins Verbal Learning test; BLE = Basic Lower Extremity function; ALE = Advanced Lower Extremity function; SPPB = Short Physical Performance Battery; HGS = Habitual Gait Speed; F8W = Figure of 8 Walk. *p* Values are given for a comparison across all four groups. *N* = 430 for all parameters (*N* = 429 for BMI).

Table 2. Mean Difference Given as Betas, 95% Confidence Intervals, and *p* Values From Multiple Regression models Demonstrating the Difference in Mobility Between Those With MCI and Without MCI Among Boston RISE Participants

	Unadjusted Model		Adjusted Model 1*	
	β (CI)	*p* Value	β (CI)	*p* Value
HGS (m/s)	−0.13 (−0.17; −0.10)	<.001	−0.12 (−0.16; −0.07)	<.001
F8W (s)†	1.19 (1.13; 1.27)	<.001	1.19 (1.13; 1.27)	<.001
SPPB (4–12)	−1.39 (−1.80; −0.98)	<.001	−1.35 (−1.80; −0.90)	<.001
BLE	−4.55 (−6.84; −2.25)	<.001	−4.06 (−6.48; −1.65)	.001
ALE	−5.97 (−8.74; −3.20)	<.001	−5.57 (−8.43; −2.71)	<.001

Notes: MCI = mild cognitive impairment; CI = confidence interval; HGS = Habitual Gait Speed; F8W = Figure of 8 Walk; SPPB = Short Physical Performance Battery; BLE = Basic Lower Extremity function; ALE = Advanced Lower Extremity function.

*Adjusted for sex, race, and education.

†F8W was log2-transformed. Results are given as 2^{β}–coefficients.

with the findings seen between those with and without MCI, the differences in HGS (≥0.09 m/s) and SPPB (≥0.71 points) surpassed the threshold of clinical meaningfulness when comparing each of the subtypes of MCI to those without MCI. In addition, some of the mobility measures differed between specific MCI subtypes. Participants with nonamnestic MCI performed significantly worse on SPPB and BLE than participants with amnestic MCI.

Table 3. Mean Difference Given as Betas, 95% Confidence Intervals, and *p* Values From Multiple Regression Model Demonstrating the Difference in Mobility Between MCI Subtypes and Those Without MCI as well as the Difference Between Single Amnestic MCI and Nonamnestic MCI Among Boston RISE Participants

	HGS (m/s)		F8W (s)*		SPPB (points)		BLE		ALE	
	β (CI)	*p* Value	β (CI)	*p* Value	β (CI)	*p* Value	β (CI)	*p* Value	β (CI)	*p* Value
aMCI vs No-MCI	−0.09 (−0.14; −0.03)	<.01	1.08 (1.00; 1.17)	.054	−0.71 (−1.30; −0.13)	.02	−2.57 (−5.74; 0.60)	.11	−4.89 (−8.66; −1.12)	.01
naMCI vs No-MCI	−0.19 (−0.30; −0.08)	<.001	1.26 (1.07; 1.47)	<.01	−2.29 (−3.46; −1.11)	<.001	−9.75 (−16.16; −3.34)	<.01	−10.50 (−18.11; −2.88)	.01
mdMCI vs No-MCI	−0.13 (−0.19; −0.08)	<.001	1.31 (1.21; 1.40)	<.001	−1.79 (−2.34; −1.24)	<.001	−4.62 (−7.62; −1.63)	<.01	−5.52 (−9.08; −1.96)	<.01
naMCI vs aMCI	−0.11 (−0.22; 0.01)	.08	1.16 (0.98; 1.38)	.08	−1.57 (−2.82; −0.33)	.01	−7.18 (−13.98; −0.38)	.04	−5.61 (−13.69; 2.47)	.17
mdMCI vs aMCI	−0.05 (−0.11; 0.22)	.15	1.21 (1.10; 1.33)	<.001	−1.07 (−1.76; −0.39)	<.01	−2.05 (−5.80; 1.70)	.28	−0.63 (−5.09; 3.82)	.78
mdMCI vs naMCI	0.06 (−0.05; 0.17)	.32	1.04 (0.89; 1.22)	.61	0.50 (−0.69; 1.69)	.41	5.13 (−1.34; 11.60)	.12	4.98 (−2.71; 12.67)	.20

Notes: MCI = mild cognitive impairment; No-MCI = no MCI; aMCI = single domain amnestic MCI; mdMCI = mixed domain amnestic MCI; naMCI = nonamnestic MCI; HGS = habitual gait speed; F8W = Figure of 8 Walk; SPPB = Short Physical Performance Battery; BLE = Basic Lower Extremity function; ALE = Advanced Lower Extremity function; CI = confidence interval. The model was adjusted for sex, race, and education.
*F8W was log2-transformed. Results are given as 2^{β}–coefficients.

Further, participants with multiple MCI performed worse on F8W and SPPB than those with amnestic MCI alone. Thus, older persons with nonamnestic impairments, characterized by problems with processing speed and executive function, performed worse on mobility measures including performance-based tests and self-report measures. These findings are consistent both with a study by Bombin and coworkers (44), indicating that people with multiple domain MCI are more impaired than those with amnestic MCI and with prior studies linking executive dysfunction to disability (11,12,45). Also, in prior studies, F8W has been linked to visual scanning and set-shifting abilities (14) and HGS performance to executive function (9,12). These findings suggest that HGS and F8W may be linked to distinct patterns of cognitive impairment. Also, poorer mobility among different MCI subtypes may be due to greater severity or different patterns of peripheral neuromuscular impairments that underlie mobility. This was demonstrated in an analysis of gait analysis parameters conducted by Verghese and coworkers (11). They found that nonamnestic MCI was more related to gait parameters associated with pace of walking, whereas amnestic MCI was more associated with rhythm and variability parameters. Our study adds to this evidence by including a variety of both performance-based and self-reported mobility tests compared with a clinical assessment of one aspect of mobility, that being gait. An investigation of the severity and pattern of peripheral neuromuscular attributes, like that performed by Verghese and coworkers, was beyond the scope of this investigation but can be evaluated within future analyses of the Boston RISE cohort.

Of note, those with naMCI reported poorer health status and manifested more chronic conditions than other subtypes, which may explain their poorer performance. However, after adjusting for current health status, naMCI still performed significantly worse than aMCI on the more complex performance-based mobility measure, SPPB, suggesting that part of the difference in performance between the two groups is likely due to different cognitive deficits.

Our results have important clinical implications. Within a population-based study of community-dwelling older adults (26), the prevalence of coexisting cognitive impairment and slow gait was 7%. Our findings suggest that the rate of cognitive impairment is much higher among primary care patients undergoing screening for mobility problems. Given the likely progression from MCI to dementia (8) and the knowledge that coexisting cognitive impairment and mobility limitations increases the risk of institutionalization(3), early detection of these patients is critical for initiating preventative and ameliorative therapies. One mode of therapy that can improve mobility is exercise and rehabilitative care (46,47). However, patients with cognitive disabilities have commonly been excluded from large clinical trials evaluating exercise or rehabilitative care as therapies for preventing functional decline (47,48). Rehabilitative

therapy requires a capacity to learn; yet, learning may be challenged if MCI is present. Therefore, rehabilitative care paradigms for older adults with mobility problems should be developed that account for common types of MCI and the specific cognitive deficits indicated.

Limitations

Our study is cross-sectional and therefore we cannot infer a causal association between cognitive impairment and mobility limitations. Furthermore, the study was observational and therefore we might have missed some confounders. However, the estimates did not change meaningfully when adjusting for known confounders. The standardized scores used in the determination of MCI were not adjusted for education, which could influence the association between MCI and function. However, we did adjust for education in the multiple regression analyses. Our sample size was small for some MCI subtypes and corresponding analyses may not have been sufficiently powered to observe true differences between these groups. However, even given these small sample sizes, the differences between subgroups were statistically significant, and our hypotheses were predefined. Our study sample is representative of older adults, who had at least some evidence of mobility problems and were living within a 10-mile radius of our center, and may not generalize to older adults residing in other regions. It is possible that our sample included some individuals with mild dementia. However, we attempted to screen out those with moderate to severe dementia by using a MMSE cut point of 18 and our entry criteria required participants to have the ability to live and function independently in the community. Moreover, when adjusting for MMSE as part of a post hoc analysis, the findings were not materially altered, suggesting the burden of cognitive impairment had a minimal influence on the findings. Lastly, the neuropsychological battery utilized was circumscribed and did not evaluate other aspects of cognition that may be relevant to mobility (ie, visuoconstructional skills). Thus, there is the possibility that some individuals were misclassified with regard to MCI subtype. Despite these potential limitations, our study provides a unique contribution to the literature because of its design within primary care and use of a broad range of clinically feasible mobility measures.

Conclusions

Among older primary care patients, performance on a broad range of mobility measures is associated with MCI status. Performance is worse among those with MCI, and these differences extend across different MCI subtypes, appearing to be poorest among those with nonamnestic MCI.

Supplementary Material

Supplementary material can be found at: http://biomedgerontology.oxfordjournals.org/.

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