Physical Fitness in Hospitalized Frail Elderly Patients

Kristina Åhlund
Physical Fitness in Hospitalized Frail Elderly Patients

Kristina Åhlund

Department of Medical, Health and Caring Sciences
Linköping University, Sweden
Linköping 2020
To my family
Johan, Vilgot and Elvira

En liten darrig gumma
vill lägga sig och dö
när vinden drar i springan
och ingen skottar snö

När ingen går på stigen
och ingen bär in ved
och hon är klen och uschlig
och stel i varje led

Men när det börjar knopps
på träden i april
då vill hon gärna leva
ja, leva lite till!

Britt G Hallqvist
# CONTENTS

| Section                                                                 | Page |
|------------------------------------------------------------------------|------|
| ABSTRACT                                                              | 1    |
| SVENSK SAMMANFATTNING                                                  | 3    |
| LIST OF PAPERS                                                        | 5    |
| LIST OF CONTRIBUTIONS                                                  | 7    |
| ABBREVIATIONS                                                         | 9    |
| ACKNOWLEDGEMENTS                                                       | 11   |
| BACKGROUND                                                            | 13   |
| Demographics                                                          | 13   |
| The heterogeneity of ageing                                           | 14   |
| Multimorbidity, Disability and Frailty                                 | 16   |
| Definition of frailty                                                  | 18   |
| Frailty instruments                                                    | 19   |
| Frailty and physical fitness                                          | 19   |
| Physical activity and exercise                                         | 21   |
| AN OVERVIEW OF THE RESEARCH FIELD                                     | 23   |
| Future challenges in hospital care                                     | 23   |
| Studies in frail elderly with disability and severe multimorbidity     | 23   |
| Physical fitness and risk of decline in frail elderly individuals      | 24   |
| Conventional in-hospital care                                          | 24   |
| Comprehensive Geriatric Assessment and Care                            | 25   |
| Physical activity and exercise in the treatment of frailty             | 26   |
| Patients’ perspective on physical activity and exercise                | 27   |
| RATIONALE OF THE THESIS                                               | 29   |
| AIMS OF THE THEISIS                                                    | 31   |
| Overall aim                                                           | 31   |
| Specific aims                                                         | 31   |
| METHODS                                                               | 33   |
| Overview of the studies                                               | 33   |
| Designs and settings                                                  | 34   |
| *Study I*                                                              | 34   |
| *Study II*                                                            | 34   |
| Section                                                                 | Page |
|------------------------------------------------------------------------|------|
| Data collection and procedure                                          | 34   |
| Study I (paper 1-3)                                                    | 34   |
| Study II (paper 4)                                                     | 35   |
| Measurements study I                                                   | 38   |
| Frailty                                                                | 38   |
| Multimorbidity                                                         | 38   |
| Physical fitness                                                       | 38   |
| Handgrip strength                                                      | 39   |
| Submaximal aerobic capacity                                            | 39   |
| Functional mobility                                                    | 40   |
| Lower limb strength                                                    | 40   |
| Intervention and control group                                         | 41   |
| Intervention group                                                     | 41   |
| Control group                                                          | 41   |
| Analysis, study I                                                      | 43   |
| Sample size                                                            | 43   |
| Cut-offs and previously used reference values                         | 43   |
| Change in physical fitness                                            | 43   |
| Confounders                                                            | 44   |
| Missing data                                                           | 44   |
| Overview of statistical methods used                                  | 45   |
| Analysis, study II                                                     | 46   |
| ETICS                                                                  | 47   |
| Ethical approval                                                       | 47   |
| Ethical considerations                                                 | 47   |
| RESULTS                                                                | 49   |
| Results study I (paper 1-3)                                           | 49   |
| Population                                                             | 49   |
| Physical fitness                                                       | 51   |
| Paper 1                                                                | 51   |
| Paper 2                                                                | 52   |
| Paper 3                                                                | 54   |
## Results study II (paper 4) ................................................................. 58

### DISCUSSION

Summary and discussion of the main findings ........................................... 61
Benefits of assessment of physical fitness in medical in-hospital care .......... 62
Aspects of importance within CGA .......................................................... 63
The role of the physical therapist ............................................................... 64
Meaningfulness in relation to physical activity and exercise in frail elderly patients .................................................................................. 65
Methodological considerations ................................................................. 66

- **Internal validity** ................................................................................. 66
- **External validity** ............................................................................... 69
- **Trustworthiness** ............................................................................... 69

### CONCLUSIONS .................................................................................. 71

### FUTURE IMPLICATIONS ................................................................. 73

### REFERENCES ..................................................................................... 75
Physical Fitness in Hospitalized Frail Elderly Patients
ABSTRACT

Demographic research shows that the proportion of older people in society is increasing. More people age well, but there are also more people getting old with disability and multimorbidity. The large diversity in functioning illustrates the heterogeneity of aging. Accelerated aging may lead to frailty, which is a geriatric syndrome, often used as a marker of biologic age and associated with decreased physiologic reserves, increased vulnerability and the risk of adverse health outcomes. Frail elderly people are frequent visitors within emergency hospital care and physical decline is common. Unfortunately, elderly patients with substantial multimorbidity are often excluded from clinical trials.

Physical fitness comprises a set of measurable health- and skill-related outcomes, such as cardiorespiratory endurance and muscle strength. A decrease in physical fitness may affect the prognosis negatively. However, previous research indicates that it may be possible to reverse frailty and improve physical fitness. It is therefore of the utmost interest to identify frailty and study how care is best provided, in order to prevent, reduce and postpone adverse health consequences.

The overall aim of this thesis is to study physical fitness in a group of frail elderly patients, within clinical hospital health care. The patients’ physical fitness will be evaluated and compared in different care settings during and after hospitalization. The aim is also to study the long-term consequences of changes in physical fitness in relation to mortality. To better understand the underlying factors for participation in physical activity and exercise, patients’ perceptions of the phenomena will be explored.

This thesis consists of four papers based on two studies comprising frail elderly patients with substantial multimorbidity, in connection with an in-hospital episode.

**Paper 1** was an observational study with a cross-sectional design (n=408). Different components of physical fitness were measured during an index hospital stay and the results showed that hospitalized frail elderly patients performed below previously described age-related reference values. Furthermore, physical fitness was associated with the degree of frailty, rather than the chronological age.

**Paper 2** was a prospective controlled trial, with two parallel groups. The patients included in the intervention group (n=206) were cared for at an emergency medical care unit providing care according to Comprehensive Geriatric Assessment and
Physical Fitness in Hospitalized Frail Elderly Patients

care (CGA). The control group (n=202) was cared for at conventional emergency medical care units. The multi-professional care approach at the CGA unit was shown to be beneficial, in terms of a greater proportion of patients who preserved or improved their function during the first three months after discharge from hospital, compared with conventional care.

Paper 3 had a prospective approach when evaluating the association between physical fitness and one-year mortality in those 390 patients discharged alive from a hospital care episode. The results showed that physical fitness during in-hospital care and the change in physical fitness during the first months after discharge were associated with one-year mortality.

In Paper 4, the patients’ perspective in terms of physical activity and exercise was explored. The theme of “Meaningfulness and risk of harm in an aging body” emerged, followed by the three categories of physical activity as part of daily life, goals of physical activity and exercise and prerequisites for physical activity and exercise.

These studies highlight the importance of a greater focus on physical fitness in hospitalized elderly patients. A careful assessment and a multi-professional approach may lead to beneficial results and better survival even in a group of frail elderly patients with severe multimorbidity. To increase physical activity and exercise in this group of patients, health care probably needs to improve the means of communicating the benefits and goals of exercise and facilitating them so that the risk of harm is reduced.

Key words: Physical fitness, frailty, in-hospital care, comprehensive geriatric assessment
SVENSK SAMMANFATTNING

Demografisk forskning visar att andelen äldre i samhället ökar. Fler människor åldras välmående, men det är också fler människor som åldras med funktionshinder och multisjuklighet. Det finns en stor variation i fysisk funktionsförmåga hos äldre, vilket speglar åldrandets heterogenitet. Hos människor med ett snabbt åldrandeförlopp ses en påverkan på fysiologiska faktorer, vilka ofta är förknippade med en högre biologisk ålder och sköhet. Sköhet (frailty på engelska) är ett geriatristiskt syndrom, associerat med minskade fysiologiska reserver, ökad närvarande och ökad risk att drabbas av negativa hälsoutfall. Sköra äldre anses ha ett ofta återkommande behov av akutsjukvårdens resurser och fysisk försämring är vanligt. Kunskap om sköra äldre med betydande multisjuklighet är begränsat då de ofta är excluderade från kliniska studier.

Fysisk kapacitet innefattar flera olika mätbara hälsos och skicklighetsrelaterade utfall, t.ex. kardiorespiratorisk kapacitet och muskelstyrka. Fysisk kapacitet påverkas negativt av sköhet och en minskning i fysisk kapacitet är associerat med en försämrad prognos. Tidigare forskning har visat att det är möjligt att förbättra fysisk kapacitet och därmed påverka graden av sköhet. Därför är det av största betydelse att identifiera sköra individer och att studera hur vården bäst bör utformas för att förebygga, minska och skjuta upp negativa hälsoutfall.

Det övergripande syftet med denna avhandling är att studera fysisk kapacitet i en grupp sköra äldre patienter inom akutm medicinsk sjukhusvård. Patienternas fysiska kapacitet utvärderas och jämförs i olika vårdformer, under och efter utskrivning från sjukhus. Syftet är också att studera långtidsresultaten av förändring i fysisk kapacitet avseende dödlighet. För att bättre förstå de underliggande faktorerna för deltagande i fysisk aktivitet och träning studeras patienternas egna uppfattningar av fenomenet.

Denna avhandling består av fyra artiklar som baseras på två studier innefattande sköra äldre patienter med betydande multisjuklighet, i anslutning till ett akutmedicinsk vårdtillfälle på sjukhus.

Artikel 1, baserades på en observationsstudie med tvärsnittsdesign (n=408). Olika komponenter av fysisk kapacitet mättes under ett index-vårdtillfälle och resultatet visade att sköra äldre patienter på sjukhus presterade under tidigare beskrivna åldersrelaterade referensvärden. Vidare, var fysisk kapacitet associerat med graden av sköhet snarare än kronologisk ålder.
Artikel 2, baserades på en prospektiv, kontrollerad studie med två parallella grupper. Patienterna som inkluderades i interventionsgruppen (n=206) fick akutmedicinsk sjukhusvård enligt Strukturerat Omhändertagande av Äldre (på engelska förkortat CGA). Kontrollgruppen (n=202) fick akutmedicinsk vård på en konventionell invärtesmedicinsk vårdavdelning. Det multiprofessionella omhändertagandet som kännetecknar CGA var fördelaktigt jämfört med konventionell vård och en större andel patienter bibehöll eller förbättrade sin fysiska kapacitet de första tre månaderna efter utskrivning från sjukhus.

Artikel 3, baserades på den kontrollerade studien och syftade till att prospektivt analysera associationen mellan fysisk kapacitet och 1-års mortalitet hos de 390 patienter som var i livet vid utskrivning från indexvårtdiftället. Resultaten visade att fysisk kapacitet under vårdtiden på sjukhus och förändringen i fysisk kapacitet de tre första månaderna efter utskrivning, båda var associerade med 1-års mortalitet, där låg fysisk kapacitet och försämring medförde högre dödlighet.

Artikel 4, baserades på en intervjustudie och utforskade patientperspektivet gällande fysisk aktivitet och träning. Analysen visade på temat ”Meningsfullhet och risk för skada i en äldre kropp”, baserat på tre kategorier; ”fysisk aktivitet som del av dagligt liv”, ”mål med fysisk aktivitet och träning” och ”förutsättningar för fysisk aktivitet och träning”.

Resultaten belyser vikten av att tydligt fokusera på fysisk kapacitet hos sköra äldre patienter som vårdas på sjukhus. En noggrann bedömning och ett multiprofessionellt omhändertagande tycks leda till fördelaktiga resultat, även hos sköra äldre patienter med en betydande multisjuklighet. Sjukvården behöver sannolikt förbättra kommunikationen angående fysisk aktivitet och träning, för att patienter bättre ska förstå fördelar och mål med träning och att de upplevda riskerna för skada ska minskas.
1: Åhlund K, Ekerstad N, Öberg B, Bäck M. Physical performance impairments and limitations among hospitalized frail older adults. J Geriatric Physical Therapy 2018; 41:230-235

2: Åhlund K, Bäck M, Öberg B, Ekerstad N. Effects of comprehensive geriatric assessment on physical fitness in an acute medical setting for frail elderly patients. Clinical Interventions in Ageing. 2017; 12:1929–1939

3: Åhlund K, Ekerstad N, Bäck M, Karlson B.W , Öberg B. Preserved physical fitness is associated with lower 1-year mortality in frail elderly patients with a severe comorbidity burden. Clinical Interventions in Ageing. 2019; 14:577–586

4: Åhlund K, Öberg B, Ekerstad N, Bäck M. A balance between meaningfulness and risk of harm in an ageing body – frail elderly patients’ perceptions of physical activity and exercise – an interview study. In manuscript

Papers 1-3, were reprinted according to the statements from the corresponding copyright holders/publishers. Paper 1 was reprinted according to the Copyright © 2018, The Academy of Geriatric Physical Therapy, APTA. Wolters Kluwer permits reuse in a thesis and a license was not required. You are free to use the final peer-reviewed manuscript in your print thesis directly and in your electronic thesis 12 months after the article's publication date.

For papers 2-3, authors are free to redistribute or adopt their published work for non-commercial purposes according to Attribution-Non Commercial 3.0 Unported (CC BY-NC 3.0). You must give appropriate credit, provide a link to the license: http://creativecommons.org/licenses/by-nc/3.0/us/ or send a letter to Creative Commons, PO Box 1866, Mountain View, CA 94042, USA and indicate if changes were made.

Some additional calculations are added in the result section of this thesis.
List of Contributions

LIST OF CONTRIBUTIONS

Paper 1
Study design: Kristina Åhlund, Niklas Ekerstad, Birgitta Öberg, Maria Bäck
Data collection: Kristina Åhlund, Björn Karlson, Niklas Ekerstad
Data analysis: Kristina Åhlund, Niklas Ekerstad, Birgitta Öberg, Maria Bäck, Henrik Hedevik
Manuscript writing: Kristina Åhlund, Niklas Ekerstad, Birgitta Öberg, Maria Bäck
Manuscript revision: Kristina Åhlund, Niklas Ekerstad, Birgitta Öberg, Maria Bäck

Paper 2
Study design: Kristina Åhlund, Maria Bäck, Birgitta Öberg, Niklas Ekerstad
Data collection: Kristina Åhlund, Björn Karlson, Niklas Ekerstad
Data analysis: Kristina Åhlund, Niklas Ekerstad, Birgitta Öberg, Maria Bäck, Henrik Hedevik
Manuscript writing: Kristina Åhlund, Maria Bäck, Birgitta Öberg, Niklas Ekerstad
Manuscript revision: Kristina Åhlund, Maria Bäck, Birgitta Öberg, Niklas Ekerstad

Paper 3
Study design: Kristina Åhlund, Maria Bäck, Niklas Ekerstad, Björn Karlsson, Birgitta Öberg
Data collection: Kristina Åhlund, Niklas Ekerstad, Björn Karlson
Data analysis: Kristina Åhlund, Maria Bäck, Niklas Ekerstad, Björn Karlsson, Birgitta Öberg, Henrik Hedevik
Manuscript writing: Kristina Åhlund, Niklas Ekerstad, Maria Bäck, Björn Karlsson, Birgitta Öberg
Manuscript revision: Kristina Åhlund, Niklas Ekerstad, Maria Bäck, Björn Karlson, Birgitta Öberg

Paper 4

Study design: Kristina Åhlund, Birgitta Öberg, Niklas Ekerstad, Maria Bäck

Data collection: Kristina Åhlund

Data analysis: Kristina Åhlund, Birgitta Öberg, Niklas Ekerstad, Maria Bäck

Manuscript writing: Kristina Åhlund, Birgitta Öberg, Niklas Ekerstad, Maria Bäck
ABBREVIATIONS

ADL  Activities of Daily Living
CCI  Charlson’s Comorbidity Index
CFS  Clinical Frailty Scale
CGA  Comprehensive Geriatric Assessment
CI  Confidence Interval
CONSORT  Consolidating Standards of Reporting Trials
COREQ  Consolidated Criteria for Reporting Qualitative Research
ED  Emergency Department
FI  Frailty Index
FRESH  FRail Elderly Support research group
HS  Handgrip Strength
HR  Hazard Ratio
IADL  Instrumental Activities of Daily Living
ICC  Intra Correlation Coefficient
METs  Metabolic Equivalents
MNA  Minimal Nutrition Assessment
MÄVA  Medicinsk Äldrevårdsavdelning (In Swedish)
NU  NÄL-Uddevalla Hospital Group
OR  Odds Ratio
Peak VO₂  Maximal Oxygen Consumption
RM  Repetition Maximum
RPE  Rate of Perceived Exertion
SOC  Sense of Coherence
STROBE  Strengthening the Reporting of Observational studies in epidemiology
TREEE  Is the Treatment of Frail Elderly Patients Effective in an Elderly Care Unit
TUG  Timed Up-and-Go
WHO  World Health Organization
5-STS  Five-Times Sit-to-Stand Test
6-MWT  The Six-Minute Walk Test
ACKNOWLEDGEMENTS

Many people have been involved in making this work possible. My deepest gratitude to all of you who have supported me in different ways during these years. I would like to express my special thanks to the following people.

My main supervisor, Maria Bäck, you are a role model, who with great enthusiasm and knowledge inspires me constantly to develop and become as good as I can. From the start, you were the one who convinced me that I was capable of doing this. Thanks for your helpful and positive mind!

Co-supervisor Niklas Ekerstad, through your dedication and ability to carry out large research projects, you have laid the foundations for my dissertation. Thank you for all the wise advice and valuable knowledge that have contributed to my ability to see a larger whole. I am very happy that I was asked to be part of your project!

Co-supervisor Birgitta Öberg, with your welcoming mind you made me love Linköping and the Unit of Physiotherapy already at the first meeting. Thank you for all your wisdom which, with a few words, could solve the greatest problem. Your extensive knowledge and vast experience have been a great asset.

All the participating patients and all the coworkers within the TREEE study research group. Without your helpful contributions, this work would not have been possible. Special thanks to Björn Karlson at MÄVA and Maria Ljunggren at the Department of Physiotherapy in Uddevalla for great support with data collection.

I would also like to thank the Department of Research and Development, NU Hospital Group, and especially Ninni Sernert. With your helpful, positive mind, you have supported me with many practical things and, not least, the time to enable research. Having a dedicated unit at home that supports and understands the process the doctoral student goes through is very valuable. I have always felt welcome in every aspect and I am really looking forward to continued cooperation.

The Department of Physiotherapy, NU Hospital Group, including all my colleagues who supported and encouraged me when I needed it the most. Thomas Johansson, thank you for believing in me and for your benevolent
attitude in freeing up time for this work to be possible. I really hope that my newly acquired knowledge will be useful in our department in the future. **Kikki Lundborg** for being the best colleague and friend. Our running workouts are more about talking than speed, which I really have appreciated. **Elisabeth Arkel**, because you made me focus on further education. Without your persuasion, it probably would not have happened right then. **Marta Radomska**, you are a rock that allowed me to concentrate entirely on research during intense periods. I am so happy to work together with you!

Special thanks to **Henrik Hedevik** at the unit of Physiotherapy in Linköping, for your great statistical knowledge and commitment in my studies. Your helpfulness and patience have been invaluable. Seeing you in-action in front of the computer, is really impressing!

**The Unit of Physiotherapy**, Linköping University, which has always made me feel that I am one of you, even though I had a long journey and could not always be present. It has been educative and interesting to have taken part in all the rewarding discussions at the unit’s seminars. From the perspective of all the different research areas, in addition to research, I have learned a lot about physical therapy.

My mom **Kerstin**, dad **Christer** and my sister **Maria** with family, for your great support. You have always believed in me, as only parents can. You have supported me with everything from kind words to practical chores, when I have been busy working or traveling. You have made me believe in my own capability, see opportunities and believe that everything is possible. I would also like to extend warm thanks to **Mona** and **Bosse**. It means a lot to have a big family around, who supports and takes care of everyone.

Finally, grateful thanks to my family, **Johan**, for spreading warmth and tranquility and for your ability to make me feel valuable. You made me love the forest and running out there together during the winter was great, when my head needed to rest and my legs needed to work, after many hours in front of the computer. I really hope we will continue to have fun and enjoy doing things together, I love you!

My beloved children, **Vilgot** and **Elvira**, for your great patience with your working mother. I am grateful for your ability to encourage me. Just by being there, you make me see more aspects of life and making me focus on things that are more important than work. I am so proud of you!
BACKGROUND

Demographics
For health care and research purposes, older adults are often sub-divided into three categories: young-old (65-74 years old), old-old (75-84 years old) and oldest-old (≥ 85 years old)\(^1\). In statistical contexts where social economy is included, divisions with five-year groups for age are often used and the proportion over or under 80 is discussed \(^2,3\).

Nowadays, elderly people are surviving longer than ever before and the number of elderly individuals in each category is increasing throughout the world. From an international perspective, older adults (≥80 years) will represent 12% of the European Union population by 2060 \(^3\). In Sweden, the number of people 80 years or older is estimated to increase dramatically over the next 20 years. In 2040, there will be almost one million Swedes above 80 years of age \(^2\).

![Graph showing the forecast of the number of people aged 65-79 years and 80+ in Sweden](image)

**Figure 1: Forecast of the number of people aged 65-79 years and 80+ in Sweden**

*The number of people in Sweden aged 65-79 and 80 years or older in 1960-2013 and a forecast for 2014–2060.*

*Source: Statistics in Sweden* \(^2\)
The heterogeneity of aging

The World Health Organization (WHO) uses the term “intrinsic capacity” to describe the composite of an individual’s total physical and mental capacity. This will change during the life course and is influenced by different aspects in life. There is a peak in intrinsic capacity during early adulthood and, from midlife onwards, decline is common. The trajectory tends to show great variability, where some components may decline to a greater extent, while others remain stable or even increase. This leads to great diversity in health and functional conditions in older people, only weakly associated with chronological age, which means that old people can have levels of both physical and mental capacity similar to those of a much younger person ⁴⁻⁵, see Figure 2. In order to explain the heterogeneity of older people, the term “biologic age” is sometimes used ⁶. Also perceived quality of life was found to vary widely within groups of elderly people of the same age ⁷.

Figure 2: The diversity of intrinsic capacity increases with age (WHO)

*WHO Clinical Consortium on Healthy Ageing. Report of consortium meeting 1–2 December 2016 in Geneva, Switzerland. Geneva: World Health Organization; 2017 (WHO/FWC/ALC/17.2). Licence: CC BY-NC-SA 3.0 IGO ⁴.*
Aging is associated with a decline in physical fitness, such as decreased muscle strength, cardiovascular function, lung function and balance, and the presence of diseases and age-related disabilities becomes more common. A change in body composition occurs, leading to an increased fat mass and decreased muscle mass. After the age of 30, the muscle mass decreases by about 1-2% annually. After 60 years, the annual loss of muscle mass is estimated to be around 1.5-3% and, after age 75, the loss increases further. Cardiorespiratory fitness (peak VO$_2$) is found to decline with age, even after adjustments for physical activity habits. The loss accelerates with increasing age from approximately 3% per decade after 20 years, to > 20% after 70 years. Potential factors implicated in the decline include both central and peripheral aspects of aging. However, the rate by which maximum heart rate is reduced is fairly constant at 4-6% per decade. In older ages, probably impaired oxygen utilization intrinsic to the muscles has a large impact.

An accelerated loss of physical fitness may occur in relation to lifestyle, such as sedentary behavior and diseases. Sarcopenia, or the progressive loss of skeletal muscle, is sometimes pathophysiologically regarded as an organ failure or “muscle insufficiency”, which can occur temporarily, e.g. during bedrest, or become a chronic condition. Sarcopenia is thought to play an important etiological role in the frailty syndrome and has been found related to several adverse health outcomes, decreased strength and exercise tolerance, general weakness and fatigue and may affect the ability to perform activities in daily living.
**Multimorbidity, Disability and Frailty**

![Venn diagram showing the relationships between multimorbidity, disability, and frailty.](image)

**Figure 3: Comorbidity, disability and frailty are all separate states, but they partially overlap**

Prevalences—and overlaps—of comorbidity, disability, and frailty among community-dwelling men and women 65 years and older. Percents listed indicate the proportion among those who were frail \( n = 368 \), who had comorbidity and/or disability, or neither. Total represented: 2762 participants who had comorbidity and/or disability and/or frailty. \( +n = 368 \) frail participants overall. \( *n = 2576 \) overall with 2 or more of the following 9 diseases: myocardial infarction, angina, congestive heart failure, claudication, arthritis, cancer, diabetes, hypertension, chronic obstructive pulmonary disease. Of these, 249 (total) were also frail. \( **n = 363 \) overall with an activity of daily living disability; of these, 100 (total) were also frail.

*This figure is reused with permission from Oxford University Press: Fried et al. The Journals of Gerontology: Series A, Volume 59, Issue 3, March 2004, Pages M255–M263*

Previously, when describing elderly individuals with increased vulnerability and a need for enhanced care, the terms multimorbidity/comorbidity, disability and frailty were often used interchangeably, probably because of their similarity and coexistence rate \(^{13}\). They are now identified as three different, but partially overlapping conditions, see Figure 3. Each condition individually or in combination is associated with negative health consequences \(^{12,13}\) and healthcare implications have to be adopted for the specific condition.
Multimorbidity is common, especially in people who are older. In Sweden, almost half the population live with a chronic disease and 25% are estimated to have two or more conditions. Multimorbidity is defined as “the co-occurrence of multiple chronic or acute diseases and medical conditions within one person.” Moreover, the term “comorbidity” is common in elderly research and means the occurrence of two or more chronic or acute diseases related to a specific index condition. The term “comorbidity burden” is sometimes used to describe the overall importance of the conditions and can be measured using validated instruments, such as Charlson’s Index, which may provide an indication of future prognosis. A severe comorbidity burden is associated with mortality and can be seen as a risk factor for frailty.

The WHO defines disability as an “impairment, activity limitation or participation restrictions” that may affect different domains, such as cognition, mobility and self-care. The physical components of disability are found to increase with age and are commonly diagnosed by self-reporting. Objectively, disability can be identified using instruments measuring activities of daily living (ADL) or instrumental activities of daily living (IADL). Disability can be seen as an outcome of frailty.

There is a growing understanding of frailty as a complex system. Most probably, frailty is a multifactorial consequence of cumulative decline in many bodily systems at the same time. Many components, such as inflammation, neuromuscular dysfunction, endocrine dysregulation, immune dysfunction, abnormalities in energy metabolism and failure of the central nervous system, are believed to play significant roles.

Frailty reflects vulnerability and decreased physiologic reserves and is often used as a marker of biologic age. Frailty is assumed to herald physical decline and it often involves a downward spiral of worsening physical function and poorer prognosis, comprising dependence, reduced autonomy, risk of falling, hospitalization, institutionalization and death. A frail person runs the risk of rapid deterioration when exposed to external stressors, such as acute illness, which is illustrated in Figure 4. However, frailty is a dynamic syndrome where deterioration is common, but the individual course of frailty varies and the degree of frailty can be improved even in old age.
Definition of frailty

According to the WHO, frailty is conceptually defined as “a clinically recognizable state in which the ability of older people to cope with everyday or acute stressors is compromised by an increased vulnerability brought by age-associated declines in physiological reserve and function across multiple organ systems”.

In research, there is no consensus definition of the frailty syndrome, but most researchers agree that it can be psychologic and physical, or a combination. The occurrence of sarcopenia and diminished muscle strength is a frequently mentioned and important discriminatory characteristic. In community-dwelling elderly individuals (≥65 years), a systematic review found an average prevalence of physical frailty of just under 10%, with a higher prevalence when psychosocial aspects were also included. More women than men were frail and the incidence increased significantly after 80 years of age and is estimated to be > 25% among those over 85 years of age.

Two main approaches are used to describe the syndrome. The first is the cumulative deficit model created by Rockwood, which encompasses an assortment of up to 70 symptoms, impairments, diseases and disabilities accumulated during the life course. The patient is evaluated clinically using a comprehensive assessment and a Frailty Index is created.
The frailty phenotype model by Fried is based on five criteria related to the reduced physiologic reserve and focuses on weakness (e.g., low handgrip strength), exhaustion, slow walking speed, low physical activity and weight loss, which are signs of an underlying physiologic state of multisystem and energy dysregulation. If a person fulfills ≥ 3 of these criteria, he or she is considered frail. If 1-2 criteria are fulfilled, the patient is considered pre-frail.

**Frailty instruments**

To improve care for elderly patients, frailty screening should be better integrated in clinical practice. There is a discussion relating to how this screening should be conducted and what purpose should be achieved. Many frailty instruments are validated as risk stratification instruments applicable in different settings and regarding different outcomes. Some elderly patients describe outcomes, which they considered worse than death. Frailty screening can facilitate clinical decisions about treatment and outcome measurements and assist in care planning. To be able to fulfill the purpose of risk stratification, the instrument needs to capture degrees of frailty and measure adequate domains so that good generalizability and usefulness in clinical practice can be achieved.

There is no screening instrument for frailty that can be regarded as the gold standard. Instead, there is an assortment of single- and multi-items tools that reflect one or more domains of the frailty syndrome. The most used frailty instruments in the acute care setting are the Clinical Frailty Scale (CFS), Fried’s phenotype frailty scale, and the Frailty Index (FI). In clinical practice, there is a need for a brief and accurate screening tool, which is also suitable for non-ambulatory patients. Screening instruments, such as the Clinical Frailty Scale, based on the FI, or the FRail Elderly Support research group (FRESH) screening instrument, based on the frailty phenotype, are also useful.

In this thesis, the FRESH screening instrument was used to identify frailty.

**Frailty and physical fitness**

Physical function and physical fitness are closely related concepts, but it is important to realize that they are not interchangeable. Physical function is defined as “The capacity of an individual to carry out the physical activities of daily living. Physical function reflects motor function and control, physical fitness, and habitual physical activity.” Physical function is usually evaluated with instruments measuring activities of daily living, but different instruments exist. Impaired physical function may lead to disability, institutionalization, mortality and poor health-related quality of life.
In frailty research, the term “physical performance” is commonly used. Physical performance measurements were previously used objectively to assess the performance of various activities in daily living (ADL) or physical tasks in the clinic, in contrast to self-reported ADL instruments. Only recently, a position paper formulated a clear definition: “An objectively measured body function related to mobility.” Physical performance is a multidimensional concept, including several aspects involved in performance, such as bone, balance and other neurology, cardiovascular aspects and motivation.

Physical fitness is usually defined as “A set of attributes that are either health or skill related. Physical fitness is operationalized as a set of measurable health- and skill related attributes that include cardiorespiratory fitness, muscular strength and endurance, body composition and flexibility, balance, agility, reaction time and power.” The degree to which people have these attributes can be measured with specific tests. The health-related domain of physical fitness comprises five different components, cardiorespiratory endurance, muscle endurance, muscular strength, body composition and flexibility, which do not have to be consistent, meaning it is possible to be strong and have poorer flexibility at the same time. The skill-related components comprise agility, balance, coordination, speed, power and reaction time.

People with different levels of physical fitness will react differently to physical activity that is fixed at an absolute intensity. The perceived rate of exertion and breathlessness for a given activity is determined by its oxygen cost relative to a person’s peak VO\textsubscript{2}. Individuals who in their daily living are near the margin of their peak ability, e.g. aerobic capacity or muscle strength, are more vulnerable than those who have a greater margin between what they can best achieve and what they need to perform in their daily life. When a task is perceived as strenuous, it tends to be avoided. Especially in elderly and deconditioned individuals, it may initiate a vicious cycle that further reduces aerobic capacity, causing further avoidance of physical activity and further loss of physical fitness.

As a result, accelerated loss of physical fitness components may lead to decreased muscle strength, low physical activity, slow walking speed and early fatigue, which describe four of the five criteria used to define the frailty phenotype.
Physical activity and exercise

In the literature, the two concepts of physical activity and exercise are often confused and used interchangeably, but it is important to note that they are not synonymous 47.

Physical activity is usually defined as “Any bodily movement produced by skeletal muscles that results in energy expenditure” 52. This is a complex behavior comprising more or less most of the things we do in life and can be divided into four sub-groups of activities; occupational, leisure, transport and household physical activity. Sedentary behavior is any waking behavior characterized by an energy expenditure of ≤ 1.5 metabolic equivalents (METs), while in a sitting, reclining or lying position 56.

Exercise is an activity people do with the intention of maintaining or improving fitness and is defined as “A subset of physical activity that is planned, structured and repetitive and has a final or an intermediate objective, the improvement or maintenance of physical fitness” 52.

Both concepts include skeletal muscle activities resulting in energy expenditure, but they differ in terms of the ability to maintain or improve fitness. Sporting activities are usually performed with the aim of maintaining or improving physical fitness, while occupational, household activities and many daily tasks are usually performed in the most efficient way possible, i.e. the way that requires the least energy, and without the goal of maintaining or improving physical fitness 52.

To maintain and improve health and physical fitness in adults, exercise needs to be of moderate or vigorous intensity or a combination and beyond daily physical activities 47. In older adults, exercise with moderate intensity, 20-30 min most days of the week, proved to be of greater benefit in relation to physical function, compared with those who were physically active every day but did not exercise57.
OVERVIEW OF THE RESEARCH FIELD

The following overview is based on the topics representing two clinical studies that form the basis of the four papers included in this thesis; first, frail elderly individuals in relation to physical fitness and in-hospital care and, secondly, patients’ perspective of physical activity and exercise.

Future challenges in hospital care

The demographic forecast, medical-technological developments and society’s expectations in relation to care are thought greatly to influence the need for health care. The present population forecast shows that life expectancy will increase, while morbidity will not decrease. Medical improvements in the acute phase of diseases have led to better survival rates but also to an increasing number of people with disability and chronic conditions. These patients are stable during certain periods, but they may gradually or suddenly experience an exacerbation and acute hospital care may be necessary. Frail elderly individuals with multimorbidity and disability are frequent visitors to acute medical hospital departments. In this group of patients, admissions are often inevitable, they often require a longer length of stay compared with their younger counterparts and the re-admission rate is high. In 2017, the proportion of people 65 years or older accounted for almost 20% of the Swedish population, but they accounted for half of all hospital admissions and 55% of all care given. One challenge in future health care is to be prepared when it comes to managing an increasing number of frail elderly patients.

Studies of frail elderly individuals with disability and severe multimorbidity

Frail elderly individuals with disability and severe multimorbidity are often excluded from clinical trials. The reported reasons include difficulties due to recruitment, high drop-out rates and problems related to transportation. Excluding elderly people with substantial disability and multimorbidity, who are seen every day at acute medical hospitals, results in poor generalizability to a clinical population of frail elderly individuals.
Physical fitness and risk of decline in frail elderly individuals

Each component of physical fitness affects some aspect of health and it is well known that low cardiorespiratory fitness and muscle strength individually and in combination are associated with increased mortality in adults 69-71. In addition to the risk of premature death, the accelerating decline in physical fitness with increasing age has consequences in daily life. To manage independent living, sufficient aerobic capacity and muscle strength are necessary 10,72.

During hospitalization, low physical activity and bedrest are common. It has been found that, in connection with hospital care for acute medical conditions, elderly patients who prior to hospital admission walked independently spend about 83% of their hospital stay in bed and 12% of their time on a chair 73. This has been found to be independently associated with adverse outcomes, such as longer length of stay, functional decline, disability, institutionalization and mortality 74-77. Frailty is a state of increased vulnerability which increases the risk of physical decline in connection with acute illness and in-hospital care and the recovery rate appears to be low 75,78-81. To counteract this trajectory, early mobilization is suggested. Early mobilization was shown to improve physical function and has been described as feasible and safe to execute 82.

In frailty research, ADL questionnaires are the most common method used to evaluate physical function 83. Objectively measured components of physical fitness usually involve selected groups of elderly people with less frailty and multimorbidity and often include an exercise intervention 84,85. Patients with severe multimorbidity and those who are not able to walk are usually excluded 86,87. The reference values for physical fitness tests are often divided into age strata and are described for community-dwelling older adults related to chronological age 87-90. However, there are examples of studies with a more clinical focus. Martin-Ponce et al. 91 studied the prognostic value of physical performance tests in hospitalized elderly patients, 60 years or older. The authors found that poor performance and the inability to perform walking tests and handgrip strength tests were associated with increased mortality.

Conventional in-hospital care

The form in which care is provided appears to be important. Today, limited healthcare resources may affect frail elderly patients adversely. The triaging system, where the most acute conditions are supposed to receive help first, may lead to long waiting times at the emergency room. This risks further deterioration in frail patients and the condition may both become more difficult and have greater consequences than in the first stage 44,92. The conventional acute medical ward is usually a specialized, organ-specific unit with the goal of providing care according
Overview of the Research Field

to national and international evidence-based guidelines, adapted for specific diseases. On these wards, the rehabilitation varies a great deal, but regular assessments of physical function in all patients are not usually part of routine care. Organizationally, physical therapists and occupational therapists are linked to the wards, but they often use a consultative approach and, first after discussion with nurses and physicians, they meet those patients who are considered to have a pronounced need, usually prior to discharge. Team meetings involving all healthcare professionals are rare.

However, physical therapy interventions are considered beneficial in acute hospital care to prevent deterioration and re-admissions. Specifically in connection with the transition process, contributions appear to be valuable in assessing, communicating and coordinating rehabilitation needs with other healthcare providers. They also play a role in prescribing assistive devices and exercise programs and providing information to both patients and their relatives.

Comprehensive Geriatric Assessment and Care

A Comprehensive Geriatric Assessment (CGA) is a process of assessment and care often referred to as “best practice” in relation to frail elderly patients. One common definition of a CGA is: “A multidimensional interdisciplinary diagnostic process intended to determine a frail elderly person’s medical, psychological and functional capabilities and limitations, in order to develop an overall plan for treatment and long-term follow-up.”

The CGA concept is characterized by the early identification of people running a large risk of complications and adverse health outcomes, followed by assessment, care and a follow-up plan. A CGA is made using a person-centered, holistic and multi-disciplinary approach, in addition to conventional evidence-based care, and it explicitly implies standardized instruments and an early rehabilitation perspective. The team commonly comprises physicians with both medical and geriatric competence, nurses, physical therapists, occupational therapists, social workers and dieticians who meet regularly, but all the players are sometimes not included.

To a varying extent, a CGA has proven to be beneficial, in terms of mortality, disability and cognitive functions in different settings. During in-hospital care, a CGA at admission carried out on specialized acute ward units was found to be more effective than a CGA carried out by mobile teams. Baztan et al. found that a CGA was effective compared with conventional care in reducing functional decline (ADL) at discharge and increasing the probability of living at home both at discharge and three months later, in elderly patients admitted to acute medical care.
Within a specialized CGA unit, physical therapists and occupational therapists work closely with other professions on the ward. These professionals implement a structured early rehabilitation strategy and, soon after admission, every patient is assessed regarding physical fitness and individualized treatments are provided. When needed, information is given to patients and their relatives to reduce the risk of concern and uncertainty related to physical activity. One goal is keeping the patient ambulatory and independent, to the greatest extent possible. The close collaboration between different healthcare professionals on the ward enables the sharing of information and experience, in order to use a more consistent, person-centered approach towards each patient.  

Physical activity and exercise in the treatment of frailty

An increased amount of physical activity, exercise, adequate protein intake and appropriate medication are thought to be the first-line therapies in the management of frailty and comprehensive and individualized prescribed treatment interventions can improve or slow down the deterioration.  

Regarding exercise, several systematic reviews of frail elderly individuals conclude that structured and individually prescribed exercise is beneficial with regard to several different outcome measurements, e.g. frailty status, disability, muscle strength, balance and rate of falls. Studies of institutionalized frail elderly patients found that even those with cognitive and physical impairments gained from resistance, balance and functional exercise programs. The authors advocated moderate to high-intensity exercise, meaning that the participants were encouraged to exercise at an intensity of 40-80% of 1 repetition maximum (RM) and to increase the load progressively.  

However, there is no “golden standard” for exercise programs in frail elderly individuals, but it has been reported that multi-component exercise interventions, including resistance exercise, aerobic, balance and flexibility exercises, are effective in improving physical fitness in pre-frail and frail older adults. Individualized and specific exercise appears to be important and a prescription should first be implemented after an examination of the patients’ current health and fitness status and include progression and a follow-up plan.
Patients’ perspective of physical activity and exercise

Older people are generally less physically active than younger adults. They spend more time sitting and have been shown to be mainly engaged in lower-intensity activities and rarely in activities of high intensity, compared with younger adults. Multimorbidity and disability are thought to further reduce the level of physical activity.

Previous studies of elderly people described barriers to participating in exercise programs related to poor health, fear of falling and a perceived need for rest. Moreover, the expectations of the exercise intervention and problems related to transportation to the exercise facility were important aspects. A systematic review of both quantitative and qualitative research highlighted problems related to lack of evidence in terms of barriers and motives for exercise in the oldest population and in frail elderly individuals with severe multimorbidity, as their perceptions may differ from those of less frail community-dwelling older people.
RATIONALE OF THE THESIS

According to the WHO, the maintenance of physical function is fundamental. It gives older adults an opportunity to be and do what they have reasons to value\(^5\). Old people constitute a heterogeneous group and age, multimorbidity and frailty are supposed to influence functioning.

Frail elderly individuals are frequent visitors to medical acute hospitals. Frailty means increased vulnerability, which may lead to adverse outcomes, such as physical deterioration, in connection with acute illness and hospitalization. Interventions to prevent or slow down the deterioration process, before leading to poorer physical function or disability, should therefore be important concerns for health care. It is unfortunate that frail elderly patients with severe multimorbidity are often excluded from clinical trials, which leads to an existing gap in knowledge, specifically regarding physical fitness in a hospital setting.

There are good examples of acute medical care units tailored to match the holistic needs of frail elderly patients. These units work on the basis of CGA and involve physical therapists to a greater extent, compared with conventional care. Previous evaluations show beneficial results in a hospital setting for different outcome measurements, such as return home, disability (ADL), mortality and readmission rates.

Physical fitness is closely related to physical function and, to improve in physical function, it is necessary to improve the components of physical fitness. Physical fitness has also been shown to be related to future prognosis. To our knowledge, there is no study that has thoroughly examined the effects of CGA on physical fitness or the impact of preservation/improvement in connection to hospital care from a longer perspective.

The effects of physical activity and exercise are compelling, even at older ages. However, there are still challenges when it comes to making frail elderly patients more physically active and few frail elderly patients participate in regular exercise. In order to better design rehabilitation programs for these patients, it is also important to explore the patients’ perspective. Qualitative research can provide valuable knowledge and add patients’ expertise to the way care may be improved.
Aims

AIMS

Overall aim
The overall aim of this thesis is to study physical fitness in a group of frail elderly patients, within clinical hospital health care. The patients’ physical fitness will be evaluated and compared in different care settings during and after hospitalization. The aim is also to study the long-term consequences of changes in physical fitness on mortality. To better understand the underlying factors for participation in physical activity and exercise, patients' perceptions of the phenomena will be explored.

Specific aims

1. To, in a Swedish context, describe measurements of physical fitness in hospitalized frail older adults in relation to the degree of frailty.

2. To compare physical fitness during the acute care of frail elderly patients at a CGA unit versus conventional care and at a three-month follow-up.

3. To analyze 1) the association between physical fitness measurements and one-year mortality and 2) the association between preserved physical fitness during the first three months after discharge from emergency hospital care and one-year mortality.

4. To explore the perceptions of physical activity and exercise among frail elderly patients with a severe comorbidity burden after acute hospital care.


**METHODS**

**Overview of the studies**

This thesis contains four papers based on two studies comprising frail elderly patients with experience of an acute period in a hospital care setting. Papers 1-3 are from Study I and Paper 4 is based on Study II.

**Table 1: An overview of the studies in the thesis**

| | Study I | Study II |
|---|---|---|
| **Design** | Prospective controlled trial, with two parallel groups | Interview study |
| **Participants** | Frail elderly patients in an acute medical in-hospital setting, n=408 | Frail elderly patients, who survived an acute medical hospital stay, n=390 |
| **Methods** | Measurements of physical fitness in connection with a medical in-patient care episode (index) | First, index values of physical fitness and, second, change in physical fitness during the first months after discharge were analyzed in relation to one-year mortality. |
| **Physical fitness measurements** | Handgrip strength Six-minute walk test Timed up-and-go Five times sit-to-stand | Handgrip strength Six-minute walk test Timed up-and-go |
| **Data analysis** | Descriptive statistics. Unpaired tests and post-hoc analysis | Descriptive statistics, multivariate Cox proportional hazard regression analysis |
| **Ethical approval** | Dnr: 8883-12 | Dnr: 8883-12 |
| **Status** | Published in J Geriatr Phys Therapy 2018;41:230-235 | Published in Clin Interv in Ageing. 2019:14 577–586 |

**Methods**
Designs and setting

Study I
This study was part of the prospective controlled clinical trial entitled “Is the Treatment of Frail Elderly Patients Effective in an Elderly Care Unit” (TREEE), carried out at the NÄL-Uddevalla (NU) Hospital Group, in western Sweden. Patients were recruited to the study between March 2013 and July 2015 in connection with a medical in-hospital care episode. For information on the design of each paper, see Table 1.

Study II
This study was derived from the TREEE research project and, during the ongoing recruitment process to the TREEE study, a qualitative interview study was also conducted. Content analysis with an inductive approach inspired by Krippendorff was chosen. The method searches for patterns in the material and involves an unprejudiced analysis of texts, based on the informants’ experiences. For additional information on Paper 4, see Table 1.

Data collection and procedure

Study I (Papers 1-3)
A total of 408 patients were included for evaluation in the study. The inclusion criteria were age ≥ 75 years, assessed as being in acute need of in-hospital treatment and frail according to the FRESH screening instrument, comprising five questions related to tiredness, falls, endurance, needing support while shopping and three or more visits to the emergency department in the past 12 months. If two or more of these questions were answered with a yes, the patient was considered to be frail. Patients with a life-threatening acute illness suitable for specialized hospital units, e.g. acute myocardial infarction or sepsis, were excluded from the study, as were patients whose informed consent could not be obtained.

When the staff on the ambulance or at the primary healthcare center identified a patient who met the inclusion criteria, they phoned a senior physician at the CGA unit or, if it was at night, the on-call physician. If the physician agreed that the patient fulfilled the inclusion criteria of the study protocol and there was a bed available at the CGA unit, the patient was admitted there directly and allocated to the intervention group. If no bed was available at the CGA unit, the patient was admitted to a conventional acute medical ward via the emergency room and allocated to the control group. As soon as possible after admission, complete information about the study was given orally and in writing and, if necessary,
repeated, by healthcare professionals working within the study. Some of the frail older adults were cognitively impaired, especially in the acute stage of illness. In these cases, informed consent was given by next of kin.

All tests of physical fitness were performed during the index hospital stay and again in connection with the follow-up visit at the hospital or in the patients’ home. It was not possible to standardize the day of testing, but the intention was to see the patient at the end of the hospital stay and the return visit was planned to be after three months ±14 days. Physical therapists primarily performed the tests, but in some cases they were performed by trained physicians. The test procedure was well practiced in advance and the performance was repeated several times during the study, in order to make the procedure standardized, throughout the study.

**Study II (Paper 4)**

This was a qualitative interview study, where the participants were originally included in the TREEE study. For inclusion and exclusion criteria, please see Study I. Additional exclusion criteria in this study were moribund patients and patients whose cognitive or communicative ability made participation difficult, such as severe dementia, aphasia or difficulty participating in an interview in Swedish.

To capture representative perceptions of the phenomenon of physical activity and exercise, a strategic sampling procedure was performed with the aim of including frail elderly patients, both men and women, with varying functional status, in both urban and rural living. The intention was to include 15-20 participants, as this was considered appropriate for capturing both common patterns and unique variations in relation to this context. In this population of frail elderly patients with severe multimorbidity, it was reasonable to calculate with a certain dropout rate. A total of 23 patients gave their informed consent to participate in the study, of which 18 finally conducted an interview.

The participants were enrolled to this interview study in connection with an acute hospital care episode. Three months after discharge from hospital, each patient was contacted by phone to decide the time and place of the interview. The participants were able to choose whether the interview would be at their homes or in a secluded room at the hospital in connection with a return visit. If the participant wanted to bring a relative, he or she was asked to remain silent during the interview.

A semi-structured interview guide was developed with the emphasis on the patients’ perceptions of physical activity and exercise, their goals and needs, perceived barriers/facilitators, perceptions of exertion and information from health care. The interview began with the following entry question: “How has your body functioned, since your discharge from hospital?” After four interviews had been performed, the study group met and discussed the interview guide and
Physical Fitness in Hospitalized Frail Elderly Patients

Interview technique. No important changes were needed, apart from adding clearer follow-up questions such as “How did you experience it” and “Can you tell me more” to further deepen the dialogue and make the patients give a more elaborate narrative.

The interviews lasted for a median of 28 minutes (range 20 to 43) and they were all tape-recorded and transcribed verbatim.

For information on the population related to each of Papers 1-4, please see Table 1.

For a flowchart relating to the population and data collection, Papers 1-4, please see Figure 5.
Methods

Figure 5: Flowchart of population and data collection (Papers 1-4)
Measurements, Study I

Clinical and demographic characteristics were collected from medical records. All the participants performed tests of physical fitness during the index hospital stay. In connection with a follow-up visit at the hospital or in the patient’s home three months later, the same variables were assessed. After one year, information on date of death was taken through the medical records or the National Cause of Death Register.

Frailty

The FRESH screening instrument is based on Fried’s phenotype frailty scale. Originally, it comprised five questions related to endurance, tiredness, falls, needing support while shopping and ≥ 3 visits to the emergency department (ED) in the past 12 months. When two or more questions were answered with a yes, the person was considered frail. The four physical questions (ED visits excluded) were later validated to identify frailty and were found to exhibit excellent clinical value in screening out frail older adults in an emergency care setting (sensitivity 84% and specificity 75%) compared with the phenotype frailty indicators. The fifth question relating to visits to the ED was of no additional value and may be omitted from the FRESH screening. In Study I, we chose to assess the degree of frailty using the four-question version of the instrument.

The FRESH screening was performed by a physician or a nurse at the time of inclusion.

Multimorbidity

Charlson’s Comorbidity Index (CCI) is a commonly used instrument for assessing the comorbidity burden and predicting short- and long-term mortality. It consists of 19 conditions, each of which is given a severity weighting (1-6) depending on the risk of dying associated with this condition. From this, an index is produced, which may give an indication of the prognosis. A CCI of ≥ 5 is often interpreted as a severe condition consistent with a poor prognosis, but even a CCI of ≥ 3 may be regarded as a substantial comorbidity burden. The CCI has been validated for use in elderly patients in an acute medical setting.

In this study, the physician completed the CCI before discharge and again at the three-month follow-up visit.

Physical fitness

In Study I, physical fitness was measured with four different tests; Muscle strength: Handgrip strength test (HS) in the papers 1-3, Submaximal aerobic capacity: Six-minute walk test (6-MWT) in the papers 1-3, Functional mobility:
Timed up-and-go test (TUG) in the papers 1-2 and lower-limb strength: Five-times sit-to-stand test (5-STS) in paper 1.

**Handgrip strength**

Isodynamic handgrip strength (HS) is a validated measurement of muscle strength in the elderly \(^{127}\).

The handgrip strength test was performed using a hand-held hydraulic dynamometer (SAEHAN, MVS In Motion, Willebroek, Belgium) with the option of an individually adapted grip position. The patient had to be in a sitting position with his/her arm next to his/her body, the elbow flexed at 90° and the wrist in a neutral position and he/she was then instructed to squeeze the dominant hand as hard as possible and then relax. The result was the peak value (kg) of three attempts, with a short rest (about one minute) between each attempt. A few patients did not manage to sit independently. They were allowed to lie in bed with their head end raised and their elbow supported.

The test of handgrip strength has been shown to have good test-retest reliability in community-dwelling elderly and in older persons with dementia (ICC = 0.97) \(^{127,128}\).

**Submaximal aerobic capacity**

The six-minute walk test (6-MWT) was originally designed to measure submaximal aerobic capacity in patients with cardiorespiratory diseases \(^{129}\) and it is also considered to be suitable for those with severe cardiovascular disease and severe multimorbidity \(^{130}\).

The 6-MWT measures the total distance covered, during a six-minute walk. The test was performed indoors, in a long, flat, straight corridor with a hard surface. The walking course was 30 m in length, with marks on the floor every 5.0 m and the turnaround points were clearly marked. The patient was given an instruction to walk as far as possible during six minutes and choose his/her own intensity of walking. Encouragement was limited, but short information, such as “well done”, “only one minute left”, was accepted \(^{129}\). In the present study, the patients were allowed to stop and continue during the test, but the test was interrupted if the patient was unable to continue, mostly due to dyspnea and strong dizziness. The walking distance was recorded in meters and calculated to the nearest full meter according to standardized mathematic rounding. In this study, no heart rate monitor was used, but, after finishing the test, all the patients rated their perceived exertion using the Borg rating of perceived exertion (RPE) scale \(^{131}\). Walking aids were allowed.
The 6-MWT has shown good test-retest reliability in community-dwelling elderly (ICC = 0.95) \(^8\).

**Functional mobility**

The timed up-and-go test has been shown to be a valid measurement of functional mobility in community-dwelling elderly adults and it correlates well with scores of gait speed (Pearson’s r=0.75) and balance (Pearson’s r=−0.72) but also with physical function (ADL) (Pearson’s r=−0.79) \(^1\). The TUG measures the time spent, in seconds, when the patient rises from a standard armchair (approx. 46 cm), walks three meters, turns around and walks back to the chair again. The three-meter distance should be clearly marked with tape that deviates from the floor color \(^2\). In the present study, the patients were instructed to walk as quickly and as safely as possible and walking aids were allowed. The TUG has been shown to have good test-retest reliability (ICC = 0.99) for community-dwelling older adults \(^8\).

**Lower-limb strength**

Rising from a seated to a standing position requires lower-extremity muscle strength. If it is performed quickly, it can also be used as a test of lower-extremity function, such as muscle power \(^3,4\). The stand chair test was identified as an important predictor of falls in elderly individuals \(^5\). There are several variants of stand chair tests. In this study, the five-times sit-to-stand test (5-STS) was used. The patient first attempts to stand up once from a standard armless chair (approx. 46 cm) with his/her arms folded across his/her chest. If the patient manages to do this, he/she rises and sits down five times in a row and the time is recorded. The test measures the time spent in seconds, from sitting position before first rising until the person stands up after the fifth rising \(^3\). The 5-STS has been shown to have good test-retest reliability (ICC = 0.96) for older adults \(^6\).
Methods

**Intervention and control group**

In Study I (Paper 2), the outcome measurements were evaluated and compared between the groups to which the patients were allocated; intervention or control group. For comparisons between the intervention and control group, see Table 2.

**Intervention group**

The intervention was care in a CGA unit. Within the NU Hospital, there are two wards specializing in care for the elderly (in Swedish, Medicinsk ÄldreVårds-Avdelning, MÄVA). In addition to care according to illness-specific, evidence-based guidelines, they worked according to the principles of an interdisciplinary CGA with evidence-based procedures and an holistic approach, where patient-centered care was the focus. The MÄVA had the opportunity to enroll patients directly, without passing the emergency room. There were dedicated discharge nurses who, at an early stage during the hospital stay, planned the discharge and a good reception in primary and municipal health care.

At the CGA unit, the teamwork was well established. Physical therapists and occupational therapists were closely linked to the unit and the team met daily. The team worked together towards the goal of making the patient independent to the greatest degree possible. There was an explicit early rehabilitation strategy and almost all the patients were assessed for physical fitness, as soon as possible after admission. On the ward, the physical therapists worked with assessments, assistive device testing and prescribing information to patients and their relatives. The aim was that the patients and their relatives should feel safe in relation to performing physical activity. In-hospital training usually consisted of functional tasks, such as mobility strategies, walking and balance exercises. Although the patients did not receive a home-based exercise program, they received structured and individualized advice regarding physical activity and exercise, as part of the intervention.

**Control group**

The patients in the control group were admitted to a ward of conventional internal medicine, where medical procedures according to national and international evidence-based guidelines were followed. Patients were admitted to the ward via the emergency room and the central care planning unit at the hospital was contacted just prior to discharge. There was no pronounced interdisciplinary collaboration, with regular team meetings between health professionals. Occupational therapists and physical therapists were linked to each of these wards, but they worked on a consultative basis, which meant that they were only contacted after a doctor or nurse felt that there was a need for an assessment or rehabilitation.
Table 2: Comparison of the management in the intervention group (CGA) and the control group (conventional acute medical care)

| Department and facilities                      | Comprehensive geriatric assessment and care                                                                 | Conventional acute medical care                                                                 |
|------------------------------------------------|------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|
| Two MÄVA (acute elderly care CGA units) wards with a total of 48 beds; one, two, or four-bed rooms | Wards of internal and emergency medicine; one, two, or four-bed rooms                                    | Division of Internal Medicine and Emergency Care                                                                 |
| Division of Internal Medicine and Emergency Care |                                                                                                            |                                                                                                   |
| Team members                                    |                                                                                                            |                                                                                                   |
| Physicians                                      | Yes. Specialists in internal medicine, family medicine and/or geriatrics                                   | Yes. Specialists in internal medicine                                                                |
| Licenced practical nurses                       | Yes. Including specialized admission and discharge nurses                                                | Yes. Including specialized admission and discharge nurses                                             |
| Occupational therapists                         | Yes. Including specialized admission and discharge nurses                                                | No. Only counseling                                                                                  |
| Physiotherapists                                | Yes. Including specialized admission and discharge nurses                                                | No. Only counseling                                                                                  |
| Nutritionists                                   | No. Only counseling                                                                                       | No. Only counseling                                                                                  |
| Treatment                                       | Systematic, structured interdisciplinary comprehensive geriatric assessment and care by validated instruments focusing on: somatic and mental health, medication review, functional and activity ability including early rehabilitation, social situation Early discharge planning | Following routines at departments of internal medicine and emergency care in accordance with guidelines |
| Admission route                                 | Directly to the MÄVA ward via ambulance or primary care                                                  | Via the emergency ward                                                                                |

For both groups, standard management procedures in accordance with national and international evidence-based guidelines were followed.

Copyright © 2017. Dove Medical Press. This table was published by Ekerstad N, et al. Clin Interv Aging. 2017. This work is published and licensed by Dove Medical Press Limited under the Creative Commons Attribution-Non Commercial 3.0 United States License. To view a copy of this license, visit http://creativecommons.org/licenses/by-nc/3.0/us/ or send a letter to Creative Commons, PO Box 1866, Mountain View, CA 94042, USA
Methods

Analysis study I

The data were computerized and analyzed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 22.0, Armonk, NY: IBM Corp). The tests used were two-sided and the statistical significance level was set at $p \leq 0.05$.

Sample size

A sample size calculation was made prior to inclusion in Study 1. It was based on change in ADL (Katz index), which was the primary outcome in the TREEE study. The effect size was based on the difference in ADL-change, between groups, from baseline to three months after discharge. No previous study with an identical primary variable was found, but one similar study which focused on ADL function during hospitalization in less frail patients provided a basis for the calculation. Using a two-sided test, 80% power and a significance level of $\alpha = 0.05$, it was necessary to include 150 patients in each study group. To compensate for the uncertainty, due to longer follow-up times which may affect the expected effect size, it was estimated that 200 patients in each study group, 400 in total, had to be included.

Cut-offs and previously used reference values

In Paper 1, cut-offs were chosen due to previously described cut-offs or age-related reference values in elderly research. For handgrip strength, cut-off values defining sarcopenia were chosen (<20 kg women and <30 kg men). For the 6-MWT, the cut-off was set at 300m based on previous research on old patients with heart failure, where ≤ 300m was considered poor aerobic capacity. A time to perform the TUG of >30 sec had previously indicated an increased risk of falling and dependence in ADL and, for the 5-STS, a time to perform of > 14.8 sec was interpreted as poorer than average in an old population (80-89 years). In Paper 3, cut-offs were used to dichotomize physical fitness into normal vs. low handgrip strength and again the sarcopenia definition was used (<20 kg women and <30 kg men). In Paper 3, the cut-offs used were based on the results from Paper 1 and the groups were categorized as 0-100m, 101-200m and >200m.

Change in physical fitness

To the best of our knowledge, there were no previously described definitions for the minimal detectable change, or the minimal clinically important change in relation to these measurements of physical fitness in hospitalized frail elderly patients with severe multimorbidity. In Papers 2 and 3, the 0- to three-month changes were trichotomized as decline, stability and improvement. Both improved and stable physical fitness were regarded as positive results in this population,
while a decline was an undesirable result. The values for change in each test were stipulated from a statistical viewpoint. As a result, the 0- to three-month change in the study population was used and, if it had decreased by one quartile or more, it was assumed to be a relevant decline. For HS, *decline* was defined as a change of -2 kg or more, *stable* as a change between the values -1 kg to +2 kg and *improved* as a change of +3 kg or more. In 6-MWT a *decline* was defined as a change of -50 m or more, *stable* as a change between the values -49 m to +23 m and *improved* as a change of +24 m or more. For the TUG a *decline* was defined as a change of +1.3 sec or more, *stable* as a change between the values +1.2 sec to -6.3 sec and *improved* as a change of -6.4 sec or more.

**Confounders**

There were several factors that could have influenced the results. From clinical experience, factors that may influence the outcome, such as age, gender and comorbidity burden, were regarded as important to consider and were included as confounders in the regression analysis (Paper 2) and in the Cox proportional hazard regression analysis (Paper 3). In the analysis of change, the index value of measurement (HS, 6-MWT or TUG) was included in the analysis as well.

**Missing data**

Many patients were unable to perform tests of physical fitness, due to an acute illness or a chronic condition. In addition, some patients were unavailable, e.g. early discharge, which meant that the results had to be separated into “unable to perform” and “missing”. In Papers 1 and 2, no imputation was made. In Paper 3, patients who were “unable to perform” were categorized in the lowest group, i.e. low handgrip strength and walking distance of < 100m. In the analysis of the 0- to three-month change in physical fitness in relation to mortality, an imputation was made, where patients who were unable to perform the tests were categorized with a value of 10 kg and 25 m respectively for the tests.
Overview of statistical methods used

Study I had a quantitative approach. An overview of the different outcome variables and statistical methods used is shown in Table 3.

Table 3: Overview of the variables and statistical methods used in Papers 1-3

| Paper 1 | Dependent variable | Independent variable | Statistical method |
|---------|--------------------|----------------------|--------------------|
| Paper 1 | Index measurements of physical fitness: HS, 6-MWT, TUG, 5-STS | FRESH screening (categorized into three groups) | Descriptive statistics, One-sample t-test (95% CI of the mean), Chi-square test between groups (categorical variables), One-way ANOVA between groups (continuous variables), Bonferroni post-hoc test |
| Paper 2 | Change in physical fitness (0-3 months): HS, 6-MWT, TUG | Type of care given: 1) CGA unit, 2) Conventional care | Descriptive statistics, Chi-square test (categorical variables), Student’s t-test between groups (continuous variables), Logistic regression models |
| Paper 3 | Events within one year | 1) Physical fitness at index (HS, 6-MWT), 2) Change in physical fitness 0-3 months (HS, 6-MWT) | Descriptive statistics, Cox proportional hazard regression analysis, 1) Hazard ratios in relation to index values of physical fitness, 2) Hazard ratios in relation to 0- to three-month changes in physical fitness |

Abbreviations:

*HS: Handgrip Strength, 6-MWT: Six-Minute Walk Test, TUG: Timed Up-and-Go, 5-STS: Five-times Sit-To-Stand, FRESH screening: FRail Elderly Support researcH group screening*
Analysis, Study II (Paper 4)

The qualitative analysis was performed using content analysis inspired by Krippendorff. It had an inductive approach and was performed in a manifest way, close to the text. The analysis process incorporated the following phases.

1) Text preparation: the first author (Kristina Åhlund) transcribed all the interviews and read the texts several times before starting to identify meaning units in each interview that related to the studied phenomenon. KÅ also began to code these units. A code is a label that briefly describes the meaning and is created with regard to the context and purpose of the study.

2) Analysis process: all the other authors (Maria Bäck, Birgitta Öberg and Niklas Ekerstad) read the transcripts to obtain a sense of the whole. MB also identified meaning units and labeled them with codes. After this, KÅ and MB met, compared the codes and created preliminary categories and sub-categories, which were presented to BÖ and NE. A triangulation process was performed and the categories were abstracted to find the latent meaning of the phenomenon, after which a theme finally emerged. The process included an iterative procedure which was on going until consensus was reached.

3) Reporting data: writing a qualitative research article reflects the iterative nature of qualitative research and the analysis continues while writing. The results have to be described to ensure trustworthiness, which usually comprises credibility, transferability, dependability and confirmability. The reporting of data in this study followed the consolidated criteria for reporting qualitative research (COREQ).
ETHICS

Ethical approval
In Study I, ethical approval was required and given by the regional ethical review board in Gothenburg (December 12, 2012). The study was also registered at the Swedish National Database of Research and Development; identifier 113021. Nov 4, 2012. http://www.researchweb.org/is/vgr/project/113021

Study II was part of Study I and only additional approval was required.

Study I: Dnr: 8883-12
Study II: Dnr: 8883-12, with additional approval: T784-13

Ethical considerations
General ethical principles according to the Declaration of Helsinki were followed. All the study participants received study information both orally and in writing from trained professionals within the research group. In connection with acute illness, frail elderly patients often need to be given information repetitively and sometimes together with their next of kin. In cases where patients had dementia or difficulty signing informed consent, this study approved consent given by proxy.

According to the Swedish Ethical Review Act (2003: 460)\textsuperscript{141}, informed consent must form the basis of research in humans. Four principles have been formulated to provide good research ethics; the principle of autonomy, the principle of non-maleficence, the principle of beneficence and the principle of fairness \textsuperscript{142}. The principle of autonomy is considered decisive when it comes to conducting research in humans and highlights the importance of respecting the individual's right to decide for him/herself. However, there is a section in the Swedish Ethical Review Act\textsuperscript{141} that regulates the opportunity to conduct research where illness or any other condition prevents the patients from giving consent themselves. Certain conditions have to be met; the results are expected to be of benefit either to the patient or to others with similar illness and the patient’s next of kin must be asked and give their permission.

In the long run, the case of no research in certain groups of patients may be disadvantageous for the group concerned. Frail elderly adults with multimorbidity, disability and cognitive impairments are unfortunately frequently excluded from scientific research \textsuperscript{61}. According to the principle of fairness, all groups in society should be offered fair and equal care, which also means that research should include all groups in society \textsuperscript{142}. 
Assessments of physical fitness may have caused some discomfort to the patients. The tests were performed at self-selected speeds and the patients were allowed to interrupt them if necessary. No patients withdrew from the study due to adverse events related to the tests of physical fitness.
RESULTS

The overarching results from this thesis are that frail elderly patients in connection with acute medical in-hospital care had poor physical fitness, which was associated with their degree of frailty rather than their chronological age, but there is still rehabilitation potential. Assessment and care in a CGA unit is superior to conventional medical care when it comes to preserving and improving physical fitness, such as submaximal aerobic capacity, handgrip strength and functional mobility. Moreover, the preservation of or improvement in physical fitness during the first three months after discharge is independently associated with the one-year prognosis. From the patients’ perspective, the perceptions of physical activity and exercise were described as a balance between what is perceived as meaningful to the individual and the risk of harm, in relation to an aging body.

Results, Study I (Papers 1-3)

Population
The population consisted of 408 older adults, 230 women (56%), with a mean age of 85.7 years (75 to 99 years). At index, all the participants were frail according to the FRESH screening and a total of 382 participants (94%) had a severe comorbidity burden, with a Charlson’s Index of ≥ 5. The most common diseases were renal failure (87%), hypertension (71%), heart failure (40%), ischemic heart disease (30%) and cerebrovascular disease (26%). The screening of nutritional status revealed that almost 64% of the population were malnourished or at risk of malnutrition. Women rated poorer health-related quality of life and lived alone to a greater extent, as compared to men. No other gender-related differences were reported. The average number of hospital days during the index care episode was 10.2 (± 6.6). Eighteen patients (4.4%) died during the index care episode. The post-hospitalization mortality was calculated for those 390 patients discharged alive. During the first three months after discharge, 11.5% of the patients died and, after one year, mortality was 37.9%.

In Paper 2, the patients were divided into two groups; the intervention group (CGA unit, n=206) and the control group (conventional care, n=202). There were no statistically significant differences between the groups, apart from a higher comorbidity burden (CCI 7.4 ± 2.1 vs 6.2 ± 1.5, p<0.001) and a longer mean length of hospital stay at index (11.2 days vs. 9.2, p=0.002) in the intervention group as compared to the control group. After three months, there were no differences between the groups (p=0.648) related to the number of hospital days, due to fewer
re-admissions in the intervention group. Regarding physical fitness, an unadjusted analysis found no differences between groups at baseline, except for the TUG, with the control group performing less well, compared with the intervention group (p<0.05). For study characteristics of the population, see Table 4.

Table 4: The study characteristics of the population

| Variable                               | Total N | Intervention group N | Control group N | P       |
|----------------------------------------|---------|----------------------|-----------------|---------|
| Age, mean ±SD                          | 408     | 206                  | 202             | 0.850   |
| Female, n (%)                          | 408     | 206                  | 202             | 0.241   |
| Frailty screening, median (min-max)    | 408     | 206                  | 202             | 0.149   |
| Charlson’s Index (CCI), mean ±SD       | 408     | 206                  | 202             | <0.001***|
| Dementia, n (%)                        | 408     | 206                  | 202             | 0.247   |
| Nutrition (MNA), mean ±SD             | 391     | 201                  | 190             | 0.492   |
| EQ-VAS, mean ±SD                       | 373     | 181                  | 192             | 0.247   |
| Lived alone, n (%)                     | 408     | 206                  | 202             | 0.055   |
| Nursing homes, n (%)                   | 408     | 206                  | 202             | 0.604   |
| Own living without home-help service, n (%) | 408 | 206                  | 202             | 0.002** |
| Number of hospital days during index care episode, mean ± SD | 408 | 206                  | 202             |         |

Nominal data are presented as n (%). Continuous data are presented as mean ± 1 SD or median with minimum to maximum. Abbreviations, SD: Standard deviation, MNA: Mini Nutritional Assessment, EQ-VAS: Euro Qol- Visual Analogue Scale. * p < 0.05, ** p < 0.01, *** p < 0.001

Copyright © 2017. Dove Medical Press. This table was adapted and reproduced from Ekerstad N, Clin Interv Aging, 2017[27]. This work is published and licensed by Dove Medical Press Limited under the Creative Commons Attribution-Non Commercial 3.0 United States License. To view a copy of this license, visit http://creativecommons.org/licenses/by-nc/3.0/us/ or send a letter to Creative Commons, PO Box 1866, Mountain View, CA 94042, USA
Physical fitness

The main results (Papers 1-3) related to physical fitness are presented below.

Paper 1

The STROBE checklist\(^{143}\) was followed, when reporting data in this paper.

In Paper 1, we found that the degree of frailty had an impact on physical fitness, while chronological age did not. Compared with previously used age-related reference values and cut-offs for the tests used, this population of frail elderly patients had poorer physical fitness, see Table 5.

Table 5: The association between frailty status and physical fitness measurements

| Variable                        | FRESH screening 1 or 2 yes | FRESH screening 3 yes | FRESH screening 4 yes | p   |
|---------------------------------|----------------------------|-----------------------|-----------------------|-----|
|                                 | N  | 95% CI          | N  | 95% CI          | N  | 95% CI          |     |
| Age (years), mean ± SD          | 80 | 85.4 ± 5.7      | 161| 85.3 ± 5.3      | 138| 86.1 ± 5.3      |     |
| Hand grip (kg), mean ± SD       | 77 | 20.7 ± 8.6      | 142| 18.5 ± 7.1      | 118| 16.8 ± 7.0      | 0.001|
| Low hand-grip, n (%)            | 77 | 57 (74.0)       | 142| 113 (79.6)      | 118| 98 (83.1)       | 0.312|
| Unable to perform test of hand-grip strength, n (%) | 80 | 3 (3.8)         | 161| 19 (11.3)       | 138| 20 (14.5)       | 0.048*|
| TUG (sec), mean ± SD            | 70 | 29.6 ± 30.1     | 119| 32.6 ± 22.7     | 84 | 37.4 ± 26.2     | 0.164|
| TUG ≥ 30 sec, n (%)             | 70 | 18 (25.7)       | 119| 51 (42.9)       | 84 | 42 (50.0)       | 0.008**|
| Unable to perform TUG, n (%)    | 81 | 11 (13.6)       | 159| 40 (25.2)       | 135| 51 (37.8)       | <0.001***|
| 6-MWT (m), mean ± SD            | 62 | 200 ± 114       | 103| 144 ± 91        | 77 | 122 ± 93        | <0.001|
| 6-MWT ≤ 300 m, n (%)            | 62 | 46 (74.2)       | 103| 96 (93.2)       | 77 | 73 (94.8)       | <0.001***|
| Unable to perform 6-MWT, n (%)  | 77 | 15 (19.5)       | 153| 50 (32.7)       | 136| 59 (43.4)       | 0.002**|
| 5-STS (sec), mean ± SD          | 43 | 23.8 ± 12.4     | 49 | 24.3 ± 8.4      | 30 | 30.2 ± 15.3     | 0.050*|
| 5-STS > 14.8 sec, n (%)         | 43 | 33 (76.7)       | 49 | 46 (93.9)       | 30 | 29 (96.7)       | 0.010**|
| Unable to perform 5-STS, n (%)  | 81 | 38 (46.9)       | 158| 109 (69.0)      | 139| 109 (78.4)      | <0.001***|

Nominal data are presented as n (%). Continuous data are presented as mean ± 1 SD.

Abbreviations: SD: Standard Deviation, FRESH: FRail Elderly Support research group instrument, TUG: Timed Up-and-Go test, 6-MWT: Six-Minute Walk Test, 5-STS: Five-time Sit-To-stand test. Low handgrip strength: W <20 kg, M <30 kg. * p < 0.05, ** p < 0.01, *** p < 0.001

Copyright © 2018 Academy of Geriatric Physical Therapy, APTA. This table is reproduced from Åhlund, et al. J geriatric Physical Therapy, 2018\(^{144}\)
Many participants were not able to perform all the tests of physical fitness during the hospital stay, due to an inability to walk without the assistance of another person, unstable medical condition and exhaustion, for example. All the tests of physical fitness were associated with the degree of frailty, where the most frail patients had the poorest performance. ADL ability and poor nutritional status were significant factors for not being able to perform tests including ambulation, see Table 6.

Table 6: Characteristics of the patients who were unable to perform tests of physical fitness during the index care episode

| Variable                     | Hand-grip strength, n=380 | TUG , n=375 | 6-MWT, n=366 | 5-STS, n=378 |
|------------------------------|----------------------------|-------------|--------------|--------------|
| Able to perform              | Unable to perform          | p-value     | Unable to perform | p-value |
| Age, mean ± SD               | 85.7 ± 5.4                 | 85.7 ± 4.5  | 0.99         | 85.4 ± 5.2   | 86.1 ± 5.6  | 0.35         | 86.4 ± 5.0   | 86.2 ± 5.4  | <0.01*       |
| Female, n (%)                | 147 (43.6)                 | 194 (44.2)  | 0.45         | 159 (58.2)   | 52 (51.0)   | 0.21         | 143 (59.1)   | 66 (53.2)   | 0.28         | 71(58.2)     | 142 (55.5)  | 0.28         |
| FRESH median (min-max)       | 3.0 (2-4)                  | 3.5 (2-4)   | 0.01*        | 3.1 (2-4)    | 3.5 (2-4)   | <0.01*       | 3.0 (2-4)    | 3.0 (2-4)   | <0.01*       | 3.0 (2-4)    | 3.0 (2-4)   | <0.01*       |
| 1-2 Yes, n (%)               | 77 (98.7)                  | 1 (1.3)     |              | 62 (25.6)    | 15 (12.1)   |              | 43 (35.2)    | 38 (14.8)   |              |
| 3 Yes, n (%)                 | 142 (88.8)                 | 18 (11.3)   |              | 103 (42.6)   | 50 (40.3)   |              | 49 (40.2)    | 109 (42.6)  |              |
| 4 Yes, n (%)                 | 118 (86.1)                 | 19 (13.9)   |              | 84 (30.8)    | 51 (50.0)   |              | 30 (24.6)    | 109 (42.6)  |              |
| CCI, median ± SD             | 6.8 ± 1.9                  | 7.0 ± 1.8   | 0.70         | 6.8 ± 1.9    | 6.9 ± 1.8   | 0.52         | 6.9 ± 1.9    | 6.7 ± 1.7   | 0.40         | 6.8 (1.8)    | 6.9 (1.9)   | 0.85         |
| ADL median (min-max)         | 4.0 (0-9)                  | 6.0 (3-9)   | <0.01*       | 4.0 (0-9)    | 8 (1-9)     | <0.01*       | 4.0 (0-9)    | 7.0 (0-9)   | <0.01*       | 3 (0-8)      | 5 (0-9)     | <0.01*       |
| MNA, mean ± SD              | 10.2 ± 3.0                 | 8.5 ± 2.9   | <0.01*       | 10.4 ± 2.9   | 8.7 ± 3.3   | <0.01*       | 10.5 ± 2.8   | 8.7 ± 3.3   | <0.01*       | 10.9 ± 2.6   | 9.5 ± 3.2   | <0.01*       |

Nominal data are presented as n (%). Continuous data are presented as mean ± 1 SD or median with minimum to maximum.

Abbreviations: SD: Standard Deviation, TUG: Timed Up-and-Go test, 6-MWT: Six-Minute Walk Test. 5-STS: Five-time Sit-To-Stand test, ADL: Activities of Daily Living, MNA: Minimal Nutrition Assessment, FRESH: FRail Elderly Support researcH group instrument, CCI: Charlson’s Comorbidity Index. * p<0.05

Paper 2
The Consort checklist was followed when reporting data in this paper.

The analysis was performed in two steps, first in continuous values and then dichotomized into the categories of decline and stable/improvement. The adjusted analysis found that the intervention group had improved significantly in all components of physical fitness. The patients in the control group improved in the TUG but declined in handgrip strength and the 6-MWT. Comparing groups, there were significant advantages for the intervention group in all components of physical fitness; handgrip strength, p<0.001, 6-MWT, p<0.001 and TUG, p=0.042.
The dichotomized analysis revealed significant differences between groups for all three components of physical fitness. The intervention group declined to a lesser extent compared with the control group; handgrip strength, p<0.001, 6-MWT, p<0.001, TUG, p=0.003. For a visual picture of the results, see Figure 6.

**Figure 6: Changes in physical fitness in the CGA unit and conventional care**

*Abbreviations: 6MWT: Six-Minute Walk Test, TUG: Timed Up-and-Go test, CGA: Comprehensive Geriatric Assessment*

*Copyright © 2017. Dove Medical Press. Reproduced from Åhlund, et al. Clin Interv Aging. 2017 146.* This work is published and licensed by Dove Medical Press Limited under the Creative Commons Attribution-Non Commercial 3.0 United States License. To view a copy of this license, visit http://creativecommons.org/licenses/by-nc/3.0/us/ or send a letter to Creative Commons, PO Box 1866, Mountain View, CA 94042, USA

In the regression analysis, the odds ratios (OR) showed the extent to which the outcome was influenced by the intervention. After adjustment, the ORs for decline were handgrip strength OR 4.4 (CI 95% 2.2 to 9.1), 6-MWT OR 13.9 (CI 95% 4.2 to 46.2) and TUG OR 2.5 (CI 95% 1.1 to 5.4) for the tests respectively, see Table 7.
Table 7: Decline in physical fitness 0-3 months

| Variable                  | Intervention group | Control group | OR (CI 95%) |
|---------------------------|--------------------|---------------|-------------|
|                           | n                 | n (%)         | Unadjusted  | Adjusted    |
| Decline                   |                    |               |             |             |
| Handgrip strength         | 133               | 23 (17.3)     | 3.2 (1.7 to 6.1) | 4.4 (2.2 to 9.1) |
| (≥ 2.0 kg or more)        | 108               | 46 (42.6)     |             |             |
| 6-MWT                     | 83                | 9 (10.8)      | 7.0 (2.8 to 17.7) | 13.9 (4.2 to 46.2) |
| (≥ 50 m or more)          | 52                | 26 (50.0)     |             |             |
| TUG                       | 105               | 18 (17.1)     | 2.8 (1.3 to 5.9) | 2.5 (1.1 to 5.4) |
| (+1.3 sec or more)        | 70                | 26 (37.1)     |             |             |

Abbreviations: 6-MWT: Six-Minute Walk Test, TUG: Timed Up-and-Go test

The 0- to 3-month change presented as dichotomized variables, decline versus non-decline, which denote preserved or improved physical fitness. Adjusted analyses were made with age, female gender, Charlson’s Index and baseline value of measurement as covariates. The data are presented as the number (%), odds ratios and a 95% confidence interval.

Copyright © 2017. Dove Medical Press. Reproduced from Åhlund, et al. Clin Interv Aging, 2017446. This work is published and licensed by Dove Medical Press Limited under the Creative Commons Attribution-Non Commercial 3.0 United States License. To view a copy of this license, visit http://creativecommons.org/licenses/by-nc/3.0/us/ or send a letter to Creative Commons, PO Box 1866, Mountain View, CA 94042, USA

Paper 3

In Paper 3, it was found that both physical fitness (handgrip strength and the 6MWT) at index and the change during the first three months after discharge from hospital were associated with one-year mortality.

The adjusted hazard ratios for one-year mortality were HR6MWT 3.3 (95% CI 1.9 to 5.8), p<0.001, where those with a walking distance at index of < 100m ran a higher risk of dying than those who walked > 200m. For handgrip strength, those with low handgrip strength at index ran a higher risk of dying than those with normal handgrip strength. HRHS low 2.4 (95% CI 1.3 to 4.3), p=0.003, see Table 7.

Patients who declined in walking distance during the first three months ran a higher risk of a poorer one-year prognosis than those who improved in walking distance, HR6MWT change decline 3.8 (95% CI 1.4 to 10.1), p=0.007. Patients who declined in handgrip strength during the first three months ran a higher risk of a poorer one-year prognosis than those who improved in handgrip strength, HRS decline 2.2 (95% CI 1.1 to 4.6), p=0.032, see Table 8 and Figure 7.

In addition, each adjusted analysis for both components of physical fitness showed that a high comorbidity burden at index (CCI ≥ 8) and male gender were associated with higher mortality, but the degree of frailty and age did not have a significant influence.
Table 8: One-year mortality in relation to performance in HS and 6-MWT

| Index | 1-year mortality in relation to physical fitness at index | 1-year mortality in relation to change in physical fitness during the first 3 months after discharge |
|-------|--------------------------------------------------------|-----------------------------------------------------------------------------------------------|
|       | Unadjusted HR (95% CI) p                               | Adjusted HR (95% CI) p |
| n     |                                                        | 0-3 months change n Unadjusted HR (95% CI) p                                                 | Adjusted HR (95% CI) p |
| 6-MWT |                                                        |                                                                |                                |
| >200m | 76 1.47 (0.77 to 2.82) 0.243 1.60 (0.83 to 3.09) 0.165 |                               |                                |
| 101-200m | 81 1.47 (0.77 to 2.82) 0.243 1.60 (0.83 to 3.09) 0.165 |                               |                                |
| 0-100 m | 197 3.29 (1.91 to 5.66) <0.001*** 3.31 (1.89 to 5.78) <0.001*** |                               |                                |
| HS    |                                                        |                                                                |                                |
| Normal | 66 1.39 (0.78 to 2.48) 0.261 1.73 (0.94 to 3.19) 0.077 |                               |                                |
| Low   | 301 2.57 (1.45 to 4.54) 0.001*** 2.39 (1.33 to 4.27) 0.003** |                               |                                |

Abbreviations: 6-MWT: Six-Minute Walk Test, HS: Handgrip Strength, HR: Hazard Ratio, CI: Confidence Interval

1-year mortality was adjusted for gender, age, CCI and frailty. 1-year mortality related to the 0-3 months change was adjusted for gender, age, CCI, frailty screening and the index value of measurement (HS or 6-MWT). The data are presented as hazard ratios and a 95% confidence interval. * p < 0.05, ** p < 0.01, *** p < 0.001

For HS, decline was defined as a change of -2 kg or more, stable as a change between the values -1 kg to +2 kg and improved as a change of +3 kg or more. In 6-MWT a decline was defined as a change of -50 m or more, stable as a change between the values -49 m to +23 m and improved as a change of +24 m or more. Normal HS was defined as >20 kg (women) and >30 kg (men). HS below these values was defined as low.

Copyright © 2019. Dove Medical Press. This table was reproduced from Åhlund, et al. Clin Interv Aging, 2019. This work is published and licensed by Dove Medical Press Limited under the Creative Commons Attribution-Non Commercial 3.0 United States License. To view a copy of this license, visit http://creativecommons.org/licenses/by-nc/3.0/us/ or send a letter to Creative Commons, PO Box 1866, Mountain View, CA 94042, USA
Figure 7: One-year mortality in relation to 0- to three-month change in physical fitness

6-MWT: Six-Minute Walk Test, HS: Handgrip Strength
In this group of patients, both improvements in and the preservation of physical fitness were defined as positive results and a decline or remaining with poor function was a non-desirable result. If the results for change were dichotomized into two categories; decline/stable with low fitness versus improved/stable instead of the previous three, a poorer prognosis was found for those patients who declined in function or retained low function, $HR_{\text{decline or } \leq 100\text{m}}$ 3.6 ($95\%\ CI$ 1.86 to 6.84), $p <0.001$ and $HR_{\text{decline or stable low HS}}$ 2.4 ($95\%\ CI$ 1.2 to 4.7), $p=0.011$, see Table 9.

Table 9: One-year mortality in relation to dichotomized values for 0- to three-month change

| 0-3 months change | Unadjusted | Adjusted |
|-------------------|------------|----------|
|                    | n          | HR (95% CI) | p       | HR (95% CI) | p       |
| 6-MWT              |            |            |         |            |         |
| Declined or stable ≤100 m | 168 | 2.90 (1.62 to 5.21) | <0.001*** | 3.57 (1.86 to 6.84) | <0.001*** |
| Improved or stable >100m | 83 | 1 | 1 |
| HS                 |            |            |         |            |         |
| Declined or stable low | 214 | 2.06 (1.14 to 3.75) | 0.017* | 2.41 (1.23 to 4.72) | 0.011* |
| Improved or stable normal | 62 | 1 | 1 |

Abbreviations: 6-MWT: Six-Minute Walk Test, HS: Handgrip Strength, HR: Hazard Ratio, CI: Confidence Interval

1-year mortality related to the 0-3 months change was adjusted for gender, age, CCI, frailty screening and the index value of measurement (HS or 6-MWT). The category declined or stable ≤100 m included those patients who remained at the level of 100m or below in walking distance, at both index and 3-month follow-up. The category declined or stable low included those patients who had low HS at both index and at 3-month follow-up.

Normal HS: >30 kg men, >20 kg women. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$
Results, Study 2 (Paper 4)

Eighteen interviews were conducted in Study II. The characteristics of the population are presented in Table 10.

Table 10: Characteristics of the study population (Paper 4) (N=18)

| Characteristic                                      | Value          |
|-----------------------------------------------------|----------------|
| Age (years), median (min-max)                       | 85.5 (75-94)   |
| Female, n (%)                                       | 9 (50 %)       |
| Frailty, FRESH screening, median (min-max)          | 3 (2-5)        |
| CCI, median (min-max)                               | 6 (5-11)       |
| Living alone, n (%)                                 | 10 (56)        |
| Home service, n (%)                                 | 6 (33 %)       |
| Assistive device indoors n (%) (walker/crutches)    | 12 (67 %)      |

Nominal data are presented as n (%). Continuous data are presented as the median (min-max).

Abbreviations: CCI: Charlson’s Comorbidity Index, FRESH screening: Frail Elderly Support Research group screening

The results are presented in an overall theme, three main categories and eight sub-categories, see Figure 8.

“Meaningfulness and risk of harm in an aging body”

“Physical activity and exercise as part of daily life”
- Occupational and household PA in daily life
- Previous experiences of exercise
- Adaptation

“Goals of physical activity and exercise”
- Perceived importance
- Information

“Prerequisites for physical activity and exercise”
- Facilitators
- Barriers
- Strategies

Figure 8 – A summary of overall team, categories and sub-categories

Abbreviations: PA: Physical Activity
In this group of frail elderly patients with substantial multimorbidity, the perceptions of physical activity and exercise were described as a balance between what they perceive as meaningful to themselves and the risk of harm in relation to their aging body. Physical activity and exercise as part of daily life, goals of physical activity and exercise and prerequisites for physical activity and exercise were separate categories that contributed to this theme. The results are described in detail in the manuscript of Paper 4 (pages 8-13).
DISCUSSION

Summary and discussion of main findings

This thesis provides a picture of the physical fitness status in frail elderly patients during an acute care event and reflects how different forms of care may affect physical fitness during the first months after discharge from hospital. Furthermore, the long-term consequences of both poor initial physical fitness status and deterioration in connection with an in-hospital stay were studied. To deepen this understanding, the patients’ perceptions of physical activity and exercise were also explored.

We found that measurements of physical fitness were related to the degree of frailty rather than the chronological age. Greater focus should be placed on physical fitness within hospital care, including an individualized assessment of each patient to make tailored interventions to prevent deteriorations in physical function possible.

We also found that the organization of health care had an impact on outcomes related to physical fitness. An holistic care approach through a CGA was shown to have a positive effect on components of physical fitness, such as muscle strength, submaximal aerobic capacity and functional mobility. In Paper 3, we found that physical fitness was associated with the long-term prognosis. Greater physical fitness (submaximal aerobic capacity and muscle strength) in connection with an emergency medical in-hospital stay and the preservation of or improvement in physical fitness during the first months after discharge were both independently associated with one-year survival. As it is known that it is possible to affect the physical fitness status, even in frail and multimorbid elderly patients, preventing a deterioration in connection with emergency medical in-hospital care should be a top priority, in order to achieve a better prognosis.

The evidence relating to the benefits of physical activity and exercise is compelling, but few frail elderly patients are still sufficiently physically active and participation in exercise programs is low. In Study II, the findings describe a balance between what the patients perceive as meaningful and the risk of harm in an aging body. This includes aspects related to physical activity and exercise as part of daily life, goals for physical activity and exercise and the prerequisites needed to enable physical activity and exercise. In order to improve patients’ understanding of the benefits of physical activity and exercise and to reduce the perception of risk, the healthcare system should develop routines for the way physical activity and exercise are best communicated to each patient.
Benefits of assessment of physical fitness in medical in-hospital care

In order to provide health care that takes account of the heterogeneous nature of elderly patients, we first have to identify those patients that risk a deterioration in connection with in-hospital care. It is recommended that frailty screening to identify frailty and facilitate risk stratification should be performed with instruments that capture multiple domains of the frailty syndrome. Since frailty is strongly related to progressive disability, additional assessments focusing on components of physical fitness should also be made of patients identified as frail. Greater attention to the physical domains, at an early stage during the hospital stay, would probably facilitate the tailoring of interventions adapted to suit each patient.

Based on clinical experience, today’s acute emergency in-hospital care often involves a brief evaluation of physical function that determines further assessment, such as whether the patient is self-ambulatory on the ward, or whether the patient or relatives state a need for increased assistance in their home after discharge. The CGA was first developed as a diagnostic process to identify people who would benefit from enhanced treatment. In the care of cardiovascular diseases, different assessments of frailty screening, as well as single measurements of physical fitness, are discussed. This information is thought to be helpful in clinical decision-making relating to invasive strategies based upon risk stratification, nutrition therapy and tailoring secondary prevention, including physical activity advice and exercise-based cardiac rehabilitation programs.

Questionnaires (e.g. the Katz ADL index or the Barthel ADL index) are common when measuring self-reported physical function in hospitalized frail elderly patients. Self-reports are often used in large studies because they are easy to administer and capture the patient’s own perspective of functioning. However, there is a risk of over- and underestimation, recall bias and social desirability. Objective measurements of physical fitness are thought to be more precise. Although performance-based measurements for use in clinical settings are less accurate than laboratory-based tests, they have been shown to be applicable and valuable in detecting impairments at an early stage, before they affect overall physical function and become visible in an ADL index. Performance-based measurements have also been found to be able to discriminate across a larger spectrum of physical fitness and to be capable of measuring changes over time to a greater extent, compared with a self-reported ADL-index.

Instruments for use in a clinical setting need to be feasible and without a need for advanced equipment, time efficient and easy to perform. Previously, reference values for the 6-MWT, HS and TUG, for example, were established in different settings, but only in relation to chronological age. To improve the interpretability and enable the identification of impairments related to different
components of physical fitness, clinical reference values are needed for physical fitness tests, to which the results can be compared\textsuperscript{154}. It could be claimed that age-related reference values are most beneficial during the period of healthy aging. To be valuable in tailoring exercise programs for use in a clinical in-hospital setting, in addition to chronological age, it is important to consider frailty.

\textbf{Aspects of importance within CGA}

In Paper 2, a CGA was found to be beneficial in preserving physical fitness, which is consistent with previous and more recent research that found that a CGA was beneficial for many outcomes, e.g. physical function and disability\textsuperscript{83,95,102,138}. In a multifactorial intervention, such as a CGA, there are many factors that may have an impact on the outcome. Exactly which components within a CGA that are actually beneficial is not clear, but there are some differences within the CGA unit compared with conventional care, such as the multi-professional team approach, structured early rehabilitation strategy, including assessment and careful care planning, and educational efforts, which may play an important role. It is likely that components other than those directly related to physical fitness also contribute to improved hospital outcomes. A CGA also includes more structured work in other aspects of care, such as pharmaceutical reviews and the use of direct admissions.

Studies have shown that frail and disabled elderly patients with substantial multimorbidity are likely to benefit from hospital care provided in a more holistic approach\textsuperscript{93}. The CGA is now the accepted “gold standard” in caring for frail elderly patients in hospitals\textsuperscript{155}. However, in the literature, there are discussions about who a CGA will benefit most\textsuperscript{102,155,156}. In Paper 2, elderly patients aged \geq 75 years, considered frail according to the FRESH screening instrument and acutely admitted to hospital, were the target population. Patients in need of acute organ-specialized care were excluded and the intention-to-treat principle was followed. With few exclusion criteria, the study population was considered to be a good representation of clinical practice. Recently, Parker et al.\textsuperscript{155} performed an umbrella review of CGA and found that the evidence of beneficial effects in terms of disability, institutionalization and death is specifically derived from hospitalized older people with acute illness. A CGA performed in other settings, such as a post-hospital discharge CGA, did not show the same beneficial results, with no effects on mortality or physical function\textsuperscript{102}. These interventions were primarily based on assessments, discharge planning and in-home follow-ups by trained geriatric nurses and they were only eventually supplemented by visits by other professionals, including physical therapists. In hospital, a CGA may also be made in different ways. The two most common are within a dedicated ward, with direct responsibility for the patient, or by mobile teams, which provide a more consultative approach\textsuperscript{102}. 
A meta-analysis\textsuperscript{157} found that mobile teams were beneficial in terms of short-term survival but less effective regarding physical function, re-admission rates and length of hospital stay. The included studies were considered to be lacking in their description of the composition of the team and the frequency of interdisciplinary meetings. Moreover, the frequency of patient visits varied greatly. Other factors of importance for the results may be related to the use of an advisory model, which may affect adherence to the recommendations given by the geriatric team. Having control of the care process is thought to be one of the key differences between the two CGA models and could be one reason why the CGA unit is effective and mobile teams are not.

A stroke unit is an example of a well-established complex multidisciplinary hospital intervention. Evaluations of stroke units have shown beneficial outcomes regarding survival, returning home and regaining independence\textsuperscript{158}. When evaluating components that make a stroke unit effective, the results are almost the same as those found for the CGA unit; structured assessment procedures for all team members, an early mobilization and rehabilitation strategy, regular multidisciplinary team meetings and early planning for discharge\textsuperscript{159}.

**The role of the physical therapist**

From the physical fitness perspective, physical therapists should probably play a more prominent role on the acute medical ward. In the CGA unit, physical therapists are part of the team, which enables an early rehabilitation strategy on the ward. Unpublished data from the TREEE project showed that the proportion of patients that received physical therapy was about 90% in the intervention group and about 47% in the control group. Just as with other conditions in emergency care, it is likely to be important to meet specialist health professionals, even in the area of physical function. Physical therapists are trained to identify functional impairments in geriatric patients, such as slowness in walking and muscle weakness\textsuperscript{160}, and are thought to be experts in prescribing exercise to optimize physical function\textsuperscript{94}.

A recent study found that frail elderly patients of advanced age have obvious benefits from participating in exercise, even if they begin late in life\textsuperscript{161}. Moreover, exercise interventions during the in-hospital stay have been shown to increase the proportion of patients discharged to their homes and to reduce the length and cost of hospital stays for hospitalized older medical patients\textsuperscript{98}. Furthermore, physical therapy comprising \(\geq 0.5\) contacts/day was shown to be an independent predictor of functional improvement and shorter hospital stays, compared with those who had fewer contacts\textsuperscript{97}. In Paper 2, the patients did not attend exercise programs at the hospital, but assessments, careful planning and educational efforts probably meant that more focus was placed on patients’ understanding of their situation regarding physical fitness/function. They also received assistance in
finding strategies for managing barriers, such as appropriate assistive devices and, when planned for discharge, patients may have found goals of interest to manage to return home.

Twenty years ago, Landi et al. \(^{162}\) evaluated the effects of introducing a structured rehabilitation program by physical and occupational therapists within the emergency medical ward. After having worked together and learning the skills and competence of each professional, in addition to better patient-related outcomes, they also found an increased interest in geriatric rehabilitation within the team. It is likely that wards with a more structured team approach are better at developing understanding and collaboration, which may lead to improved continuity for each patient regarding rehabilitation, information and goal setting \(^{102}\).

Needless to say, the availability of rehabilitation after hospital discharge may have influenced the results of the study. The work in both study groups reflected clinical practice in emergency health care. Both groups were similar in that physical therapists did not have the opportunity to follow patients after discharge regarding physical activity and exercise. When needed, information on the patient's physical function was reported to the rehabilitation professionals within municipal care and what was offered differed depending on the municipality. The patients in the study lived in many different municipalities and the representation was similar in both groups. The structured work within the CGA unit probably led to more information about physical function and physical fitness in the hospital epicrisis. Within Study I, no information on rehabilitation outside the hospital was available.

**Meaningfulness in relation to physical activity and exercise in frail elderly patients**

“Meaningfulness” is a concept that is often used as meaning “a meaningful life” and it is relevant to discuss this in relation to aging. Meaningfulness includes all the things that create or constitute meaning for a person \(^{163}\). Subjectively, a person’s life is meaningful if he/she feels that it is and it is not possible for anyone else to interpret what meaningfulness means to another person. There are many things that influence making life meaningful. Among others, the content of life, such as activities, experiences and relationships, that lead us forward to a specific and valuable goal is regarded as important \(^{163}\).

What makes life meaningful may differ in frail elderly individuals compared with younger persons. A Canadian study by Hoover et al. \(^{164}\) found that almost 50\% of adults aged 85 years or older living at home rely on others to help them perform their daily activities. In the present study, patients described their goals for physical activity and exercise, in terms of being able to maintain independence in daily life. Many elderly people probably feel that they are on the verge of becoming more dependent. As dependency is related to life satisfaction \(^{165}\), the
patients in the present study probably found their goal for physical activity and exercise meaningful. In frail elderly individuals, loneliness is a problem of great concern \(^{166}\). Sjöberg et al. \(^{167}\) studied the meaning of existential loneliness in frail elderly individuals in long-term care facilities. The results were presented in terms of “being trapped in a frail and deteriorating body”, “being met with indifference”, “having nobody to share life with” and “lacking purpose and meaning”. In our study (Paper 4), the patients also described goals for physical activity and exercise in terms of meeting friends by participating in activities with others. After studying the patients’ stories, it is likely that, in old age, sufficient physical function is a cornerstone of independence in daily life and an important facilitator when it comes to maintaining autonomy related to social interaction.

In Paper 4, physical activity and exercise were described as a balance between what the patients perceived as meaningful and the risk of harm in an aging body. The concept of “Sense of Coherence” (SOC)\(^{168}\) has been shown to be an important determinant of life satisfaction and highlights three components related to perceived SOC and meaning; comprehensible, manageable and meaningful, which can be applied to the results of the study. Comprehensibility is related to an understanding of the purpose and knowing how to perform physical activity and exercise. It affects the benefits an individual sees and the valuable goals he/she sets. The individual also needs to perceive physical activity and exercise as manageable, which means being able to handle the demands related to the activity, e.g. risk of falls, illness or other symptoms related to the aging body. According to SOC, meaningfulness is something an individual personally values and it is related to motivation.

To enable participation in physical activity and exercise in frail elderly individuals, we have to clearly communicate the purpose of it and also give careful instructions on how they should actually perform it. A discussion about finding strategies for making participation possible is also necessary. Finally, they may need assistance in formulating valuable goals, which make physical activity and exercise meaningful for the individual.

**Methodological considerations**

**Internal validity**

The results of this thesis need to be considered in relation to the study limitations. In Study I, some systematic errors need to be addressed, as they might lead to an under- or overestimation of the results. To interpret the results properly, the large proportion of missing data may be important to consider, even though it is in line with previous research including physical fitness tests in hospitalized, frail, elderly patients \(^{91}\). Prior to the inclusion of patients, a power calculation was performed. This primarily relied on other outcomes in the TREEE study and was
described in detail in Paper 2. Compared with previously performed exercise interventions in frail elderly patients, including evaluations of physical fitness, a fairly large number of participants completed the tests.

The opportunity to make an imputation of values in the analysis was discussed. In Paper 1, imputation was not appropriate, as the aim was to describe the physical fitness status in clinical in-hospital care. In Paper 2, the reason for no imputation was due to the probability that it was the most severely ill patients who did not manage to perform the tests. If they were excluded from the analysis, the potential to maintain fitness would probably be better and a difference between the two groups might be a little more difficult to detect. If there was still a difference, it probably reflected a “true” difference. In Paper 3, there were two separate analyses. In the first, all the patients who survived the index hospital stay were included. Those who were not able to perform the tests of physical fitness represented the lowest group of function. In the second analysis, imputations were made. Those who were unable to perform the tests were assigned values of 10 kg and 25 m, which were considered low and relevant, due to the varying status of acutely admitted frail elderly patients.

The patients were allocated to the intervention group or the control group based on the availability of hospital beds, which was assumed to be the most clinically feasible method for including and evaluating patients, representative of today’s emergency hospital care. To reduce the risk of selection bias, a computerized randomization procedure is recommended. However, it was considered too difficult to implement and it is known to be challenging when evaluating clinical practice in complex hospital health care. If the allocation procedure had been computerized, it would have been necessary to give informed consent in the ambulance, which appeared to be very difficult in this group of patients with severe multimorbidity. Additionally, due to the situation with a shortage of available beds within emergency care, many patients were excluded due to there being no available bed on the ward that the lottery procedure had chosen, which would in turn probably have made the inclusion procedure very lengthy. The allocation procedure might anyway be regarded as random to a satisfactory degree, as no one in the study group was able to influence the procedure. Different physicians were involved in the allocation; this also included on-call physicians if it was night time and the patients had been admitted to the same ward, even outside the study.

Cumulative comorbidities have been considered to be highly related to reduced exercise capacity in the elderly. In Paper 2, both groups were highly affected by diseases, but the intervention group had a slightly higher comorbidity burden at index, which should mean poorer initial conditions for improvements in physical fitness. However, the patients in the intervention group managed to perform the tests to a greater extent at index, compared with the control group. This could perhaps be related to slightly longer hospital stays and also closer teamwork on the
ward, which made it easier to find opportunities to perform the tests. In turn, better initial results may lead to difficulty improving still further.

Another potential source of bias is that there was no opportunity to use blinding, as the intervention and control wards were situated in different hospital buildings. However, during the follow-up test procedure, the previous results for physical fitness were not available to the assessors.

In this specifically frail population, it would probably have been useful to have one more test accepted for non-ambulatory patients. In Paper 1, only 30% of the patients managed to perform a 5-STS test. It can be hypothesized that the 30s stand chair test would have been more valuable, as the patients would then already have had a result after one rising.

Limitations due to the chosen study measurements are almost inevitable in clinical trials. The intention was to measure different components of physical fitness, although performance-related components are part of the evaluation. The tests were previously found to have good validity when measuring different components of physical fitness and were commonly used in elderly research. Moreover, the reliability of the tests was thought to be good. However, no data on measurement properties were found for this specific group of hospitalized frail elderly patients with severe multimorbidity. In the present study, the assessors were all trained to perform the tests as similarly as possible and there were training sessions both before the data collection started and repetitively during the study period.

The lack of studies of objectively measured physical fitness in hospitalized frail elderly patients sometimes made it difficult to decide on cut-offs and relevant clinically important changes in relation to the specific tests. The disadvantage of categorization due to cut-offs is that it only offers two options and makes small differences difficult to identify. Identifying meaningful changes is challenging and depends on the contexts, such as the baseline level of function and disease considerations. In this study, we had to stipulate relevant limits for change from a statistical viewpoint beyond the standard error of measurement. The minimal clinically important change can be defined as a change that has clinical or practical importance for the persons studied. For functional performance-based tests, it should be large enough for a person to perceive the change, in daily life or improved prognosis, for example. The changes used in Study I actually resulted in changes that were fairly similar or even greater than those previously reported in elderly populations and they could be considered clinically important, as they managed to identify change related to survival.
**External validity**

Generalizability is the extent to which the results can be transferred to other populations. In the TREEE study, patients who were in acute need of medical in-hospital care and fulfilled the criteria for inclusion were enrolled consecutively. As there were few exclusion criteria and the main purpose of TREEE was to evaluate existing hospital care, we feel that the population effectively represented clinical hospital care in Sweden. To be able to include even cognitively impaired patients, it was possible to give consent through proxy.

Paper 1 reflected the clinical picture related to physical fitness measurements. A substantial proportion of the patients were unable to perform the test during the hospital stay, but there were also patients who performed quite well in relation to previously described age-related reference values. The analysis found large standard deviations for all tests. The variation in physical fitness probably mirrors the heterogeneity in this group of patients and the degree of frailty appears to be important, with slightly larger variations in less frail patients. In Paper 2, all the patients who managed to perform two measurements of physical fitness were included in the analysis. The results appear to be generalizable to patients in clinical practice who are able to ambulate, at least short distances, and to those able to follow instructions to a satisfactory extent. Overall, in the clinical context of Swedish medical emergency hospital care, the generalizability is thought to be good.

**Trustworthiness**

In qualitative research, trustworthiness, including the terms credibility, transferability, dependability and confirmability, is a quality criterion and can be compared with the reliability and validity in quantitative studies. In addition, reflexivity is an integral part, ensuring the quality and transparency of the findings. Trustworthiness answers the question, is it true? 139.

To explore the patients’ perspectives of physical activity and exercise, Study II (Paper 4) had a qualitative approach. Credibility is concerned with the aspect of truth, which means the reliability of the data and the interpretations within the analysis process 139. The patients in the study were admitted by strategic sampling with the aim of including both men and women with frailty, of varying ages and functional status and living in both urban and rural settings. This was considered appropriate in order to capture both common patterns and unique variations in relation to this context. In the analysis, an investigator triangulation was used, meaning that the data were coded, analyzed and interpreted step by step by all researchers until consensus was reached. The researchers’ various past experiences enriched the analysis, as more perspectives were weighed up.

Transferability is the applicability of the research 139. Writing a qualitative article mirrors the iterative process of continuous analysis and it also encompasses
questions of trustworthiness. There should be a broad description of the participants, the research process and the context in which the research was conducted. In our study, the characteristics of the study population are described, together with descriptions of the inclusion and exclusion criteria, the interview procedure and the interview guide. The description of the research has to be comprehensive enough for a reader to understand and decide whether the findings are transferable to his/her own setting.

*Dependability* includes the aspect of consistency, which means ensuring compliance with the particular method of analysis. *Confirmability* refers to neutrality and means that the interpretation should reflect the researchers’ own viewpoints but should still be well grounded in the data. Both dependability and confirmability are addressed by enabling transparency in the analysis process. The researchers should describe the process that produced their findings, such as coding schedule and quotations, on which their interpretations are based.

Krippendorff states that the text obtains its meaning through the reader and the interpretation of the informants’ perceptions has to be carefully managed with consciousness of the context. *Reflexivity* means examining the different assumptions and preconceptions and values that influence decisions in the research process. In Paper 4, all the interviews were performed by the same author (KÅ) who used a semi-structured interview guide to ensure that the interviews focused on the studied phenomenon. As a physical therapist, the preconception in relation to physical activity and exercise may be a positive experience beneficial to elderly people. The interview guide helped the interviewer to stay focused and neutral during the interviews and the fact that the triangulation process involved more perspectives was a strength.
CONCLUSIONS

This thesis highlighted the importance of considering physical fitness in clinical hospital health care, with special emphasis on hospitalized frail elderly patients with multimorbidity.

- The results showed that, among frail elderly patients in medical emergency in-hospital care, a substantial proportion of the patients were found to have poor physical fitness. Furthermore, physical fitness was associated with the degree of frailty, rather than the chronological age, which makes frailty important to consider when physical activity and exercise are discussed.

- A CGA was found to be beneficial in terms of the preservation of or improvement in physical fitness. It was hypothesized that the multi-professional approach and an early rehabilitation strategy, including an assessment of physical fitness and physical function and care tailored to suit each patient, were important components of the CGA, in relation to these outcomes.

- Physical fitness in connection with in-hospital care was associated with one-year mortality. Furthermore, preserved or improved submaximal aerobic capacity and muscle strength during the first months after an in-hospital episode were associated with an improved long-term prognosis. This means that frail elderly patients with a severe comorbidity burden can benefit from interventions aiming to preserve and/or improve physical fitness.

- Patients’ perceptions of physical activity and exercise, as a balance between what is perceived as meaningful and the risk of harm, highlight the need for improved information and interventions with respect to the goals and prerequisites of each patient.
FUTURE IMPLICATIONS

- Greater focus on the systematic assessment of frail elderly patients in terms of frailty, physical function and physical fitness within hospital care is vital. It is important to identify patients at risk of functional decline in connection with in-patient hospital care. Assessments of physical fitness and physical function should be offered routinely as the basis of an individualized tailored intervention.

- To enhance the preservation of and/or improvement in physical fitness in hospitalized elderly patients, a multi-professional healthcare team, including physical therapists, who are trained to assess and prescribe exercise in elderly patients, is recommended.

- Hospital care according to a CGA is considered to be “best practice” care even for frail elderly patients with substantial multimorbidity and needs to be introduced to a greater extent in hospitals, to increase access to more available patients.

- Within a comprehensive intervention such as a CGA, it is difficult to pinpoint one factor of particular importance to the outcome, even though we believe that the role of physical therapists is important. In order to use the available resources in the best possible way, future research should be designed more specifically to analyze the importance of physical therapy within a CGA.

- There is a need for improved communication about physical activity and exercise to frail elderly patients with multimorbidity, within hospital health care. The team around the patient has to be consistent in communicating benefits, risks and guidance towards realistic and valuable goals. In order to succeed with this, future research should also explore how the team around the patients perceive the patients’ needs for physical activity and exercise.
REFERENCES

1. Crews DE, Zavotka S. Aging, disability, and frailty: implications for universal design. J Physiol Anthropol. 2006;25(1):113-118.

2. Statistiska Centralbyrån (SCB). The future population of Sweden 2014–2060 (in Swedish). 2014. BE 18 SM 1401.

3. The European Commission. The 2012 Ageing Report: Underlying Assumptions and Projection Methodologies. 2011.

4. World Health Organization (WHO). Clinical Consortium on Healthy Ageing. Report of consortium meeting 1-2 December 2016 in Geneva, Switzerland. Geneva: World Health Organization 2017. License: CC BY-NC-SA 3.0 IGO.

5. World Health Organization (WHO). World report on ageing and health. 2015. ISBN 978 92 4 156504 2.

6. Mitnitski AB, Graham JE, Mogilner AJ, Rockwood K. Frailty, fitness and late-life mortality in relation to chronological and biological age. BMC Geriatr. 2002;2:1.

7. Kojima G, Iliffe S, Jivraj S, Walters K. Association between frailty and quality of life among community-dwelling older people: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(7):716-721.

8. Spirduzo WW FK, Mac Rae PG. Physical dimensions of aging. 2nd ed. Champaign, IL: Human Kinetics; 2005.

9. Hughes VA, Frontera WR, Roubenoff R, Evans WJ, Singh MA. Longitudinal changes in body composition in older men and women: role of body weight change and physical activity. Am J Clin Nutr. 2002;76(2):473-481.

10. Fleg JL, Morrell CH, Bos AG, et al. Accelerated longitudinal decline of aerobic capacity in healthy older adults. Circulation. 2005;112(5):674-682.

11. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010;39(4):412-423.
12. Theou O, Rockwood MR, Mitnitski A, Rockwood K. Disability and co-morbidity in relation to frailty: how much do they overlap? Arch Gerontol Geriatr. 2012;55(2):e1-8.

13. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. J Gerontol A Biol Sci Med Sci. 2004;59(3):255-263.

14. Statistiska Centralbyrån (SCB). Vård och omsorg om äldre (in Swedish). 2019. 2019-3-18.

15. Bayliss EA, Edwards AE, Steiner JF, Main DS. Processes of care desired by elderly patients with multimorbidities. Fam Pract. 2008;25(4):287-293.

16. Valderas JM, Starfield B, Sibbald B, Salisbury C, Roland M. Defining comorbidity: implications for understanding health and health services. Ann Fam Med. 2009;7(4):357-363.

17. Feinstein AR. The Pre-Therapeutic Classification of Co-Morbidity in Chronic Disease. J Chronic Dis. 1970;23(7):455-468.

18. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-383.

19. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146-156.

20. Hanlon P, Nicholl BI, Jani BD, Lee D, McQueenie R, Mair FS. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493 737 UK Biobank participants. Lancet Public Health. 2018;3(7):e323-e332.

21. Federici S, Bracalenti M, Meloni F, Luciano JV. World Health Organization disability assessment schedule 2.0: An international systematic review. Disabil Rehabil. 2017;39(23):2347-2380.

22. Bleijenberg N, Zuithoff NPA, Smith AK, de Wit NJ, Schuurmans MJ. Disability in the Individual ADL, IADL, and Mobility among Older Adults: A Prospective Cohort Study. J Nutr Health Aging. 2017;21(8):897-903.

23. Kojima G. Frailty as a predictor of disabilities among community-dwelling older people: a systematic review and meta-analysis. Disabil Rehabil. 2017;39(19):1897-1908.
24. Junius-Walker U, Onder G, Soleymani D, et al. The essence of frailty: A systematic review and qualitative synthesis on frailty concepts and definitions. *Eur J Intern Med.* 2018;56:3-10.

25. Clegg A, Young J, Iliffe S, Rikker MO, Rockwood K. Frailty in elderly people. *Lancet.* 2013;381(9868):752-762.

26. Schaap LA, Pluijm SM, Deeg DJ, et al. Higher inflammatory marker levels in older persons: associations with 5-year change in muscle mass and muscle strength. *J Gerontol A Biol Sci Med Sci.* 2009;64(11):1183-1189.

27. Wilson D, Jackson T, Sapey E, Lord JM. Frailty and sarcopenia: The potential role of an aged immune system. *Ageing Res Rev.* 2017;36:1-10.

28. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ.* 2005;173(5):489-495.

29. Ferrucci L, Guralnik JM, Simonsick E, Salive ME, Corti C, Langlois J. Progressive versus catastrophic disability: a longitudinal view of the disablement process. *J Gerontol A Biol Sci Med Sci.* 1996;51(3):M123-130.

30. Gill TM, Gahbauer EA, Han L, Allore HG. Trajectories of disability in the last year of life. *N Engl J Med.* 2010;362(13):1173-1180.

31. Kojima G. Frailty as a predictor of hospitalisation among community-dwelling older people: a systematic review and meta-analysis. *J Epidemiol Community Health.* 2016;70(7):722-729.

32. Vermeiren S, Vella-Azzopardi R, Beckwee D, et al. Frailty and the Prediction of Negative Health Outcomes: A Meta-Analysis. *J Am Med Dir Assoc.* 2016;17(12):1163 e1161-1163 e1117.

33. Kojima G, Taniguchi Y, Iliffe S, Jivraj S, Walters K. Transitions between frailty states among community-dwelling older people: A systematic review and meta-analysis. *Ageing Res Rev.* 2019;50:81-88.

34. Tonet E, Pavasini R, Biscaglia S, Campo G. Frailty in patients admitted to hospital for acute coronary syndrome: when, how and why? *J Geriatr Cardiol.* 2019;16(2):129-137.

35. Cesari M, Calvani R, Marzetti E. Frailty in Older Persons. *Clin Geriatr Med.* 2017;33(3):293-303.

36. Morley JE, Vellas B, van Kan GA, et al. Frailty consensus: a call to action. *J Am Med Dir Assoc.* 2013;14(6):392-397.
37. Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: a systematic review. *J Am Geriatr Soc.* 2012;60(8):1487-1492.

38. Song X, Mitnitski A, Rockwood K. Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. *J Am Geriatr Soc.* 2010;58(4):681-687.

39. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. *Sci World J* 2001; 1: 323–36.

40. Rockwood K, Theou O, Mitnitski A. What are frailty instruments for? *Age Ageing.* 2015;44(4):545-547.

41. Afilalo J, Alexander KP, Mack MJ, et al. Frailty assessment in the cardiovascular care of older adults. *J Am Coll Cardiol.* 2014;63(8):747-762.

42. Theou O, Squires E, Mallery K, et al. What do we know about frailty in the acute care setting? A scoping review. *BMC Geriatr.* 2018;18(1):139.

43. de Vries NM, Staal JB, van Ravensberg CD, Hobbel JS, Olde Rikkert MG, Nijhuis-van der Sanden MW. Outcome instruments to measure frailty: a systematic review. *Ageing Res Rev.* 2011;10(1):104-114.

44. Theou O, Campbell S, Malone ML, Rockwood K. Older Adults in the Emergency Department with Frailty. *Clin Geriatr Med.* 2018;34(3):369-386.

45. Eklund K, Wilhelmsson K, Landahl S, Ivanoff-Dahlin S. Screening for frailty among older emergency department visitors: Validation of the new FRESH-screening instrument. *BMC Emerg Med.* 2016;16(1):27.

46. Wilhelmsson K, Duner A, Eklund K, et al. Design of a randomized controlled study of a multi-professional and multidimensional intervention targeting frail elderly people. *BMC Geriatr.* 2011;11:24.

47. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc.* 2011;43(7):1334-1359.

48. Beswick AD, Rees K, Dieppe P, et al. Complex interventions to improve physical function and maintain independent living in elderly people: a systematic review and meta-analysis. *Lancet.* 2008;371(9614):725-735.
49. Hernandez-Luis R, Martin-Ponce E, Monereo-Munoz M, et al. Prognostic value of physical function tests and muscle mass in elderly hospitalized patients. A prospective observational study. *Geriatr Gerontol Int.* 2018;18(1):57-64.

50. Pongiglione B, De Stavola BL, Kuper H, Ploubidis GB. Disability and all-cause mortality in the older population: evidence from the English Longitudinal Study of Ageing. *Eur J Epidemiol.* 2016;31(8):735-746.

51. Beaudart C, Rolland Y, Cruz-Jentoft AJ, et al. Assessment of Muscle Function and Physical Performance in Daily Clinical Practice: A position paper endorsed by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). *Calcif Tissue Int.* 2019;105(1):1-14.

52. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep.* 1985;100(2):126-131.

53. Howley ET. Type of activity: resistance, aerobic and leisure versus occupational physical activity. *Med Sci Sports Exerc.* 2001;33(6 Suppl):S364-S369; discussion S419-S420.

54. Ayis S, Gooberman-Hill R, Bowling A, Ebrahim S. Predicting catastrophic decline in mobility among older people. *Age Ageing.* 2006;35(4):382-387.

55. Rhodes RE, Warburton DE, Murray H. Characteristics of physical activity guidelines and their effect on adherence: a review of randomized trials. *Sports Med.* 2009;39(5):355-375.

56. Tremblay MS, Aubert S, Barnes JD, et al. Sedentary Behavior Research Network (SBRN) - Terminology Consensus Project process and outcome. *Int J Behav Nutr Phys Act.* 2017;14(1):75.

57. Brach JS, Simonsick EM, Kritchevsky S, et al. The association between physical function and lifestyle activity and exercise in the health, aging and body composition study. *J Am Geriatr Soc.* 2004;52(4):502-509.

58. Newdick C. *Who should we treat?: rights, rationing and the resources in the NHS.* 2nd ed ed. New York: Oxford University Press; 2005.

59. Coulter A HC. *The global challenge of health care rationing.* Buckingham: Open University Press; 2000.
60. DALYs GBD, Collaborators H, Murray CJ, et al. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990-2013: quantifying the epidemiological transition. *Lancet.* 2015;386(10009):2145-2191.

61. Swedish Council on Health Technology Assessment (SBU). *Comprehensive Geriatric Assessment and Care of Frail Elderly.* 2014: 221.

62. Global Burden of Disease Study Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet.* 2015;386(9995):743-800.

63. Legramante JM, Morciano L, Lucaroni F, et al. Frequent Use of Emergency Departments by the Elderly Population When Continuing Care Is Not Well Established. *PLoS One.* 2016;11(12):e0165939.

64. Aminzadeh F, Dalziel WB. Older adults in the emergency department: a systematic review of patterns of use, adverse outcomes, and effectiveness of interventions. *Ann Emerg Med.* 2002;39(3):238-247.

65. Hastings SN, Whitson HE, Sloane R, Landerman LR, Horney C, Johnson KS. Using the past to predict the future: latent class analysis of patterns of health service use of older adults in the emergency department. *J Am Geriatr Soc.* 2014;62(4):711-715.

66. Roberts DC, McKay MP, Shaffer A. Increasing rates of emergency department visits for elderly patients in the United States, 1993 to 2003. *Ann Emerg Med.* 2008;51(6):769-774.

67. Knechel NA. The challenges of enrolling older adults into intervention studies. *Yale J Biol Med.* 2013;86(1):41-47.

68. Rothwell PM. External validity of randomised controlled trials: "to whom do the results of this trial apply?". *Lancet.* 2005;365(9453):82-93.

69. Kodama S, Saito K, Tanaka S, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. *JAMA.* 2009;301(19):2024-2035.

70. Leong DP, Teo KK, Rangarajan S, et al. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet.* 2015;386(9990):266-273.
71. Kim Y, White T, Wijndaele K, et al. The combination of cardiorespiratory fitness and muscle strength, and mortality risk. *Eur J Epidemiol.* 2018;33(10):953-964.

72. den Ouden ME, Schuurmans MJ, Arts IE, van der Schouw YT. Physical performance characteristics related to disability in older persons: a systematic review. *Maturitas.* 2011;69(3):208-219.

73. Brown CJ, Redden DT, Flood KL, Allman RM. The underrecognized epidemic of low mobility during hospitalization of older adults. *J Am Geriatr Soc.* 2009;57(9):1660-1665.

74. Brown CJ, Friedkin RJ, Inouye SK. Prevalence and outcomes of low mobility in hospitalized older patients. *J Am Geriatr Soc.* 2004;52(8):1263-1270.

75. Covinsky KE, Pierluissi E, Johnston CB. Hospitalization-associated disability: "She was probably able to ambulate, but I'm not sure". *JAMA.* 2011;306(16):1782-1793.

76. Surkan MJ, Gibson W. Interventions to Mobilize Elderly Patients and Reduce Length of Hospital Stay. *Can J Cardiol.* 2018;34(7):881-888.

77. Zisberg A, Shadmi E, Sinoff G, Gur-Yaish N, Srulovici E, Admi H. Low mobility during hospitalization and functional decline in older adults. *J Am Geriatr Soc.* 2011;59(2):266-273.

78. Boyd CM, Landefeld CS, Counsell SR, et al. Recovery of activities of daily living in older adults after hospitalization for acute medical illness. *J Am Geriatr Soc.* 2008;56(12):2171-2179.

79. Creditor MC. Hazards of hospitalization of the elderly. *Ann Intern Med.* 1993;118(3):219-223.

80. Socorro Garcia A, de la Puente M, Perdomo B, Lopez Pardo P, Baztan JJ. Functional status and mortality at month and year in nonagenarians hospitalized due to acute medical illness. *Eur J Intern Med.* 2015;26(9):705-708.

81. Zisberg A, Shadmi E, Gur-Yaish N, Tonkikh O, Sinoff G. Hospital-associated functional decline: the role of hospitalization processes beyond individual risk factors. *J Am Geriatr Soc.* 2015;63(1):55-62.
82. Kosse NM, Dutmer AL, Dasenbrock L, Bauer JM, Lamoth CJ. Effectiveness and feasibility of early physical rehabilitation programs for geriatric hospitalized patients: a systematic review. *BMC Geriatr.* 2013;13:107.

83. Ellis G, Gardner M, Tsiachristas A, et al. Comprehensive geriatric assessment for older adults admitted to hospital. *Cochrane Database Syst Rev.* 2017;9:CD006211.

84. Weening-Dijksterhuis E, de Greef MH, Scherder EJ, Slaets JP, van der Schans CP. Frail institutionalized older persons: A comprehensive review on physical exercise, physical fitness, activities of daily living, and quality-of-life. *Am J Phys Med Rehabil.* 2011;90(2):156-168.

85. Cooper R, Kuh D, Hardy R, Mortality Review G, Falcon, Teams HAS. Objectively measured physical capability levels and mortality: systematic review and meta-analysis. *BMJ.* 2010;341:c4467.

86. Boxer R, Kleppinger A, Ahmad A, Annis K, Hager D, Kenny A. The 6-minute walk is associated with frailty and predicts mortality in older adults with heart failure. *Congest Heart Fail.* 2010;16(5):208-213.

87. Steffen TM, Hacker TA, Mollinger L. Age- and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go Test, and gait speeds. *Phys Ther.* 2002;82(2):128-137.

88. Bohannon RW. Reference values for the five-repetition sit-to-stand test: a descriptive meta-analysis of data from elders. *Percept Mot Skills.* 2006;103(1):215-222.

89. Bohannon RW. Reference values for the timed up and go test: a descriptive meta-analysis. *J Geriatr Phys Ther.* 2006;29(2):64-68.

90. Bohannon RW, Bear-Lehman J, Desrosiers J, Massy-Westropp N, Mathiowetz V. Average grip strength: a meta-analysis of data obtained with a Jamar dynamometer from individuals 75 years or more of age. *J Geriatr Phys Ther.* 2007;30(1):28-30.

91. Martin-Ponce E, Hernandez-Betancor I, Gonzalez-Reimers E, Hernandez-Luis R, Martinez-Riera A, Santolaria F. Prognostic value of physical function tests: hand grip strength and six-minute walking test in elderly hospitalized patients. *Sci Rep.* 2014;4:7530.
92. Guttmann A, Schull MJ, Vermeulen MJ, Stukel TA. Association between waiting times and short term mortality and hospital admission after departure from emergency department: population based cohort study from Ontario, Canada. *BMJ.* 2011;342:d2983.

93. Banerjee S. Multimorbidity--older adults need health care that can count past one. *Lancet.* 2015;385(9968):587-589.

94. Falvey JR, Burke RE, Malone D, Ridgeway KJ, McManus BM, Stevens-Lapsley JE. Role of Physical Therapists in Reducing Hospital Readmissions: Optimizing Outcomes for Older Adults During Care Transitions From Hospital to Community. *Phys Ther.* 2016;96(8):1125-1134.

95. Baztan JJ, Suarez-Garcia FM, Lopez-Arrieta J, Rodriguez-Manas L, Rodriguez-Artalejo F. Effectiveness of acute geriatric units on functional decline, living at home, and case fatality among older patients admitted to hospital for acute medical disorders: meta-analysis. *BMJ.* 2009;338:b50.

96. Falvey JR, Mangione KK, Stevens-Lapsley JE. Rethinking Hospital-Associated Deconditioning: Proposed Paradigm Shift. *Phys Ther.* 2015;95(9):1307-1315.

97. Hartley P, Adamson J, Cunningham C, Embleton G, Romero-Ortuno R. Higher Physiotherapy Frequency Is Associated with Shorter Length of Stay and Greater Functional Recovery in Hospitalized Frail Older Adults: A Retrospective Observational Study. *J Frailty Aging.* 2016;5(2):121-125.

98. de Morton NA, Keating JL, Jeffs K. Exercise for acutely hospitalised older medical patients. *Cochrane Database Syst Rev.* 2007(1):CD005955.

99. Turner G, Clegg A, British Geriatrics S, Age UK, Royal College of General P. Best practice guidelines for the management of frailty: a British Geriatrics Society, Age UK and Royal College of General Practitioners report. *Age Ageing.* 2014;43(6):744-747.

100. Rubenstein LZ, Stuck AE, Siu AL, Wieland D. Impacts of geriatric evaluation and management programs on defined outcomes: overview of the evidence. *J Am Geriatr Soc.* 1991;39(9 Pt 2):8S-16S; discussion 17S-18S.

101. Solomon DH. Geriatric assessment: methods for clinical decision making. *JAMA.* 1988;259(16):2450-2452.
102. Pilotto A, Cella A, Pilotto A, et al. Three Decades of Comprehensive Geriatric Assessment: Evidence Coming From Different Healthcare Settings and Specific Clinical Conditions. *J Am Med Dir Assoc.* 2017;18(2):192 e191-192 e111.

103. Ellis G, Whitehead MA, O’Neill D, Langhorne P, Robinson D. Comprehensive geriatric assessment for older adults admitted to hospital. *Cochrane Database Syst Rev.* 2011(7):CD006211.

104. Johansson ME, Johansson P. [Elderly with multiple diseases often in contact with health services should be admitted right away. Study of 40 patients in the NU-healthcare]. *Lakartidningen.* 2012;109(20-21):1022-1023.

105. Lazarus NR, Izquierdo M, Higginson IJ, Harridge SDR. Exercise Deficiency Diseases of Ageing: The Primacy of Exercise and Muscle Strengthening as First-Line Therapeutic Agents to Combat Frailty. *J Am Med Dir Assoc.* 2018;19(9):741-743.

106. Puts MT, Toubasi S, Andrew MK, et al. Interventions to prevent or reduce the level of frailty in community-dwelling older adults: a scoping review of the literature and international policies. *Age Ageing.* 2017.

107. Dent E, Morley JE, Cruz-Jentoft AJ, et al. Physical Frailty: ICFSR International Clinical Practice Guidelines for Identification and Management. *J Nutr Health Aging.* 2019;23(9):771-787.

108. Dent E, Martin FC, Bergman H, Woo J, Romero-Ortuno R, Walston JD. Management of frailty: opportunities, challenges, and future directions. *Lancet.* 2019;394(10206):1376-1386.

109. Cadore EL, Rodriguez-Manas L, Sinclair A, Izquierdo M. Effects of different exercise interventions on risk of falls, gait ability, and balance in physically frail older adults: a systematic review. *Rejuvenation Res.* 2013;16(2):105-114.

110. Daniels R, van Rossum E, de Witte L, Kempen GI, van den Heuvel W. Interventions to prevent disability in frail community-dwelling elderly: a systematic review. *BMC Health Serv Res.* 2008;8:278.

111. de Labra C, Guimaraes-Pinheiro C, Maseda A, Lorenzo T, Millan-Calenti JC. Effects of physical exercise interventions in frail older adults: a systematic review of randomized controlled trials. *BMC Geriatr.* 2015;15:154.
112. de Vries NM, van Ravensberg CD, Hobbel JS, Olde Rikkert MG, Staal JB, Nijhuis-van der Sanden MW. Effects of physical exercise therapy on mobility, physical functioning, physical activity and quality of life in community-dwelling older adults with impaired mobility, physical disability and/or multi-morbidity: a meta-analysis. Ageing Res Rev. 2012;11(1):136-149.

113. Rosendahl E, Lindelof N, Littbrand H, et al. High-intensity functional exercise program and protein-enriched energy supplement for older persons dependent in activities of daily living: a randomised controlled trial. Aust J Physiother. 2006;52(2):105-113.

114. Jadczak AD, Makwana N, Luscombe-Marsh N, Visvanathan R, Schultz TJ. Effectiveness of exercise interventions on physical function in community-dwelling frail older people: an umbrella review of systematic reviews. JBI Database System Rev Implement Rep. 2018;16(3):752-775.

115. Lee PG, Jackson EA, Richardson CR. Exercise Prescriptions in Older Adults. Am Fam Physician. 2017;95(7):425-432.

116. Bauman A, Merom D, Bull FC, Buchner DM, Fiatarone Singh MA. Updating the Evidence for Physical Activity: Summative Reviews of the Epidemiological Evidence, Prevalence, and Interventions to Promote "Active Aging". Gerontologist. 2016;56 Suppl 2:S268-280.

117. Johansson MS, Korshoj M, Schnohr P, et al. Time spent cycling, walking, running, standing and sedentary: a cross-sectional analysis of accelerometer-data from 1670 adults in the Copenhagen City Heart Study: Physical behaviours among 1670 Copenhageners. BMC Public Health. 2019;19(1):1370.

118. Milanovic Z, Pantelic S, Trajkovic N, Sporis G, Kostic R, James N. Age-related decrease in physical activity and functional fitness among elderly men and women. Clin Interv Aging. 2013;8:549-556.

119. Buttery AK, Martin FC. Knowledge, attitudes and intentions about participation in physical activity of older post-acute hospital inpatients. Physiotherapy. 2009;95(3):192-198.

120. Franco MR, Tong A, Howard K, et al. Older people's perspectives on participation in physical activity: a systematic review and thematic synthesis of qualitative literature. Br J Sports Med. 2015;49(19):1268-1276.

121. Freiberger E, Kemmler W, Siegrist M, Sieber C. Frailty and exercise interventions: Evidence and barriers for exercise programs. Z Gerontol Geriatr. 2016;49(7):606-611.
122. Baert V, Gorus E, Mets T, Geerts C, Bautmans I. Motivators and barriers for physical activity in the oldest old: a systematic review. *Aging Res Rev.* 2011;10(4):464-474.

123. Krippendorff. *Content analysis: an introduction to its methodology.* 4th ed. Los Angeles: SAGE publications; 2018.

124. Höglund-Nielsen B GM. *Tillämpad kvalitativ forskning inom hälsa- och sjukvård (In Swedish)* 3:2 ed. Lund: Studentlitteratur AB; 2017.

125. de la Rica-Escuin M, Gonzalez-Vaca J, Varela-Perez R, et al. Frailty and mortality or incident disability in institutionalized older adults: the FINAL study. *Maturitas.* 2014;78(4):329-334.

126. Frenkel WJ, Jongerius EJ, Mandjes-van Uitert MJ, van Munster BC, de Rooij SE. Validation of the Charlson Comorbidity Index in acutely hospitalized elderly adults: a prospective cohort study. *J Am Geriatr Soc.* 2014;62(2):342-346.

127. Mathiowetz V, Weber K, Volland G, Kashman N. Reliability and validity of grip and pinch strength evaluations. *J Hand Surg Am.* 1984;9(2):222-226.

128. Alencar MA, Dias JM, Figueiredo LC, Dias RC. Handgrip strength in elderly with dementia: study of reliability. *Rev Bras Fisioter.* 2012;16(6):510-514.

129. Guyatt GH, Sullivan MJ, Thompson PJ, et al. The 6-minute walk: a new measure of exercise capacity in patients with chronic heart failure. *Can Med Assoc J.* 1985;132(8):919-923.

130. Rostagno C, Gensini GF. Six minute walk test: a simple and useful test to evaluate functional capacity in patients with heart failure. *Intern Emerg Med.* 2008;3(3):205-212.

131. Borg G. *Borg’s perceived exertion and pain scales.* New York: Human Kinetics; 1998.

132. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc.* 1991;39(2):142-148.

133. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol.* 1994;49(2):M85-94.
134. Whitney SL, Wrisley DM, Marchetti GF, Gee MA, Redfern MS, Furman JM. Clinical measurement of sit-to-stand performance in people with balance disorders: validity of data for the Five-Times-Sit-to-Stand Test. *Phys Ther.* 2005;85(10):1034-1045.

135. Buatois S, Miljkovic D, Manckoundia P, et al. Five times sit to stand test is a predictor of recurrent falls in healthy community-living subjects aged 65 and older. *J Am Geriatr Soc.* 2008;56(8):1575-1577.

136. Bohannon RW, Shove M.E, Barreca S.R, Masters L.M, Sigouin C.S. Five-repetition sit-to-stand test performance by community-dwelling adults: A preliminary investigation of times, determinants, and relationship with self-reported physical performance. *Isokinetics and Exercise Science*,. 2007;15(2):77-81.

137. Ekerstad N, Karlson BW, Dahlin Ivanoff S, et al. Is the acute care of frail elderly patients in a comprehensive geriatric assessment unit superior to conventional acute medical care? *Clin Interv Aging.* 2017;12:1-9.

138. Zelada MA, Salinas R, Baztan JJ. Reduction of functional deterioration during hospitalization in an acute geriatric unit. *Arch Gerontol Geriatr.* 2009;48(1):35-39.

139. Korstjens I, Moser A. Series: Practical guidance to qualitative research. Part 4: Trustworthiness and publishing. *Eur J Gen Pract.* 2018;24(1):120-124.

140. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *Int J Qual Health Care.* 2007;19(6):349-357.

141. Parliament S. Lag (2003:460) om etikprövning av forskning som avser människor (In Swedish). Accessed 2020-02-13.

142. Helsingforsdeklaration V. Etiska principer för medicinsk forskning som omfattar människor (In Swedish). *Läkartidningen.* 2002;99:1214-1216.

143. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg.* 2014;12(12):1495-1499.

144. Ahlund K, Ekerstad N, Oberg B, Back M. Physical Performance Impairments and Limitations Among Hospitalized Frail Older Adults. *J Geriatr Phys Ther.* 2018;41(4):230-235.
145. Turner L, Shamseer L, Altman DG, et al. Consolidated standards of reporting trials (CONSORT) and the completeness of reporting of randomised controlled trials (RCTs) published in medical journals. *Cochrane Database Syst Rev.* 2012;11:MR000030.

146. Ahlund K, Back M, Oberg B, Ekerstad N. Effects of comprehensive geriatric assessment on physical fitness in an acute medical setting for frail elderly patients. *Clin Interv Aging.* 2017;12:1929-1939.

147. Ahlund K, Ekerstad N, Back M, Karlson BW, Oberg B. Preserved physical fitness is associated with lower 1-year mortality in frail elderly patients with a severe comorbidity burden. *Clin Interv Aging.* 2019;14:577-586.

148. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of Illness in the Aged. The Index of Adl: A Standardized Measure of Biological and Psychosocial Function. *JAMA.* 1963;185:914-919.

149. Wade DT, Collin C. The Barthel ADL Index: a standard measure of physical disability? *Int Disabil Stud.* 1988;10(2):64-67.

150. Kasper JD, Chan KS, Freedman VA. Measuring Physical Capacity. *J Aging Health.* 2017;29(2):289-309.

151. Portney LG, Watkins MP. *Foundations of clinical research: applications to practice.* Vol 2: Prentice Hall Upper Saddle River, NJ; 2000.

152. Chen HM, Hsiao SM, Kuo MC, et al. Identifying early decline of daily function and its association with physical function in chronic kidney disease: performance-based and self-reported measures. *PeerJ.* 2018;6:e5286.

153. Bennell K, Dobson F, Hinman R. Measures of physical performance assessments: Self-Paced Walk Test (SPWT), Stair Climb Test (SCT), Six-Minute Walk Test (6MWT), Chair Stand Test (CST), Timed Up & Go (TUG), Sock Test, Lift and Carry Test (LCT), and Car Task. *Arthritis Care Res (Hoboken).* 2011;63 Suppl 11:S350-370.

154. Tveter AT, Dagfinrud H, Moseng T, Holm I. Health-related physical fitness measures: reference values and reference equations for use in clinical practice. *Arch Phys Med Rehabil.* 2014;95(7):1366-1373.

155. Parker SG, McCue P, Phelps K, et al. What is Comprehensive Geriatric Assessment (CGA)? An umbrella review. *Age Ageing.* 2018;47(1):149-155.
156. Ellis G, Langhorne P. Comprehensive geriatric assessment for older hospital patients. *Br Med Bull.* 2004;71:45-59.

157. Deschodt M, Flamaing J, Haentjens P, Boonen S, Milisen K. Impact of geriatric consultation teams on clinical outcome in acute hospitals: a systematic review and meta-analysis. *BMC Med.* 2013;11:48.

158. Stroke Unit Trialists C. Organised inpatient (stroke unit) care for stroke. *Cochrane Database Syst Rev.* 2013(9):CD000197.

159. Langhorne P, Pollock A, Stroke Unit Trialists C. What are the components of effective stroke unit care? *Age Ageing.* 2002;31(5):365-371.

160. Gustavson AM, Falvey JR, Jankowski CM, Stevens-Lapsley JE. Public Health Impact of Frailty: Role of Physical Therapists. *J Frailty Aging.* 2017;6(1):2-5.

161. Valenzuela PL, Castillo-Garcia A, Morales JS, et al. Physical Exercise in the Oldest Old. *Compr Physiol.* 2019;9(4):1281-1304.

162. Landi F, Zuccala G, Bernabei R, et al. Physiotherapy and occupational therapy: a geriatric experience in the acute care hospital. *Am J Phys Med Rehabil.* 1997;76(1):38-42.

163. Brülde B FF. *Vad gör ett liv meningsfullt? (In Swedish)* Online: Mittfåra & marginal. Göteborgs universitet: SOM-institutet.; 2014.

164. Hoover M, Rotermann M. Seniors’ use of and unmet needs for home care, 2009. *Health Rep.* 2012;23(4):55-60.

165. Piredda M, Matarese M, Mastroianni C, D'Angelo D, Hammer MJ, De Marinis MG. Adult Patients' Experiences of Nursing Care Dependence. *J Nurs Scholarsh.* 2015;47(5):397-406.

166. Andreasen J, Lund H, Aadahl M, Sorensen EE. The experience of daily life of acutely admitted frail elderly patients one week after discharge from the hospital. *Int J Qual Stud Health Well-being.* 2015;10:27370.

167. Sjoberg M, Beck I, Rasmussen BH, Edberg AK. Being disconnected from life: meanings of existential loneliness as narrated by frail older people. *Aging Ment Health.* 2018;22(10):1357-1364.

168. Antonovsky A. The structure and properties of the sense of coherence scale. *Soc Sci Med.* 1993;36(6):725-733.
169. Cadore EL, Casas-Herrero A, Zambom-Ferraresi F, et al. Multicomponent exercises including muscle power training enhance muscle mass, power output, and functional outcomes in institutionalized frail nonagenarians. *Age (Dordr).* 2014;36(2):773-785.

170. Torres-Sanchez I, Valenza MC, Cabrera-Martos I, Lopez-Torres I, Benitez-Feliponi A, Conde-Valero A. Effects of an Exercise Intervention in Frail Older Patients with Chronic Obstructive Pulmonary Disease Hospitalized due to an Exacerbation: A Randomized Controlled Trial. *COPD.* 2017;14(1):37-42.

171. Gluud LL. Bias in clinical intervention research. *Am J Epidemiol.* 2006;163(6):493-501.

172. Bakker FC, Olde Rikkert MG. Hospital Care for Frail Elderly Adults: From Specialized Geriatric Units to Hospital-Wide Interventions. *Interdiscip Top Gerontol Geriatr.* 2015;41:95-106.

173. Marcin T, Eser P, Prescott E, et al. Predictors of pre-rehabilitation exercise capacity in elderly European cardiac patients - The EU-CaRE study. *Eur J Prev Cardiol.* 2019:2047487319894676.

174. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. *Res Q Exerc Sport.* 1999;70(2):113-119.

175. Guralnik J B-RK, Bhasin S, Landi E, Muscedere J, Perera S, Reginster JY, Woodhouse L, Vellas B and the ICFSR task force. Clinically meaningful change for physical performance: Perspectives of the ICFFSR task force. *J. Frailty Aging.* 2019.

176. Marques A, Cruz J, Quina S, Regencio M, Jacome C. Reliability, Agreement and Minimal Detectable Change of the Timed Up & Go and the 10-Meter Walk Tests in Older Patients with COPD. *COPD.* 2016;13(3):279-287.

177. Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. *J Am Geriatr Soc.* 2006;54(5):743-749.
Papers

The papers associated with this thesis have been removed for copyright reasons. For more details about these see:

http://urn.kb.se/resolve?urn=urn:nbn:se:liu:diva-164961
