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Effectiveness of geriatrician-performed comprehensive geriatric care in older people referred to a Danish community rehabilitation unit

PhD dissertation

Dmitri Zintchouk

Health

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"We all recognize quality when we see it or particularly when we receive it. In 'cure' outcomes plays an important part of in determining quality, but it is certainly not the whole story. The really important factors are kindliness and ability to communicate on the part of all members of the medical team"

Archie Cochrane,

Effectiveness & Efficiency. Random Reflections on Health Services, 1972

PREFACE AND ACKNOWLEDGEMENTS

The present thesis is based on a randomized study of the effectiveness of geriatrician-performed comprehensive geriatric care in a Danish community rehabilitation unit. The study was conducted from 2012 to 2018 at the Research Department for Geriatrics, Aarhus University Hospital and the Department of Public Health, Section of General Medical Practice, Aarhus University, Denmark. I would like to thank the many people who have been involved in this study and who have helped me complete this work.

First, I wish to thank my main supervisor Professor Else Marie Damsgaard for giving me the opportunity to follow my dream to gain insight into research. Else Marie Damsgaard has been a continuous source of inspirational ideas, and I am grateful for her patience with me, a research novice. I am also grateful for the flexibility and support that Else Marie Damsgaard afforded me by virtue of her position as head of the Department of Geriatrics.

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Dmitri Zintchouk, December 20, 2018.

LIST OF ABBREVIATIONS

ADL	Activities of daily living
AOU	Assessment of Underutilization
ATC	Anatomical Therapeutic Chemical
CAM	Confusion Assessment Method
CCI	Charlson Comorbidity Index
CI	Confidence interval
CGA	Comprehensive geriatric assessment
CGC	Comprehensive geriatric care
CNS	Central nervous system
DL	Depression list
IG	Intervention group
CG	Control group
GP	General practitioner
HR	Hazard ratio
ED	Emergency department
IRR	Incidence rate ratio
ITT	Intention-to-treat
IQR	Interquartile range
MAI	Medication Appropriateness Index
MBI	Modified Barthel-100 Index
MCID	Minimally clinically important difference
MMSE	Mini–Mental State Examination
MTM	Medication therapy management
OR	Odds ratio
OQoL	Overall quality of life
RCT	Randomized controlled trial
SD	Standard deviation
START	Screening Tool to Alert doctors to Right Treatment
STOPP	Screening Tool of Older Persons' Prescriptions
30-s CST	30-second Chair Stand Test

LIST OF ORIGINAL PAPERS

This thesis is based on three original papers, denoted below by Roman numerals. The full texts of the papers are found in the Appendices.

Paper I

Comprehensive geriatric care versus standard care for elderly referred to a rehabilitation unit – a randomized controlled trial. Zintchouk D, Lauritzen T, Damsgaard EM

Journal of Aging Research and Clinical Practice, 2017; 6:40-47

DOI: https://doi.org/10.14283/jarcp.2016.126

Paper II

Geriatrician-performed comprehensive geriatric care in older adults referred to a community rehabilitation unit: A randomized controlled trial.

Zintchouk D, Gregersen M, Lauritzen T, Damsgaard EM

European Journal of Internal Medicine, 2018; 51:18-24

DOI: https://doi.org/10.1016/j.ejim.2018.01.022

Paper III

Impact of Geriatrician-performed Comprehensive Geriatric Care on Medication Use and Cognitive Function in Older Adults Referred to a Non-Hospital-Based Rehabilitation Unit.

Zintchouk D, Gregersen M, Lauritzen T, Damsgaard EM

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1 INTRODUCTION

1.1 REHABILITATION AS PART OF GERIATRIC MEDICINE

Sixty years ago, Marjorie Warren laid down the guiding principles of geriatric medicine[1]. She emphasized rehabilitation as a tool to help elderly people regain the best possible functional independence.

The primary objective of rehabilitation is to seek a goal for the patient, based on personality, functional ability, and social position. It must include a realistic assessment of a functional prognosis and the co-operation of the patients and professionals complementary to medicine[2].

Many different definitions of rehabilitation have been proposed. Some authors have defined what rehabilitation is not: 'The aim of rehabilitation is not the attainment of an objective, appropriate to the needs of the service (i.e., an early discharge of the patient from hospital)'[3].

1.2 IN-HOSPITAL REHABILITATION

In World Health Organization's recommendations from 2017[4], hospitals shall have specialized rehabilitation units for patients with complex needs. There is evidence that specialized rehabilitation wards for restoring functioning to older people with complex rehabilitation needs are superior to the rehabilitation provided in general wards[5]. However, persons aged ≥ 65 years already occupy approximately two-thirds of the medical beds in hospitals[6].

As patients' length of stay in hospital declines worldwide, most rehabilitation of frail older persons must be provided in community settings outside hospitals.

1.3 COMMUNITY REHABILITATION UNITS AND HOSPITAL CONTACTS

During the past decades, community-based rehabilitation units in Denmark have offered older persons an opportunity to improve their level of functioning. The goal has been to reduce re-hospitalization and restore functional ability during a 3- to 5-week rehabilitation stay. This should allow patients to return to their own homes or sheltered housing.

We did an observational study of 181 older persons referred to a community rehabilitation unit. We found that 21% of the older persons came from their own homes or from sheltered housing, 79% were referred from a hospital department because they were too unstable to be sent home directly[7]. Among the 181 persons, 137 hospital admissions and emergency department (ED) visits were registered within 3 months after start of community rehabilitation[7].

Suboptimally treated subacute medical conditions and inappropriate medication may result in visits to the ED or hospitalization. For older people, hospital admission involves a risk of rapid decline in functional and cognitive abilities[8,9]. Hospitalized patients are not only recovering from illness, they also need to recover after being exposed to the stressful hospital environment[10]. The period immediately after discharge is a high-risk period with increased vulnerability and adverse health outcomes[11].

We did a small explorative cross-sectional study of people consecutively referred from hospital or own home to a community rehabilitation unit in 2004[12]. We found an underlying serious medical or iatrogenic cause for functional decline in 95 out of 100.

A solution of the outlined problems may lie in the development of Marjorie Warren´s vision: Comprehensive Geriatric Assessment (CGA) combined with interventions now called Geriatric Comprehensive Care (CGC).

This PhD dissertation describes the background for and the effectiveness of a modified CGC model. The thesis outlines how the model was developed, implemented, and tested in an experimental design. The study population included older persons referred to a Danish non-hospital-based rehabilitation unit. The results are presented and discussed in the light of the existing literature and keeping in mind the study's methodological limitations.

2 BACKGROUND AND LITERATURE REVIEW

This chapter problematizes the increasing number of hospital contacts, and describes such common conditions in older people as multimorbidity and polypharmacy. It presents a review of interventions to reduce hospital contacts, optimize medication use, improve cognitive function, activities of daily living (ADL) function, and quality of life. Lastly, the chapter introduces concept for medication adjustment, a key element of geriatrician-led CGC in a community rehabilitation unit.

2.1 HOSPITAL ADMISSIONS OF OLDER PEOPLE

The world's population is aging as a result of decreasing fertility and mortality[13]. Healthcare needs are likely to grow because increasing age is accompanied by chronic illness and age-related disability. More survivors with chronic diseases lead to an increasing number of overlapping comorbidities and an increased risk of acute illness[14,15]. Furthermore, geriatric syndromes like confusion, polypharmacy, malnutrition, and falls contribute to acute or serious problems such as fractures, immobility, and pressure ulcers. Aging is also associated with cognitive impairment which, regardless of its cause, challenges management of daily life and compliance with medication[16]. This may contribute to an increased number of hospital contacts.

The Western population aged ≥ 65 years is expected to grow from 15% in 2010 to 25% in 2040[17]. This accounts for the large increase in hospital admissions[6] despite worldwide efforts to reduce them[18]. Up to 30% of hospital admissions of patients over 75 years were medication related. Of these up to 75% were potentially preventable[19].

In Denmark, 20% of discharges among 67+-year-old persons were followed by acute readmissions within 30 days[20]. Generally, readmission rates range from 5% to 35%, with the highest rates among geriatric patients[18]. Reducing the rates of re-hospitalization has attracted much attention from Danish policymakers as a way to cut expenses and improve quality of care. In Denmark, the effect of a home visit by a patient's general practitioner (GP) and a community nurse 1 week after discharge was examined in two studies[21,22]. One of the studies showed a positive effect in the form of a reduction in readmissions from 52% to 40% at 6 months[22]. This program is now mandatory in Denmark but does not include patients discharged to a community rehabilitation unit.

2.2 INAPPROPRIATE MEDICATION

2.2.1 Multimorbidity and medication

The disease-oriented model of medicine focuses on the theory that organ-based or system-based pathologies cause disease[23]. Due to increasing life expectancy, healthcare systems are progressively facing growing populations of older patients who often have non-disease-specific problems such as multimorbidity, polypharmacy, and disability[24]. Overcoming some of the limitations of the disease-oriented model[25] remains a challenge. Between 25 and 50% of clinical trials have a specific upper age limit, and approximately 80% of clinical trials exclude persons with comorbidities[26,27]. Disease-specific guidelines based upon such trials are often extrapolated to persons with comorbidities despite absence of evidence supporting their benefit. Even in studies that focus on older persons, the participants were not representative. They were generally more vigorous and robust than others of their age[28]. Healthier persons have a better risk-benefit balance for many medications. Studies may convey progressively more (typically favorably) distorted estimates for many treatments[28].

The combined impact of multimorbidity on an older person's capacity and healthcare utilization is often significantly greater than might be expected from the summed-up effects of each condition[29]. Older persons are more vulnerable to drug-related harms due to age-related changes in pharmacokinetics/dynamics and decreased physiological reserves[30].

Strict application of guidelines may result in multiple drug use[31], which is associated with greater healthcare costs, poorer functional status[32], and decreased cognitive capacity[33]. In frail older people, the number needed to treat for some medications exceeds the number needed to harm[34]. Several preventive treatments (e.g., statins or intensive

blood glucose control in type 2 diabetes mellitus) may therefore have limited benefit because of the patients' short life expectancies[35].

Older people with complex health care needs often receive fragmented care[36]. Physicians in hospitals mainly see patients during acute exacerbations of their chronic diseases and will naturally focus on drugs relevant to the acute illness. On the other hand, GPs who are responsible for long-term follow-up and repeat prescriptions may be reluctant to change medications initiated by hospital specialists[37,38]. As care shifts from the secondary to the primary sector, GPs are expected to manage an increasingly sick, old, and disabled population[39]. The loss of homoeostatic reserve and the need to treat multiple conditions concurrently will carry an inevitable risk of iatrogenic complications.

Avoidance and early detection of iatrogenic complications are core domains in geriatric medicine[40]. Some researchers suggest that more geriatricians need to be appointed[41]. Experts generally agree that geriatricians' efforts should be devoted to clinical care for the most vulnerable patients with the most complex medical needs. Primary care providers with appropriate critical knowledge of basic geriatric principles should manage the healthier 70% of the elderly population[42].

For many older people with multimorbidity, maintaining their functional ability may be more crucial and important than screening for illnesses and aggressive medical treatment of their chronic diseases.

2.2.2 Polypharmacy

Polypharmacy means prescribing either many or too many medications[43]. Prescribing many medications can be essential or beneficial. The problem is whether the medications have been prescribed appropriately[43,44]. The single most important indicator of *inappropriate* prescribing is the number of prescribed drugs[45]. Fulton and Allen defined polypharmacy as: 'The use of medications that are not clinically indicated'[46]. Other definitions include a medical regimen comprising at least one unnecessary medication[47], or use of medications for which harm outweighs benefits[32].

During the past 2 decades, polypharmacy has been recognized by numerous studies[48-50]. A unique quantitative definition of polypharmacy is still lacking. In a systematic review of polypharmacy definitions[51], the authors found a total of 138 definitions of polypharmacy: 111 numerical-only definitions, 15 numerical definitions incorporating duration of therapy or healthcare setting, and 12 descriptive definitions. Only 6.4% of the articles made the distinction between appropriate and inappropriate polypharmacy. The most commonly reported definition of polypharmacy was the numerical definition of five or more daily medications (46.4% of the articles). Between 1988 and 2010, the proportion of non-institutionalized Americans aged ≥ 65 years taking ≥5 medications tripled from 12.8% to 39%[52].

2.2.3 Hyperpolypharmacy

Considering the trend toward an increased use of medications, researchers now quantify 'hyperpolypharmacy exposure' as the use of ≥10 medications[53]. A population database analysis showed a 17% prevalence of hyperpolypharmacy among people aged ≥ 65 years in primary care in Scotland in 1995–2000[54]. A retrospective cross-sectional survey using data from the Norwegian Prescription Database showed that in 2008, 20% home-dwelling elderly ≥ 70 years were prescribed more than 10 different drugs daily[55]. A Danish cohort study from 2016 reported a hyperpolypharmacy prevalence of 20% in hospitalized patients aged ≥ 65 years[56]. A longitudinal cohort study conducted in Sweden and published in 2017 showed an unexpected, high share (47%) of adults that took ≥10 different drugs daily in the last year of their lives[57]. To our knowledge, the prevalence of hyperpolypharmacy in older people referred to a non-hospital community rehabilitation unit is not known.

2.2.4 Some expert-validated tools to optimize medication use

1) Although there is no standard definition of inappropriate polypharmacy, clinicians see and recognize it every day. One of the most used tools to guide clinicians is the STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment) criteria[58,59]. In one randomized controlled trial (RCT), this screening tool was examined as a physician-led intervention for prescribing appropriately [60]. When measured by the Medication Appropriateness Index (MAI)[61] and the Assessment of Underutilization (AOU)[62] index in this trial, significant improvements in hospitalized older patients were reported. This effect was sustained for 6 months after discharge. However, the study was not powered to detect a clinically significant difference between groups regarding mortality. Nor was the follow-up period long enough to allow for detection of a potentially significant reduction in the prevalence of falls or readmissions[60]. One RCT investigating pharmacist-led implementation of STOPP/START criteria in elderly residents at a chronic geriatric facility showed a reduction in the number of medications and falls compared with usual care[63]. Rates of hospitalization, functioning (FIM)[64], quality of life (SF-12)[65], and costs of medications were similar for both groups.

2) 'Deprescribing' is defined in the literature as 'the process of withdrawal of an inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes'[66]. The patient's goals and priorities are central to deprescribing, and most of patients report that they would like to stop a medicine if their doctor said they could[67]. From a clinical viewpoint, deprescribing seems most relevant in four situations: falls, delirium, cognitive impairment, and end-of-life situations[68]. In withdrawal trials, the most frequent medications were diuretics, antihypertensives, and psychotropic drugs. The tools available to support deprescribing were summarized in 2012[70] and 2017[71]. The latest review of this topic was done in Denmark in 2018. Here, the authors focused specifically on frail older persons or those with a limited life expectancy[72]. The authors found one systematic review[69] of published trials of medication withdrawal demonstrating that withdrawal of psychotropics was associated with improved cognition. A three-dimensional algorithm embracing both medication, disease, and

the patient[73] has also been shown to be effective in reducing polypharmacy, mortality, and morbidity in nursing-home residents[74] and community-dwelling[73] older patients.

However, existing evidence for medication deprescribing is scarce. While preliminary evidence suggests the tools that may reduce the use and cost of certain medications such as proton pump inhibitors[75], no randomized trial has assessed the tools' impact on patient-centered or clinical outcomes on population level of prescribing[76].

3) Reduction of the use of drugs with anticholinergic properties, particularly of psychotropic drugs, was suggested by the American Geriatrics Society 2015 Beer's Criteria Update Expert Panel[77]. A lack of consensus remains about what constitutes 'anticholinergic medication'[53]. Many psychotropic drugs have anticholinergic properties[78]. Nevertheless, physicians often attribute anticholinergic symptoms to memory deficits and confusion due to aging or age-related illness rather than to the side-effects of drugs[79].

4) One pragmatic suggestion is that GPs should review the medication lists of patients receiving 10 or more regular medicines, or more than four medicines if an additional risk factor is present[80]. A recent multicenter observational longitudinal study reported that hyperpolypharmacy predicted functional decline in older patients discharged from acute care hospitals, whereas the STOPP criteria were not associated with the outcome after adjusting for potential confounders[81].

2.2.5 Literature overview of interventions to optimize medication use in older people

Medication use in older people is recognized as a complex challenge and needs careful consideration of benefits and potential harms. Interventions to reduce polypharmacy are highly complex and vary in terms of assessment of participants' drug regimens, performance of medication reviews, forwarding recommendations to the responsible physicians, and the patients' involvement.

This overview summarizes research on the effects on hospital contacts, medication use, cognitive function, ADL function, quality of life, and mortality (safety) of interventions to reduce inappropriate polypharmacy in older people. The amount of literature on this topic is expanding. We focused on systematic reviews and meta-analyses as the primary source of information. The search strategy can be found in Appendix 2. A.

2.2.5.1 Interventions to reduce inappropriate prescribing

A 10-year-old systematic review summarized interventions launched to reduce inappropriate prescribing in the elderly. They were categorized as educational interventions, computerized support systems, pharmacist interventions, geriatric medicine services, multidisciplinary teams, regulatory policies, and multi-faceted

approaches[82]. The review concluded that CGAs in community[83] and hospital settings[84] and geriatrician-led case conference reviews[85] in residential care were among the most effective interventions to reduce inappropriate prescribing.

2.2.5.2 Outpatient pharmacist-led medication therapy management

A systematic review and meta-analysis published in 2015 evaluated the effectiveness of an outpatient pharmacist-led medication therapy management (MTM) in adults[86]. Most studies aimed to improve the quality of the medication regimen[86,87]. The MTM interventions improved medication appropriateness and reduced medication costs compared with usual care. The evidence presented was insufficient to determine the effect of interventions on drug therapy problems, adverse drug events, disease-specific morbidity, disease-specific or all-cause mortality, and harms. Of the 44 studies included in the systematic review[86], 15 RCTs focused on patient-centered outcomes. One RCT had cognitive function as an outcome but the study only included cognitively intact older adults[88]. In this study, intervention had no effect on cognitive function.

2.2.5.3 Interventions to improve appropriate use of polypharmacy

A recent Cochrane review (2014) found that various (mostly pharmacist-led) interventions could reduce inappropriate prescribing. However, no benefits were observed either in the clinical outcomes or in health-related quality of life[47]. The studies were limited by their small sample sizes and poor quality. A few geriatrician-led interventional studies suffered from suboptimal designs, such as the use of surrogate outcomes[60] or interventional studies without randomization[74,89]. A physician-led study[90] investigated computerized decision-making support. GPs were provided with automated alerts for potentially inappropriate prescribing. This intervention reduced the rate of initiation of inappropriate prescriptions, but no clinical outcomes were examined[90].

2.2.5.4 Impact of strategies to reduce polypharmacy on clinically relevant outcomes

In 2016, a systematic review and meta-analysis evaluated the impact on hospitalization and mortality of strategies to reduce polypharmacy[87]. The studies used a variety of methods for the medication review: checklists, drug-drug interaction tools (e.g. software, lists), reconciliation methods, and expert opinions based on a single pharmacist or physician or on a multidisciplinary team (case conferences with consensus-based discussion of medication quality). No strategies influencing outcomes were found[87]. The quality of the evidence assessed using the GRADE approach[91] was rated as low to very low, including the two RCTs in which a physician performed the medication review[92,93]. Two of 11 studies focused on hospitalization and found a significant effect of the intervention on this outcome.

Naunton et al.[94] evaluated pharmacist-conducted follow-up at home of high-risk elderly patients discharged from hospital. In this study, 45% of the participants in the control group were readmitted during the 90-day follow-up, compared with 28% in the intervention group ($P = 0.05$), but there was no significant difference between groups in the total number of days in the hospital ($P = 0.06$). Pitkälä et al. reported significantly fewer hospital days in an intervention group compared with participants in a control group (IRR 0.60; 95% CI 0.49–0.75, $P < 0.001$), although significant differences between groups existed at baseline, compromising the result[95].

Other systematic reviews confirmed no benefit in terms of patient satisfaction and quality of life[47,96-98].

The evidence underlines the need to test the effectiveness of these strategies in large RCTs with long follow-up[87,99].

Table 1. Recent systematic reviews of medication optimization interventions on hospital contacts, medication use, cognitive function, ADL function, quality of life, and mortality in older people.

First author /Year	Subject of study	Type of intervention	Outcomes					
№ of included studies			Hospital admissions and ED visits	Medication use	Cognitive function	ADL/ physical function	Quality of life	Mortality
Tjia, 2013[98] 15 RCTs	Interventions to reduce unnecessary medication use in frail older adults	Interventions led by pharmacists/ 5 studies involved physician-led medication reviews	↕	↕	NR	↕	NR	NR
Patterson, 2014 [47] 12 RCTs	Interventions to improve the appropriate use of polypharmacy for older people	Complex, multi-faceted interventions of pharmaceutical care/ In two studies geriatrician reviewed medication upon admission to the hospital	↕	↕	NR	NR	~	NR
Cooper, 2015[96] 8 RCTs, 2 cluster RCTs	Interventions to improve the appropriate use of polypharmacy in older people	Complex, multifaceted, pharmaceutical care-based interventions in various settings	↕	+	NR	NR	~	NR
Viswanathan, 2015[86] 44 RCTs	Medication therapy management interventions in outpatient settings	Complex, multi-faceted interventions of pharmaceutical care	~	+	NR	NR	~	NR
Johansson, 2016[87] 21 RCTs	Impact of strategies to reduce polypharmacy on clinically relevant endpoints	Pharmacist-led interventions (13 studies), multidisciplinary team-led (8 studies), physician-led (4 studies) interventions in various settings	~	+	NR	NR	NR	~
Christensen, 2016[99] 10 RCT	Medication review in hospitalized patients to reduce morbidity and mortality	Interventions led by pharmacist or a physician specialized in clinical pharmacology	~	NR	NR	NR	NR	~
Rankin, 2018[97] 18 RCTs 10 cluster RCTs	Interventions to improve the appropriate use of polypharmacy for older people	Complex, multi-faceted pharmaceutical-care based approaches in various settings	~	↕	NR	NR	~	NR

Abbreviations: CGA = Comprehensive Geriatric Assessment; RCT = Randomized controlled trial; SR = Systematic Review; ED = Emergency Department; ADL = Activities of daily living.
Systematic reviews summary impact: + = Positive Impact; − = Negative Impact; ~ = No difference, ↕ = Unable to determine/Inconsistent results; NR = Not studied or reported.

2.3 COMPREHENSIVE GERIATRIC ASSESSMENT

2.3.1 CGA and CGC

CGA can prioritize and address the complex health needs of older people. CGA is defined as 'a multidimensional, interdisciplinary diagnostic process focused on determining a frail elderly person's medical, psychological, and functional capability in order to develop a coordinated and integrated plan for treatment and long-term follow-up'[101]. CGA core components include evaluation of functional capacity, fall risk, cognition, polypharmacy, social support, goals of care, and advanced care preferences[102].

In practice, CGA is followed by an intervention and occasionally by assessment-based follow-up. The recently suggested concept of Comprehensive Geriatric Care (CGC) describes the combined assessment and follow-up of interventional process more precisely[103].

CGA and CGC are implemented across healthcare settings, ranging from specialized inpatient units in acute care facilities to shared care in primary care settings.

Several meta-analyses of RCTs have evaluated five main different CGA/CGC models: *acute geriatric care units, inpatient consultation, post-hospital discharge, home geriatric assessment, and outpatient consultation*[5,104-109].

2.3.2 Effectiveness of CGA

2.3.2.1 In inpatient setting

The effectiveness of inpatient CGA/CGC is supported by robust evidence. A meta-analysis from 2017of 29 trials reported that the patients who received the interventions in acute geriatric care units were more likely to be living at home and less likely to be admitted to a nursing home up to 1 year after their hospitalization[105]. Several key elements of the interventions were commonly used and known for their effectiveness: coordinated multidisciplinary assessment; geriatric medical expertise; identification of medical, physical, social, and psychological problems; and the making of a care plan involving appropriate rehabilitation. The interventions did not influence hospital contacts, dependence, cognitive status, risk of death, or the need for assistance with activities such as walking. However, the authors found too much variation in length of hospital stay and cognitive function to draw conclusions. None of the reported studies addressed patients' quality of life. When compared to usual care CGA, inpatient rehabilitation[5] was shown to reduce functional decline and admissions to nursing homes. Evidence for benefits of *inpatient geriatric consultations* is lacking.

2.3.2.2 In outpatient settings

CGA performed as *home visits* to outpatients[109] was shown to reduce functional decline and admissions to nursing homes when compared with usual care. Data for post-hospital discharge and outpatient geriatric consultation are scarce. A recent Danish quasi-RCT showed that *post-hospital discharge* home visits and follow-up by a geriatrician and a specialized nurse reduced the short-term readmission rate for acute medical patients by almost 50% compared with usual care[110]. In two studies, *outpatient CGA* that addresses treatment of patients at a high risk of hospitalization was shown to prevent decline in function and quality of life[111,112]. A long-term outpatient CGA model in an ambulatory setting in Sweden resulted in longer survival and fewer days in hospital compared with usual care[113].

The value of CGA by geriatricians serving as community consultants is poorly investigated and remains controversial[16]. Two studies evaluated geriatrician consultation comprising direct contact with patients[114,115]. Two other studies examined consultations that did not include direct patient contact[116,117]. The studies of direct geriatrician involvement in patient care identified target intervention subgroups of patients at high risk of frailty or patients who were high service users[114,115]. One of these studies was limited by a retrospective cohort design[114]. The second study was designed as a long-term RCT. It showed a significant reduction in the combined outcomes regarding deaths, institutionalizations, or need for home care in the subgroup of patients who were at risk of frailty. CGA was followed up by geriatric intervention by the primary healthcare[115].

Interventions in which geriatricians had direct patient contact were more likely to yield better outcomes than interventions where the interaction was limited to support of other clinicians, regardless of the setting[16].

2.3.3 Literature overview of the effectiveness of outpatient geriatrician-led CGA

The aim of this literature overview was to summarize research on the effectiveness of outpatient geriatrician-led CGA/CGC models on healthcare utilization, medication use, cognitive function, ADL function, quality of life, and mortality (safety). Systematic reviews and meta-analyses were used as the primary source of evidence. Geriatricians as outpatient consultants or as primary care providers were not directly considered in any of the identified systematic reviews.

A meta-analysis of trials of preventive home visits[106] reported favorable, but not statistically significant effects on mortality, nursing home admission, or function. After stratification of the studies on geriatrician involvement, no significant effect was found of any of the outcomes. Inclusion of a clinical examination in the home visit was associated with a reduction in functional decline (OR 0.64, 95% CI: 0.48–0.87).

A meta-analysis of 89 trials of complex interventions including 19 studies of care involving geriatricians[118] found that CGA and community follow-ups were associated with fewer nursing home admissions (RR 0.87, 95% CI: 0.83–0.90), improved physical function (standardized mean difference −0.08, 95% CI: −0.11 to −0.66), and lower risk of hospital admissions (RR 0.94, 95% CI: 0.92–0.97).

Another meta-analysis of complex interventions[107] focused on the impact on mortality of CGA, provided either as primary care or as an outpatient consultation. All interventions in the included studies involved a geriatrician. The merged data affirmed that CGA did not reduce mortality (RR 0.95, 95% CI: 0.82–1.12, *P* = 0.62).

Other reviews reported conflicting results[108,109,119]. Several systematic reviews of the effectiveness of the outpatient geriatrician-led CGA/CGC are still ongoing[120-123]. A recently published systematic review, including outpatient geriatrician-led CGA/ CGC, confirmed that CGA/CGC may facilitate clinical decisions when planning personalized care of older persons. The review concluded that further studies are needed to test the ability of CGA/CGC to improve clinical outcomes[124]. A systematic review evaluating the effectiveness of a geriatrician-led CGA model on cognition, function, and quality of life compared with usual care or other care models is ongoing[122].

Table 2. Main systematic reviews on the effectiveness of CGA including the outpatient geriatrician-led interventions on hospital contacts, medication use, cognitive function, ADL function, quality of life, and mortality.

First author /Year	Subject of study	Type of intervention	Outcomes					
№ of included studies			Hospital admissions and ED visits	Medication use	Cognitive function	ADL/ physical function	Quality of life	Mortality
Stuck, 1993[108] 28 RCTs	Meta-analysis of five CGA types	Geriatric units/inpatient and outpatient consultations/hospital-home assessment/home visits	NR	NR	NR	NR	NR	↕
Jonsson, 2003[119] 30 RCTs	Geriatric rehabilitation as an integral part of geriatric medicine in the Nordic countries	Teams/complex interventions in different settings and clinical conditions	↕	↕	↕	↕	↕	↕
Stuck, 2002[109] 18 RCTs	Home visits to prevent nursing home admission and functional decline	Primary and preventive care/home visits	↕	NR	↕	↕	NR	↕
Kuo, 2004[107] 9 RCTs	Effect of CGA on mortality	Teams/ complex interventions	NR	NR	NR	NR	NR	~
Beswick, 2008[118] 89 RCTs	Community-based complex interventions to improve function and maintain independence	Teams/ complex interventions	+	NR	~	+	NR	~
Huss, 2008[106] 21 RCTs	Multidimensional preventive home visits.	Teams/ complex interventions	NR	NR	~	~	NR	~
Eklund, 2009[125] 9 RCTs	Coordinated and integrated interventions targeting frail elderly	Teams/ complex interventions	-	NR	~	~	NR	NR
Totten, 2011[16] 28 RCTs, 10 SRs	Effect of geriatrician on outcomes of inpatient and outpatient care	Teams/complex interventions/	+	+	NR	↕	NR	~
Pilotto, 2017[124] 18 RCTs 19 SRs and MAs	CGA in different health care settings and clinical conditions	Teams/ complex interventions, Three study in outpatient or community-dwelling settings	↕	NR	+	NR	NR	+

Abbreviations: CGA = Comprehensive Geriatric Assessment; RCT = Randomized controlled trial; SR = Systematic Review; MA = meta-analysis; ED = Emergency Department; ADL = Activities of daily living.
Systematic reviews summary impact: + = Positive Impact; − = Negative Impact; ~ = No difference, ↕ = Unable to determine/Inconsistent results; NR = Not studied or reported.

2.4 SUMMARY OF THE LITERATURE OVERVIEW

The many good efforts are still in sharp contrast with the lack of robust evidence of the effectiveness of the tools used to measure inappropriate polypharmacy or of the interventions aimed at reducing it in older people. Medication misadventures, defined as medication errors and adverse drug events, remain a leading public health issue, particularly among older people[126,127]. The harm of 'drug misadventure' ranges from mild discomfort to death. It is estimated to be responsible for an average of 35% unplanned hospital readmissions[128] and up to 50% of nursing home admission[129].

According to the American Evidence-based Synthesis Program[16], geriatricians serving as primary care providers manage medication more effectively than other generalists (general internal medicine or family practice) by avoiding inappropriate medications[130].

The outpatient CGA/CGC with geriatricians in multidisciplinary teams and as consultants had mixed impacts on hospital admission and ED visits, and did not reduce mortality compared with usual care. No outpatient geriatrician-led CGA/CGC addressed the prevalence of hyperpolypharmacy as an outcome measure. Outpatient CGA/CGC with geriatricians in multidisciplinary teams and as consultants had mixed impacts on cognitive function and ADL function. Very few studies addressed quality of life as an outcome, and these studies reported inconclusive results or no effect.

A meta-analysis of complex interventions including CGAs confirmed that CGA improved physical function and reduced the risk of hospital admission and institutionalization in community settings[118].

Interventions in which geriatricians had direct patient contact were more likely to yield better outcomes than interventions where the interaction was limited to support of other clinicians, regardless of the setting[16].

The optimal components of CGA/CGC interventions and delivery remain poorly understood.

2.5 THE GERIATRICIANS' ROLE

Geriatricians are physicians who have received additional training and are certified in the care of older adults with multiple, often complex health issues. In Denmark, geriatric medicine has been a fully recognized medical specialty since 1972, in the UK since 1948, and it is currently the largest medical specialty in the UK. In the USA, geriatric medicine was approved as a subspecialty of internal medicine and family medicine in 1985.

Geriatricians' role in healthcare services ranges from serving as leaders of multidisciplinary teams to occasionally being consultants or assuming the position of the clinician holding primary care responsibility. The low number of geriatricians in most Western countries makes a strong case for using their specialist competences in the best

possible way. In 2015, 107 physicians were specialized in geriatric medicine in Denmark, which means less than one geriatrician per 8,000 Danes aged ≥ 65 years. The ratio of geriatricians is unlikely to increase sufficiently to meet the demands of the aging population. In Denmark, only 17 trainees are pursuing this subspecialty in 2018.

To exploit geriatricians' knowledge and skills, it is important to understand which geriatrician-led models of CGA are the most effective. Several systematic reviews did not separate CGA led by a geriatrician from CGA led by a nurse or primary care physician[105,106,109,131,132]. One systematic review found a beneficial effect of geriatrician-led CGA in inpatient rehabilitation[5].

The literature provides also limited insight into the components of geriatrician-led CGA/ CGC that may work best for the individual patient. The two systematic reviews of multi-disciplinary teams including geriatricians and complex interventions involving geriatricians that attempted subgroup analyses[107,118] failed to identify characteristics that were likely to yield a positive outcome.

2.6 The concept of medication adjustment as a key element of geriatrician-led CGC

Today, two-thirds of the people aged ≥ 65 years have two or more chronic conditions, often receive care from several clinicians, and take multiple medications[133]. Medication is the most frequently used and misused form of therapy in older people[134]. There is general agreement that clinicians should review the patient's medications at each visit. However, this is often not practicable due to time restrictions[123].

An evaluation of the problems and needs revealed by a CGA may simplify medication prescription by prioritizing pharmacological and healthcare requirements in older people. In this way an improved quality of prescribing and a reduction of the risk of drug-related illness may be achieved[135].

2.7 The geriatrician-performed CGC in a community rehabilitation unit

The increasing pressure to reduce the number of hospital beds by avoiding admissions and reducing length of stay motivates the effort to develop alternatives to inpatient care, e.g. care in a non-hospital-based rehabilitation unit. The staff of the Danish community rehabilitation units has expertise in the care of older people with functional decline. In collaboration with the staff, the geriatrician may be able to perform many parts of CGC. This comprises careful medication adjustment with attention to drugs that lead to iatrogenic functional deterioration. Involvement of a large team from a geriatric department may involve unnecessary costs. Therefore, it was necessary in an experimental design to develop a modified CGC model in order to test the model's effectiveness *(Paper I)*[136].

To our knowledge, no RCT has evaluated the effectiveness of geriatrician-performed CGC in a non-hospital-based rehabilitation unit with regard to healthcare utilization, medication optimization, and patient-centered outcomes like cognitive function, ADL function, and quality of life.

3 RESEARCH QUESTIONS

The present dissertation seeks to answer two main questions.

First, does a CGC comprising CGA and interventional follow-up by a geriatrician reduce the number of hospital contacts in older people referred to a community rehabilitation unit without increasing ambulatory and GP contacts, institutionalization, and mortality?

Second, does CGC optimize older people's medication use, improve their functional ability, and their quality of life?

4 AIMS

The aims of this dissertation were to examine whether a geriatrician-performed CGC in older people referred to a community-based rehabilitation unit

1) reduces the number of hospital contacts and
2) optimizes medication use, improves cognitive function, ADL function, and quality of life during the first 90 days after start of the individualized rehabilitation stay.

The intervention was compared with usual care in a Danish community rehabilitation unit.

5 HYPOTHESES

We hypothesized that a geriatrician-performed CGC established in a non-hospital-based rehabilitation unit can

1) reduce the total number of hospital admissions and ED visits without increasing the number of days in hospital, ambulatory contacts and contacts to the GP, and without increasing institutionalization and mortality within 90 days;
2) reduce the prevalence of hyperpolypharmacy and optimize medication profile within 90 days; improve cognitive function measured by the Mini-Mental State Examination; improve ADL function measured by the Modified Barthel-100 Index; and improve overall quality of life measured by the Depression List within 10, 30, and 90 days.

In testing these hypotheses, we compared the intervention with a standard rehabilitation stay with no geriatrician-led approach, but with the GP serving as back-up.

6 MATERIALS AND METHODS

In this section, the methodological considerations and principles for the modified CGC are described (*Paper I* [136]).

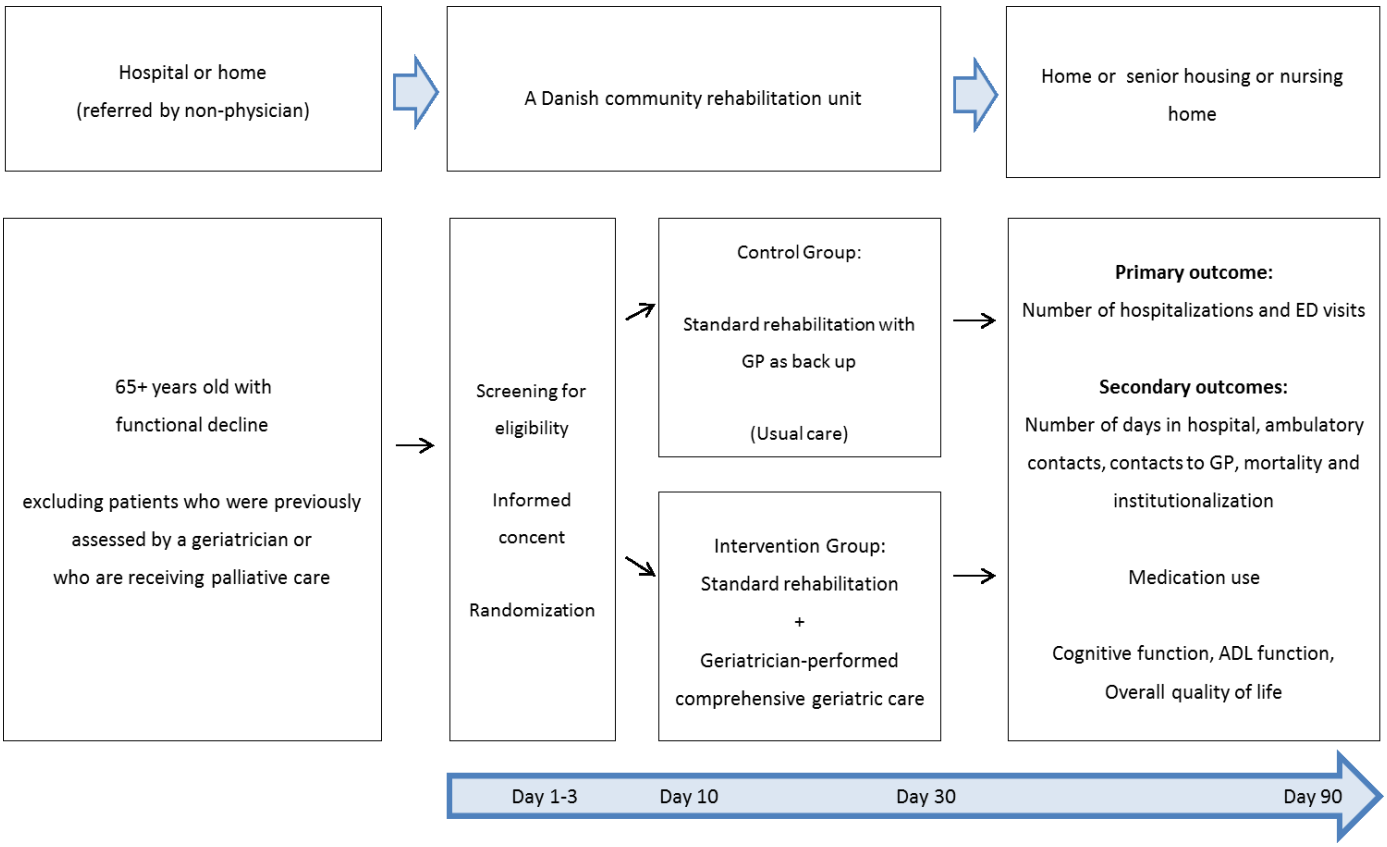
6.1 DESIGN, PARTICIPANTS, AND SETTING

The study was an open, assessor-blinded clinical RCT with two parallel groups.

The inclusion criteria were age 65 years or older and referral to a community rehabilitation unit from a hospital department or own home. The exclusion criteria were assessment by a geriatrician during the past month or receiving palliative care.

The participants were all residents of two non-hospital-based rehabilitation units, Vikærgården (64 rooms) and Thorsgården (24 rooms), in Aarhus Municipality, Denmark. The Danish rehabilitation units (hereafter referred to as 'rehabilitation units') are not part of hospitals and are run by the municipal authorities. The older people attending rehabilitation stayed overnight at the unit for the duration of the program. The staff at the unit consists of community nurses, assistant nurses, physiotherapists, occupational therapists, and nutritionists. GPs provide medical assistance on demand (Figure 1 [136]).

Figure 1. Study flow (*Paper I* [136]).



6.2 RECRUITMENT

Participants were recruited consecutively from the rehabilitation unit Vikærgården in the period from 17 January 2012 to 29 May 2015 and from the rehabilitation unit Thorsgården from 20 October 2014 to 29 May 2015. The project manager screened the participants for eligibility at the rehabilitation units and obtained written informed consent from each participant or from his/her relatives within 2 days of their arrival at the rehabilitation unit. All had 24 hours to consider or discuss with their relatives before the written informed consent was obtained.

During study enrolment, the following adjustments were made to accelerate the inclusion of participants: The inclusion age was lowered from 70+ to 65+ as of 14 May 2012 (after 58 persons had been randomized); the period for previous contact with a geriatrician, which was initially set to 3 months was reduced to 1 month from 2 December 2012 (after 84 persons had been randomized); recruitment from the rehabilitation unit at Thorsgården was initiated on 20 October 2014 (after 290 participants had been randomized).

All the changes were submitted to ClinicalTrials.gov (NCT01506219)[136].

6.3 ETHICS

Eligible participants with dementia or confusion on arrival at the rehabilitation units were also included. Under the consent procedure, the project manager assessed the person's cognitive capacities. Cognitive impairment was defined by: (1) a Mini-Mental State Examination (MMSE)[137] score of <25; (2) a Confusion Assessment Method (CAM)[138] indicating delirium; or (3) a clinical cognitive evaluation undertaken by the project manager. Eligible participants who were not cognitively impaired gave their written informed consent. Consent from cognitively impaired patients was given by a relative.

The study was approved by the Ethical Committee of the Central Denmark Region, record no. M-20110262, and conducted in accordance with the Helsinki Declaration. All data were treated confidentially and participants were assured anonymity (Danish Data Protection Agency, record no. 2012-58-006)[136].

6.4 RANDOMIZATION AND BLINDING

Randomization took place within 3 days after the participants' arrival at the rehabilitation unit. Random allocation in a 1:1 ratio to geriatrician-performed CGC (the Intervention group, IG) or to usual care (the Control group, CG) was done by an independent external organization ('TrialPartner', Public Health and Quality Improvement, Central Denmark Region, Denmark). The project manager assessed the treatment allocation by logging into the remote internet-based randomization system after having obtained written consent. The randomization sequence was computer-generated and carried out in blocks of unknown and variable size. The randomization was stratified according to sex, age (65 to 79 and 80 years and older), and place of referral.

In the IG, the geriatrician informed participants and relatives about the allocation and gave a personal contact information card to participants or relatives. Owing to the nature of this study, it was impossible to blind participants and their relatives to the allocation group. The project manager collected data on age, gender, place of referral, and comorbidity before randomization; and conducted the intervention. The project manager was blinded to the study outcomes, which were collected from the registers or by a blinded research occupational therapist. The rehabilitation units' staff, particularly physiotherapists, were not blinded.

The project manager informed the participant's GPs by letter about the persons' study participation without giving information about their allocation. In the IG, the geriatrician informed GPs briefly by mail about the treatment plan via the Electronic Patient Record[136].

6.5 STANDARD CARE IN THE REHABILITATION UNIT (CARE IN THE CONTROL GROUP)

The standard rehabilitation program lasts 3–5 weeks and is based on the resident's general situation, capability, and wishes/needs. On the first day of rehabilitation, the resident's functional status is observed by the rehabilitation unit's physiotherapists and occupational therapists, and nutritional screening is performed by the rehabilitation unit's nutritionist. The team members discuss the patient's discharge destination and necessary arrangements with the patient and his/her relatives at the mid-term meeting and again before discharge from the rehabilitation unit. A municipality nurse participates in these meetings either in person or by telephone. The decision on destination after discharge is based upon the patient's motivation and his or her functional and medical status. Rehabilitation services are not free of charge as the residents pay a moderate fee for their stay.
The typical standard rehabilitation is described in detail in Appendix 3. A.

The person's GP may be involved during the rehabilitation stay if required by the units' staff or, occasionally, on the GP's own initiative. Acute medical aid (ambulance or out-of-hours GP) is called for in case of illness after 4 p.m., on weekends, and during public holidays. Furthermore, participants can be referred to the Department of Geriatrics at Aarhus University Hospital if needed during their rehabilitation stay. After discharge from the rehabilitation units, the patient's GP is responsible for further treatment[136].

6.6 CARE IN THE INTERVENTION GROUP

The participants in the IG had the same access to usual care as participants in the CG. Additionally, a senior consultant geriatrician in collaboration with the staff of the rehabilitation units performed a CGC. The CGC consisted of a primary assessment, related medical treatments, and clinical follow-up.
The primary assessments lasted about 1 hour and included primary clinical judgment and routine blood tests, review of comorbidity conditions and prescribed medications, a life expectancy evaluation, and a decision regarding advanced care preferences.
The participant's current problems, expectations, and aims were defined in dialogue with the patient and/or any relatives. Targeted problem solving focusing on the potentially reversible causes of functional deterioration was established. Medication adjustment was based on clinical judgment and performed with particular attention to drugs that may cause iatrogenic functional deterioration. The balance of risks and benefits of the drug was explained to the participants and/or relatives. No systematic approaches to deprescribing were employed. The Beers Criteria[139] and the STOPP/START screening tool[59] were used as inspiration[59,139].

The geriatrician followed the participants with regard to changes in symptoms, signs, or results of relevant blood tests that might indicate a restart of a discontinued medication. If appropriate, the geriatrician on site carried out relevant medical treatments, including intravenous antibiotics and blood transfusions (Table 3).
The geriatrician sent the discharge summary for each IG participant to the GP.

The geriatrician was present at the rehabilitation units for 18.5 hours per week and could be contacted by phone for any reason by participants, their relatives, or the units' staff on weekdays from 8 a.m. to 3 p.m.[136].

Table 3. Care in the Intervention group versus the Control group at a Danish community rehabilitation unit (*Paper I* [136]).

Elements of CGC: The Medical Assessment	**Intervention group: CGC by geriatrician**	**Control group: Usual care**
Problem list is obtained	Yes	No
Comorbidity conditions and disease severity	• Assessed systematically • Included medical examination, primary clinical judgment, and routine blood tests*	• GP visits, if required by the staff or occasionally on the GP's own initiative • Blood pressure, pulse, weight by a rehabilitation unit nurse
Decision on advanced care	Yes	No
Medication review and adjustment	• Performed systematically within the first 3 days and during the stay if needed	• Approved by the GP, by phone, or e-mail consultation on first day and during the stay if needed
Treatments with intravenous antibiotics or blood transfusions	Yes	No
*Other paraclinical assessments** or specialist outpatient consultations*	• Electrocardiography • Referral by geriatrician with geriatric follow-up	• Referral by GP with the GP's follow-up

*Hemoglobin, leucocytes, C-reactive protein, P-albumin, P-Potassium, P-sodium, glomerular filtration rate.
**Control of cholecalciferol (Vitamin D3) if no Vitamin D3 treatment given and/if Vitamin D3 deficiency is suspected clinically deficit; control of thyroid-stimulating hormone (TSH) if TSH was not available within the past 2 months; International Normalized Ratio (INR) controls in all patients on warfarin therapy. Blood samples were analyzed at the Department of Clinical Biochemistry, Aarhus University Hospital, in the same manner as samples taken at the Department of Geriatrics, Aarhus University Hospital.

6.7 OUTCOMES AND ASSESSMENT MEASURES

6.7.1 Baseline data

Before randomization, baseline characteristics were registered manually by extraction from electronic medical records by the project manager. The baseline variables comprised age, gender, place of referral, marital status, residence, previous diagnoses, medication use, and comorbidity burden by the Charlson Comorbidity Index (CCI)[140]. The CCI was used to categorize comorbidity into three levels: 0 = low, 1–2 = moderate, and 3 or more = high.

Cognitive function, ADL function, and quality of life measures were assessed by a research occupational therapist on day 3 after admission to the rehabilitation units. Data on use of walking aids, personal social services (including practical help and shopping, transport, and emergency call), and homecare and district nurse services were obtained from the Aarhus Community Care Record by the research nurse.

6.7.2 Primary outcome *(Paper II)*

The primary outcome was the number of hospital admissions and ED visits in the first 90 days following admission to the rehabilitation units.

6.7.3 Secondary outcomes *(Papers II, III)*

The secondary outcomes included the number of days in hospital, number of ambulatory contacts (except to the Department of Radiology), number of GP contacts (daytime consultations and visits, daytime phone and email consultations, evening and night visits, evening and night phone consultations, all other services), medication use, cognitive function, ADL function, overall quality of life (OQoL), residential status, and mortality from baseline to the 90-day follow-up.

6.7.4 Data collection

6.7.4.1 Hospital contacts, days in hospital, GP contacts, residential status, and mortality

Data on hospital contacts and number of days in hospital, number of ambulatory contacts, number of GP contacts, and mortality were collected by the project manager from the National Patient Register or the Danish Psychiatric Register, the National Health Insurance Service Register, and Danish Civil Registration System, respectively.

Data on residential status were collected from the Aarhus Community Care Record by the research nurse.

6.7.4.2 Medication use

Data on medication use were obtained from the Aarhus Community Care Record by the research nurse. A medication was defined as 'regular' if it was taken according to a fixed (usually daily) schedule. 'As needed medication' was not recorded. Medication amount was categorized into three groups based on the number of

unique regular medications prescribed concurrently: nonpolypharmacy (0–4), polypharmacy (5–9), and hyperpolypharmacy (≥10 medications per day). These cut-off points were based on previous studies[141,142].

The participants' medication use was assessed by prevalence of use of at least one medication within the Anatomical Therapeutic Chemical (ATC) classes, and the presence of medication changes (discontinuation, initiation, dosage decrease or increase) within the respective ATC classes. Some medication groups were considered to be of particular interest. These included psychotropics, antihypertensives, cholecalciferol, and drugs included in the Danish Health Authority's list of drugs for which the indication should be reconsidered in older people[143].

6.7.4.3 Cognitive function

Cognitive function was assessed by the MMSE. The MMSE is a 10-minute bedside measure of impaired thinking. The items of the MMSE include tests of orientation, registration, recall, calculation and attention, naming, repetition, comprehension, reading, writing, and drawing. The MMSE sum-score indicates severe (≤9), moderate (10–18), or mild (19–23) cognitive impairment, and normal cognitive function (≥24 out of 30)[137]. The MMSE is a widely used performance-based screening test for cognitive impairment[144], but is not very accurate. The summary accuracy at a cut point of 24 was sensitivity 0.85 and specificity 0.90 for the detection of dementia in older people living in the community[145]. Age and education are associated with MMSE test performance, while gender has no impact[146]. Across different age and education subgroups, changes from at least 2 up to 3 points indicate significant (i.e., reliable) changes in MMSE test scores at a 90% confidence level, and a change of 2–3 points is considered to be of importance[146].

6.7.4.4 ADL function

ADL function was measured by the Modified Barthel-100 Index (MBI)[147]. The Barthel Index (BI) is originally developed to measure ADL function in stroke patients[148], but subsequently its use has been extended to geriatric patients[149]. BI can be repeated at regular intervals to assess changes in the overall functional ability of the disabled person, and is widely used both in clinical practice and research[150]. In Denmark, the BI version modified by Shah et al. (Barthel-100 Index MBI) is recommended since 2003 to measure functional decline in older people[151].

The MBI is a 10-item instrument that provides a score of basic daily activities (feeding, bathing, grooming, dressing, bowels, bladder, toilet use, transfer, mobility, and stair climbing). It may be used as questionnaire or in interview. It may be face to face or by telephone. However, people who may not be fully active or fully cooperate, for whatever reason, may be inaccurately scored. The scores range from 0 to 100, with a higher score indicating greater independence. Depending on the methods used, the minimal clinically important difference (MCID) is about 8 points[152]. Impairment in ADL function would be a strong indicator of dependency and in many cases indicate a need for 24-hour care or at least a need for rehabilitation[153].

6.7.4.5 Quality of life

OQoL was measured by the Depression List (DL)[154-156]. The DL is an interview-based questionnaire validated among nursing home residents. It can be completed by the participants themselves, provided they have a MMSE score ≥ 5. The DL consists of 15 questions covering emotional well-being, social relationships, life-satisfaction, comfort, functional competence, and autonomy. The scale ranges from 0 (best quality of life) to 30 (poorest quality of life).

All the functional measurements are validated for use in an elderly population. All questionnaires were performed as structured interviews. Measurement of cognitive function, ADL function, and OQoL outcomes were assessed at days 10, 30, and 90 after admission to the rehabilitation units by a blinded research occupational therapist (Table 4).

The trial outcome follow-up was completed on 27 August 2015[136].

Table 4. Data collection overview (*Paper I* [136]).

✓ Drawn from national registers ❖ Recorded through the Electronic Patient Record by the project manager ▪ Recorded through the Community Care Record by a research nurse ○ Obtained by a blinded research therapist		Before arrival to a rehabilitation unit (day 0)	Day 1-3	Day 10	Day 30	Day 90
Primary outcome	Number of hospital admissions and ED visits					✓
Secondary outcomes	Number of days spent in hospital					✓
	Number of ambulatory contacts					✓
	Number of contacts to GPs					✓
	Baseline data		❖			
	Medication use		❖			▪
	MMSE		○	○	○	○
	The 30-second Chair Stand Test *		○	○	○	○
	Modified Barthel-100 Index		○	○	○	○
	Depression List		○	○	○	○
	Residential status	▪				▪
	Mortality				✓	✓

*Not reported in this PhD Dissertation.

Data collection on the 30-second Chair Stand Test (30-s CST)[157] to measure changes in physical function was started on 10 October 2012. The 30-s CST measures body strength by determining the number of times the participant can stand up fully and sit down in 30 seconds with the arms crossed over the chest (Appendix 3. G). However, the majority of the participants were unable to perform the original version of the test or a modified version of the test, where use of an armrest is allowed.

The other originally planned pre-specified outcomes were the use of walking aids, personal social services (including practical help and shopping, transport, and emergency call), and homecare and district nurse services[136]. These outcomes are not reported in this PhD thesis because they are planned to be included in a subsequent secondary cost-effectiveness analysis.

6.8 STATISTICS

6.8.1 Power calculation

For the power calculation, we used data on hospital contacts from the Danish National Patient Register on persons receiving rehabilitation at the community rehabilitation unit Vikærgården from 1 April 2009 to 31 March 2010. There were 153 hospital contacts (hospital admissions and ED visits) among 550 persons aged ≥ 65 years within 3 months after rehabilitation admission. For the sample size calculation, we expected a 25% reduction in number of the hospital contacts, which we regarded as a clinically relevant change. The estimated dropout was set to 20% in both groups, as mortality was expected to be high. To obtain 80% statistical power and a significance level of 0.05, we therefore needed to recruit 370 participants[136].

6.8.2 Data analysis

All data except for the registers data were entered into a database (Access 2010) by the research nurse. The statistical analysis was conducted based on a predefined statistical protocol[136].

Descriptive statistics for baseline data were calculated as a percentage for categorical variables, while mean with standard deviations (SD) for normally distributed data or median, interquartile range (IQR), and range for non-normally distributed data were used for continuous variables. Distribution was checked by manually inspecting distribution curves and Q-Q plots. Categorical variables were analyzed using Pearson's chi-squared test or Fisher's exact test. Continuous variables were analyzed using Student's t-test or the Mann-Whitney U test.

The number of hospital admissions, ED visits, ambulatory contacts, and GP contacts were compared by incidence rate ratios (IRRs) with 95% confidence intervals (CI). IRRs were calculated using a negative binominal regression with adjustment for mortality by including the risk time as an exposure variable[158].

Medication status binary outcomes were analyzed in survivors using a logistic regression model and were adjusted for baseline medication values using a penalized maximum likelihood estimation method[159].

Mortality rates after 30 and 90 days were calculated as the percentage of deaths in the total population per group, and Cox regression analysis was used to calculate hazard ratios (HRs) with 95% CIs. Each patient was followed for the same period of time without censoring, and only death terminated the follow-up period. Time of death was recorded by date.

The cognitive function, ADL function, and OQoL measures at the group level were analyzed using a repeated measurements mixed model. The distribution between participants who worsened or did not change versus participants who improved their cognitive function, ADL function, or quality of life after 90 days was analyzed by creation of dichotomous variables and a logistic regression model for binary response by maximum likelihood. Results were expressed as ORs with 95% CIs. In non-survivors and in case of missing baseline observations, the missing measures were set to the worst possible values (zero points for MMSE and MBI, 30 points for DL).
The worst value imputation method was used in all other cases of missing values[158,160].

Stata 13 (StataCorp, College Station, TX, USA) was used for computation. The statistical methods and STATA codes as described below in Table 5.

The two-sided significance level of 5% was used for evaluation of statistical significance in the primary and secondary outcomes.

Table 5. Summary of the statistical methods and STATA codes.

Variable	Data type and distribution	Statistical method *STATA codes*
Only at baseline		
• Age	Continuous, normally distributed	Histogram, *hist* Student's t-test, *ttest*
• MMSE score • MBI score • DL score • CCI score	Continuous, not-normally distributed	Histogram, *hist* Mann-Whitney U-test, *ranksum*
• Gender • Place of referral • Previous diagnoses	Categorical	Pearson's chi-squared, *tab, chi* Fisher's exact if <6 observations, *tab, chi exact*
• CCI, three categories: CCI=0; CCI=1-2; CCI>2 points • MMSE, two categories: 0-18, 19-30 points • MBI, three categories: 0-49; 50-79; 80-100 points • DL, three categories: 0-9; 10-19; 20-30 points	Categorical	Pearson's chi-squared, *tab, chi*
Both at baseline and as outcomes		
Medication at day 0 and at 90 • Number of medications	Discrete count variable data	Mann-Whitney U-test, *ranksum*
• Prevalence of non-polypharmacy, polypharmacy, and hyperpolypharmacy • Prevalence of use of at least one medication within all ATC classes • Presence of medication changes within the respective ATC classes	Categorical Baseline values are perfect predictors of the outcome values	Logistic regression model, adjusted for baseline medication by the penalized maximum likelihood estimation method, *firthlogit*
Function, quality of life at day 3, 10, 30, and 90 as the mean between-group differences • MMSE • MBI • DL	Continuous, not-normally distributed	Repeated measurements mixed model, *mixed contrasts*
Difference in function and quality of life at days 3 and 90 as a binary outcome at the individual level, 'improved', or 'not improved' • MMSE • MBI • DL	Categorical	Logistic regression model for binary response by maximum likelihood, *logit, contrasts*
• Residential status at day 90	Categorical	Pearson's chi-squared, *tab, chi*
Only as outcomes		
Healthcare utilization *Measuring point/periods:* - from day 0 to the end of the individualized rehabilitation stay - from the end of the individualized rehabilitation stay to day 90 - from day 0 to day 90 *Adjustment:* for age, gender, place of referral, mortality		
• Number of admissions and ED visits • Number of ambulatory contacts • Number of classified GP services	Discrete count data, which extremely over-disperse due to the high population heterogeneity	Incidence rate ratios. Negative binominal regression adjusted for mortality by including the risk time as an exposure variable, *nbreg*
• Number of persons with 'zero' or with one and more contacts	Dichotomous	Pearson's chi-squared, *tab, chi*
• Number of days in hospital	Not-normally distributed data	Mann-Whitney U-test, *ranksum*
Mortality at day 30 and 90	Time-to-event data	Cox regression, *xi:stcox*

7 RESULTS

This chapter describes recruitment of the study participants. The baseline socio-demographic and clinical characteristics, including baseline medication use are presented. The factual medical content of the CGC is briefly described. The effect of CGC on hospital contacts, GP contacts, residential status, and mortality is presented followed by results on medication use. The effects of geriatrician-performed CGC on patient-centered outcomes are described and illustrated. The chapter ends with the presentation of the post hoc sensitivity analyses and exploratory analyses of the participants with missing measurements, and the subgroup analyses with the baseline comorbidity as predictor.

7.1 STUDY POPULATION

7.1.1 Recruitment

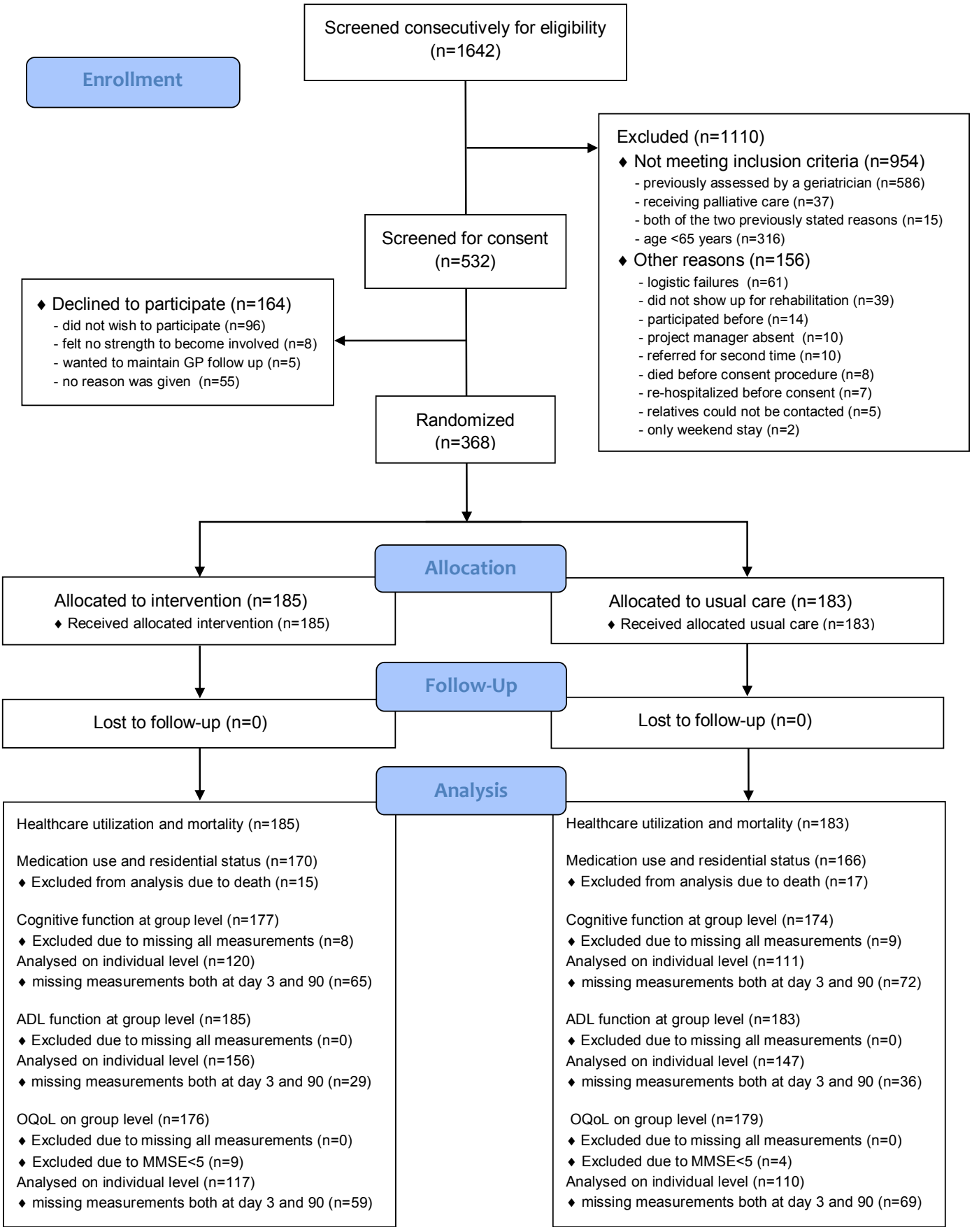
During the inclusion period, 1642 persons were referred to the rehabilitation units and screened consecutively for eligibility by the project manager (Figure 2)[136].

In all, 954 persons did not meet the inclusion criteria and 156 persons did not enter for any other reason (summarized in Figure 2). The 'logistic failures' during recruitment included situations for which the project manager was unaware or not informed of the arrival of a potential participant, mostly during a period of isolation due to a viral gastrointestinal infection in the rehabilitation unit Thorsgården in January 2015.

The inclusion criteria were met by 688 persons. In all, 164 persons (31% of those 532 who were asked for consent) declined to participate. The main reasons for decline were: 'I am not interested', 'I already has been through a lot of things, and I have no strength to become involved in the research project', 'I want to maintain the follow-up initiated by my family doctor', or no reasons were given.

Neither non-consenters nor other non-enters differed significantly from the recruited persons with respect to comorbidity burden (Appendix 2. B). Persons who did not meet the inclusion criteria (except of <65 years old persons) were significantly older, they were more frequently women, and had more often been referred from a hospital than the consenters. Those who did not enter for any other reason were significantly younger and more often men (Appendix 2. B).

Figure 2. CONSORT Flow Diagram: Participant flow *(Papers II and III)* [158,160]



7.1.2 Participants

7.1.2.1 Baseline socio-demographic and clinical characteristics

In total, 368 participants were randomly assigned to receive either geriatrician-performed CGC, n = 185, or usual care, n = 183 (Figure 2). The mean age of the participants was 78.6 (SD ± 8.1) years, 51% were women, 65% were living alone, 64% were referred from a hospital department, 28% suffered from moderate or severe cognitive impairment, 28% were substantially or completely dependent.

The main reasons given for referral to the rehabilitation units were rehabilitation need (64%), need for assessment of functional ability and clarification of future residence (25%), need for assessment of unexplained functional decline to prevent hospitalization (4%), prevention of hospital readmission (3%), and the family/spouse's need of succor (4%).

The IG and the CG did not differ with respect to socio-demographic and clinical characteristics (*Paper II,* Table 6) [158].

In total, 291 study participants had a baseline CAM assessment. Hereof, seven of the 150 (5%) IG participants suffered from delirium as did seven of the 141 (5%) CG participants.

Results of blood tests during the geriatrician's primary assessment were only complete in the IG.
Of the 183 participants with a baseline glomerular filtration rate (GFR) assessed, 60 (33%) persons had chronic renal failure defined as GFR < 60 mL/min/1.73 m^2. Of the 180 participants who had a baseline serum albumin assessment, 122 (68%) persons had hypoalbuminemia defined as serum albumin < 35 g/L.

Table 6. Baseline socio-demographic and clinical characteristics of participants *(Paper II* [158]*).*

Characteristics	Intervention group (n=185)	Control group (n=183)
Age, mean (SD)	78.8 ± 8.3	78.4 ± 7.9
Women, n (%)	93 (50)	93 (51)
Living alone, n (%)	124 (67)	116 (63)
Residence, n (%)		
Own home	170 (92)	166 (90)
Sheltered housing	14 (7.5)	17 (10)
Nursing home	1 (0.5)	0
Walking aids, n (%)		
None or stick	74 (40)	82 (45)
Walker	72 (39)	64 (35)
Wheelchair	39 (21)	37 (20)
Personal social services[1, 2], n (%)		
No	71 (38)	66 (36)
Yes	114 (62)	117 (64)
Homecare[1], n (%)		
No	86 (47)	89 (49)
Weekly	9 (5)	3 (2)
One and more times daily	90 (49)	91 (50)
Place of referral, n (%)		
Hospital department	119 (64)	115 (63)
Home	66 (36)	68 (37)
Place of rehabilitation stay, n (%)		
Vikærgården	177 (96)	171 (93)
Thorsgården	8 (4)	12 (7)
Previous diagnoses[3], n (%)		
Dementia	8 (4)	4 (2)
Previous stroke	35 (19)	30 (16)
Other cerebral diseases	24 (13)	24 (13)
Cardiovascular diseases, excluding stroke	79 (43)	77 (42)
Diabetes	25 (14)	22 (12)
Chronic obstructive pulmonary disease	18 (10)	15 (8)
Diseases of the digestive system	18 (10)	20 (11)
Chronic renal insufficiency	16 (9)	12 (7)
Charlson Comorbidity Index (CCI), median (IQR)	2 (1-3)	2 (1-3)
Low comorbidity, CCI 0, n (%)	31 (17)	34 (18)
Moderate comorbidity, CCI 1-2	101 (54)	91 (50)
High comorbidity, CCI > 2	53 (29)	58 (32)
Mini-Mental Status Examination (MMSE)[4], median (IQR)	23 (18-26)	22 (18-25)
Moderate or severe cognitive impairment, MMSE 0-18, n (%)	39 (27)	40 (29)
Modified Barthel-100 Index (MBI)[5], median (IQR)	64 (46-83)	66 (46-83)
Minimally dependent or independent, MBI 80-100, n (%)	57 (31)	52 (29)
Moderately dependent, MBI 50-79	74 (40)	83 (45)
Substantially or completely dependent, MBI 49-0	54 (29)	48 (26)
Depression List (DL)[6], median (IQR)	10 (6-14)	8.5 (5-13)
DL, sum-score 0-9 points, n (%)	65 (37)	70 (39)
DL 10-19	66 (38)	56 (31)
DL 20-30	45 (25)	53 (30)

[1] Data on personal social services and homecare were obtained in the IG for the 184 community-dwelling persons
[2] Personal social services included practical help and help for shopping, transport, and emergency call
[3] Diseases were classified according to the International Classification of Diseases, 10th edition
[4] Data on MMSE were obtained 3 days after admission to the rehabilitation units (n = 142 in the IG, n = 136 in the CG)
[5] Data on MBI were obtained 3 days after admission to the rehabilitation units (n = 185 in the IG, n = 183 in the CG)
[6] Data on DL were obtained 3 days after admission to the rehabilitation units (n = 176 in the IG, n =179 in the CG)

7.1.2.2 Baseline medication use

The IG and the CG did not differ with respect to their medication use (Table 7). Median number of drugs used was 8 drugs, range 1–22 [IQR 6–11] versus 9 drugs, range 0–19 [IQR 6–11], *P* = 0.20 in the IG versus the CG. Eighty-eight percent of the participants were taking five or more medications/day, and 38% were taking 10 or more regular medications/day at baseline.

Table 7. Regular medication in the Intervention group and the Control group at baseline (*Paper III* [160]).

Drugs users exposed for, n	Intervention group (n=185)	Control group (n=183)	OR (95% CI)	*P*-value
Total number of drugs per person,				
median	8	9		
range (IQR)	1-22 (6-11)	0-19 (6-11)		0.20
< 5 drugs/day	23	19	1.0 (0.6-1.9)	0.91
5-9 drugs/day	99	87	1.3 (0.8-1.9)	0.25
≥ 10 drugs/day	63	77	0.8 (0.5-1.2)	0.21
ATC classification system[1] class				
Gastrointestinal system	170	166	1.2 (0.6-2.4)	0.69
Cholecalciferol	21	13	1.7 (0.8-3.4)	0.17
Proton pump inhibitors	86	80	1.1 (0.7-1.7)	0.59
Blood and blood-building organs	128	136	0.8 (0.5-1.2)	0.28
Cardiovascular system	136	147	0.7 (0.4-1.1)	0.12
Loop-diuretics	52	66	0.7 (0.5-1.1)	0.10
Antihypertensives, excl. loop-diuretics	108	114	0.9 (0.6-1.3)	0.44
Urogenital system	14	21	0.6 (0.3-1.3)	0.21
Drugs for urinary frequency and incontinence	4	8	0.9 (0.5-1.6)	0.73
Endocrine system	28	35	0.8 (0.4-1.3)	0.31
Corticosteroids for systemic use	20	22	0.9 (0.5-1.7)	0.72
Systemic infections	46	51	0.9 (0.5-1.4)	0.52
Musculoskeletal system	39	31	1.3 (0.8-2.2)	0.32
Central nervous system	148	141	1.2 (0.7-2.0)	0.69
Opioids	39	42	0.9 (0.6-1.5)	0.67
Hypnotics and sedatives	9	18	0.5 (0.2-1.1)	0.08
Anxiolytics	2	2	1.0 (0.2-5.8)	0.99
Selective serotonin reuptake inhibitors	40	42	0.9 (0.6-1.5)	0.76
Tricyclic antidepressants	7	4	1.7 (0.5-5.5)	0.39
Other antidepressants	27	24	1.1 (0.6-2.0)	0.68
Antipsychotics	8	7	1.1 (0.4-3.1)	0.82
Antiepileptics	27	25	1.1 (0.6-1.9)	0.78
Respiratory system	35	29	1.2 (0.7-2.1)	0.44
Anti-asthmatic inhalers	21	22	0.9 (0.5-1.8)	0.84
Antiparasitic products, quinine	2	4	0.5 (0.1-2.6)	0.44
Dermatologicals	11	8	1.4 (0.6-3.4)	0.51
Antineoplastic and immunomodulators	4	12	0.3 (0.1-1.0)	0.05
Sensory organs	14	10	1.4 (0.6-3.2)	0.43
Various	6	3	1.9 (0.5-7.0)	0.35

[1] Anatomical Therapeutic Chemical classification system.

7.2 FACTUAL MEDICAL CONTENT OF THE CGC *(PAPER II [158])*

The median for day of start of intervention was day 3 (IQR 1–5, range 3–21 days) following arrival to the rehabilitation units. The intervention period was individualized: mean 35 (SD ± 8.1) days.

The length of attendance at the rehabilitation units was similar in both groups, mean 38 (SD ± 17) days in the IG versus 35 (SD ± 16) days in the CG, *P* = 0.13.

The medication review and adjustment was done in all participants in the IG.

The medical interventions performed by the geriatrician in IG participants during their individualized rehabilitation stay are summarized below (obtained from electronic medical records by the project manager retrospectively).

Interventions performed by a geriatrician	**No. of patients**
Routine blood tests (hemoglobin, leucocytes, C-reactive protein, P-albumin, P-potassium, P-sodium and glomerular filtration rate)	182
Additional paraclinical assessment	
Cholecalciferol (Vitamin D3)	87
Thyroid-stimulating hormone	63
Hemoglobin A1c	26
International Normalized Ratio	22
Electrocardiography	28
Arterial puncture	4
Treatments	
Intravenous antibiotics	8
Blood transfusions	9
Subcutaneous fluid therapy	9
Successful dosage reduction or discontinuation	
Antihypertensives or furosemide	78
Morphine	48
Benzodiazepines	24
Anti-asthmatic inhalers	19
Proton pump inhibitor	12
Prednisolone	7
Non-steroidal anti-inflammatory drugs	5
Anticholinergic drugs for urinary frequency and incontinence	4
Antiepileptic drugs	2
Antipsychotics	2
Catheter a demeure	14
Nasogastric feeding tube or percutaneous endoscopic gastrostomy	7
Referrals	
X-ray of lumbar spine, hip, or upper limb	6
Echocardiography	4
Cerebral computer tomography	2
Gastroscopy	2
Abdominal ultrasound	1

7.3 OUTCOMES

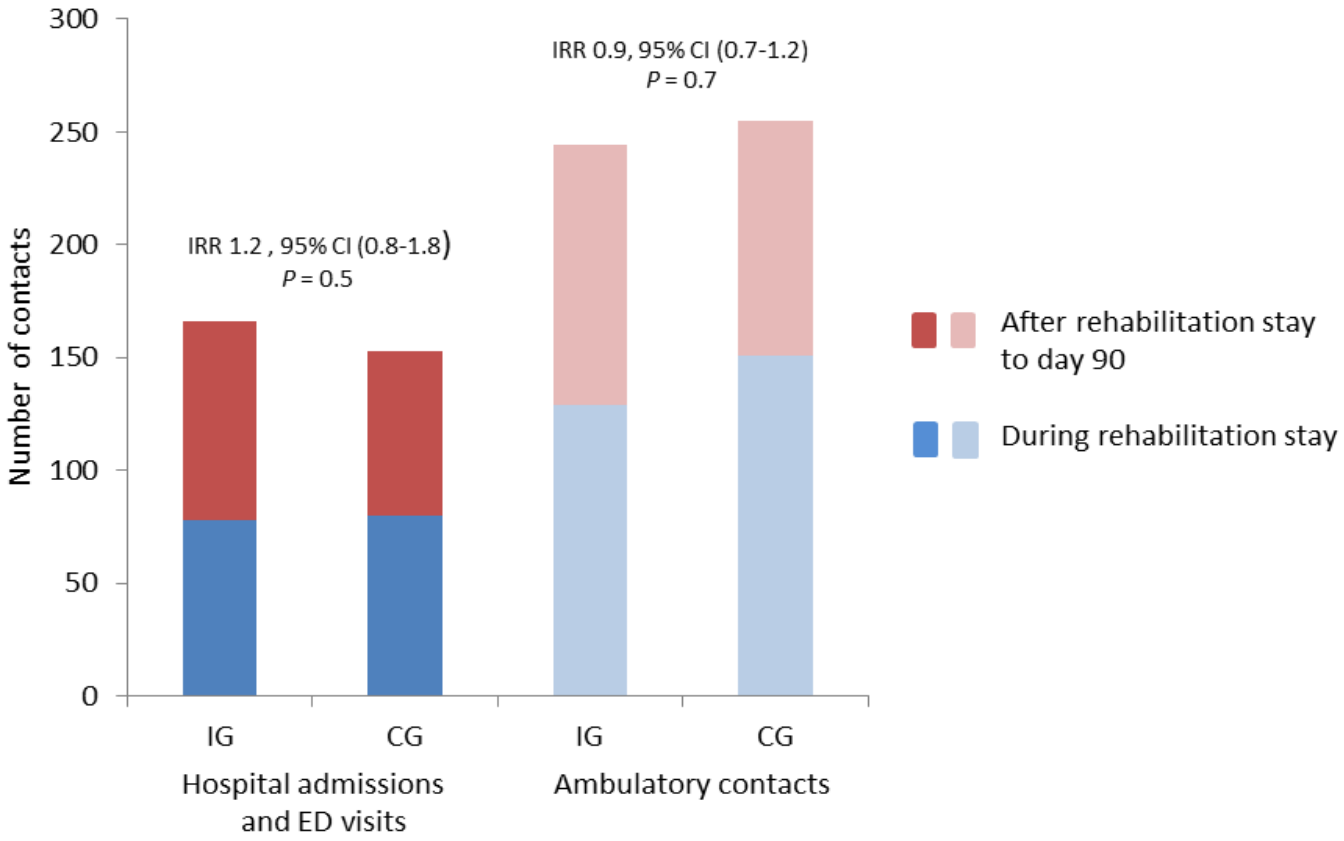
7.3.1 Hospital contacts, days in hospital, GP contacts, residential status, mortality (Hypothesis 1)

7.3.1.1 Number of hospital admissions and ED visits (the primary outcome)[158]

No significant difference in the numbers of hospital admissions and ED visits between the IG and the CG was observed in the 90-day follow-up period, IRR 1.2, 95% CI: 0.8–1.8, *P* = 0.5 (Figure 3 and Table 8).

The numbers of the hospital admissions and ED visits and the proportion of persons with no hospital admissions and ED visits did not differ between the groups during the participants' rehabilitation stay, from the end of the stay to day 90, or during the whole study period (Figure 3 and Table 8).

Figure 3. Hospital contacts obtained from the National Patient Register and the Danish Psychiatric Register.



Abbreviations: IRR, incidence rate ratio; CI, confidence intervals.

Table 8. Hospital contacts obtained from the National Patient Register or the Danish Psychiatric Register *(Paper II* [158]*).*

	Intervention group (n=185)	**Control group** (n=183)	**Incidence rate ratio (IRR)**[1] (95% CI)	***P*-value**[2]
90-day follow-up				
Hospital admissions or ED visits				
Number	166	153	1.2 (0.8-1.8)	0.5
Median (IQR)[3]	0 (0-1)	0 (0-1)		0.2
Persons without any contact (%)[4]	111 (60)	125 (68)		0.7
Persons with 1-3 contacts (%)	63 (34)	44 (24)		
Persons with ≥4 contacts (%)	11 (6)	14 (8)		
Ambulatory contacts				
Number	244	255	0.9 (0.7-1.2)	0.7
Median (IQR)[3]	1 (0-2)	1 (0-2)		0.7
Persons without any contact (%)[4]	72 (39)	70 (38)		0.4
Persons with 1-3 contacts (%)	94 (51)	93 (51)		
Persons with ≥4 contacts (%)	21 (11)	18 (10)		
Rehabilitation stay				
Hospital admissions or ED visits				
Number	78	80	1.1 (0.6-1.8)	0.8
Median (IQR)[3]	0 (0-0)	0 (0-0)		0.9
Persons without any contact (%)[4]	142 (77)	140 (77)		0.4
Persons with 1-3 contacts (%)	37 (20)	37 (20)		
Persons with ≥4 contacts (%)	6 (3)	6 (3)		
Ambulatory contacts				
Number	129	151	0.8 (0.6-1.1)	0.3
Median (IQR)[3]	0 (0-1)	0 (0-1)		0.3
Persons without any contact (%)[4]	102 (55)	96 (52)		0.4
Persons with 1-3 contacts (%)	76 (41)	81 (44)		
Persons with ≥4 contacts (%)	7 (4)	6 (3)		
After rehabilitation stay to day 90				
Hospital admissions or ED				
Number	88	73	1.21 (0.7-2)	0.5
Median (IQR)[3]	0 (0-1)	0 (0-0)		0.3
Persons without any contact (%)[4]	135 (73)	149 (81)		0.2
Persons with 1-3 contacts (%)	46 (25)	27 (15)		
Persons with ≥4 contacts (%)	4 (2)	7 (4)		
Ambulatory contacts				
Number	115	104	1.1 (0.8-1.6)	0.8
Median (IQR)[3]	0 (0-1)	0 (0-1)		0.9
Persons without any contact (%)[4]	124 (67)	122 (67)		0.3
Persons with 1-3 contacts (%)	57 (31)	56 (31)		
Persons with ≥4 contacts (%)	4 (2)	5 (3)		

Abbreviations: IQR, 25% interquartile range; IRR, incidence rate ratio; CI, confidence interval.

[1] IRR compared using negative binominal regression

[2] IRR adjusted for mortality by including the risk time as an exposure variable

[3] Number of contacts compared using the Mann-Whitney U test

[4] Number of persons with contacts compared using the chi-squared test

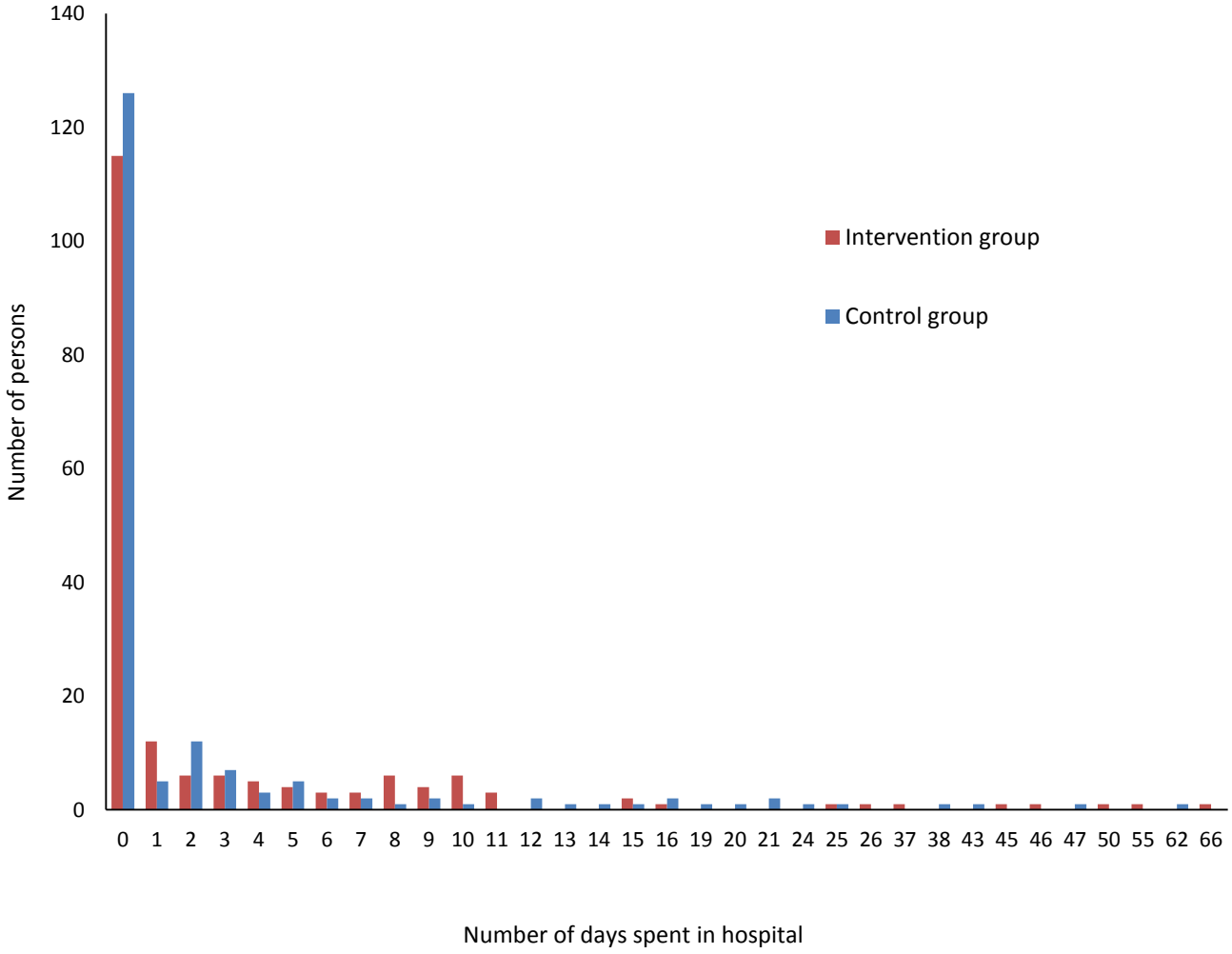
7.3.1.2 Days in hospital *(Paper II* [158]*)*

There was no significant difference between the groups in the number of days spent in hospital during the 90-day follow-up period. In total, 720 days were spent in hospital (median 0, IQR 0–3, range 0–66) in the IG versus 567 days (median 0, IQR 0–2, range 0–62) in the CG, *P* = 0.18.

In total, 115 participants (62%) in the IG and 126 participants (69%) in the CG did not spend any days in hospital (Figure 4).

An analysis of the distribution of days in hospital showed that 25 of 368 participants stayed in hospital for more than 14 days. The number of days in hospital for these participants was 367 days (13 persons) for the IG and 422 days (12 persons) for the CG. Thus, a 7% minority of the IG participants accounted for 51% of the bed days in the IG. Similarly, 7% among the CG participants accounted for 59% of the bed days in the CG (Figure 4)[158].

Figure 4. Distribution of days in hospital.



7.3.1.3 Ambulatory contacts *(Paper II [158])*

There were no significant differences in total numbers of ambulatory hospitals contacts between the IG and the CG in the 90-day follow-up period, IRR 0.9, 95% CI: 0.7–1.2, *P* = 0.7 (Figure 3 and Table 8).

The numbers of the hospital ambulatory contacts and the proportion of persons with no hospital ambulatory contacts did not differ between the groups during the participants' rehabilitation stay, from the end of the stay to day 90, or during the whole study period (Figure 3 and Table 8).

7.3.1.4 GP contacts *(Paper II [158])*

We observed a significantly lower IRR for any type of contact with the GP in the IG, except for evening and night visits and evening or night phone consultations in the 90-day follow-up period and during the individualized rehabilitation stay.

In the average 55-day post-rehabilitation period, there were no differences between the groups with respect to the rates of GP contacts, except for evening and night visits, which were higher in the IG (IRR 1.9, 95% CI: 1–3.6, *P* = 0.045). A table with details regarding the GP contacts and the proportion of persons with no GP contacts obtained from the National Patient Register or the Danish Psychiatric Register is present in the Appendix 2. E.

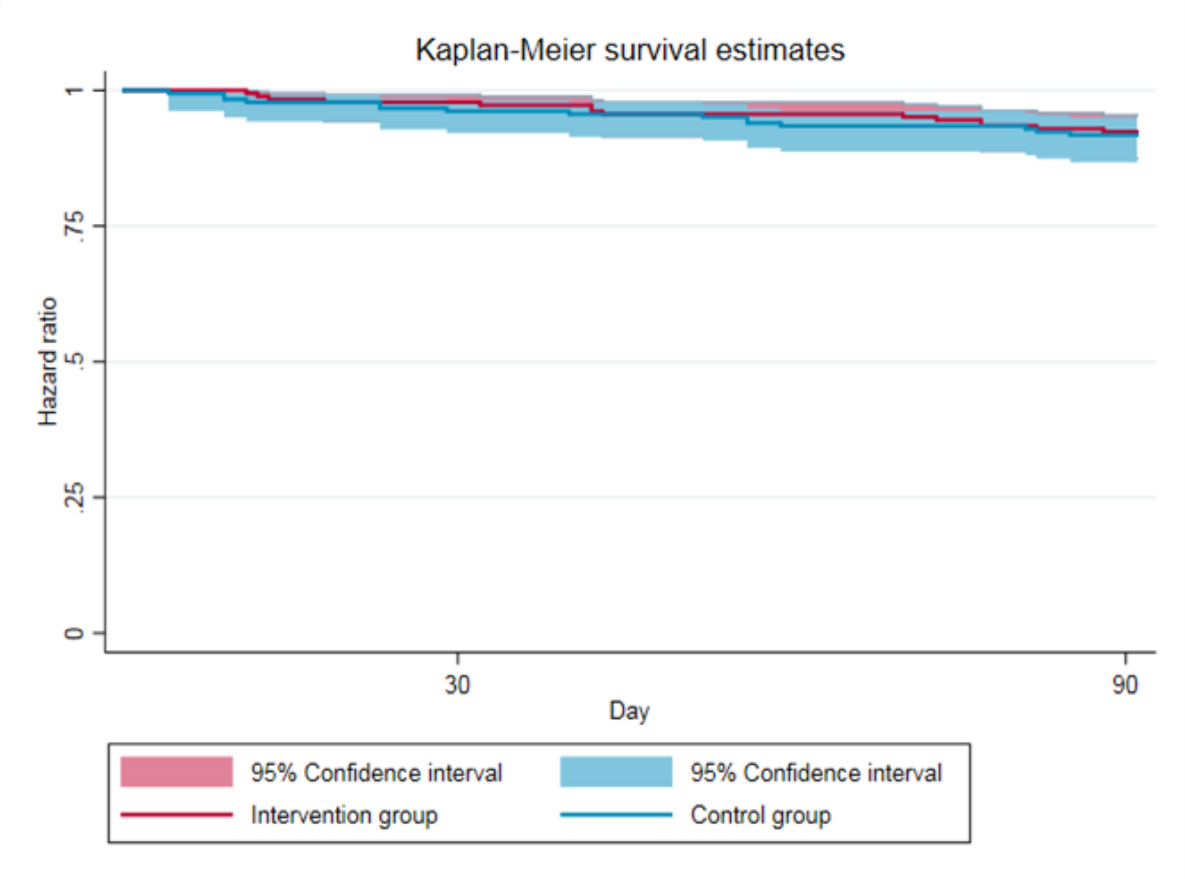
7.3.1.5 Residential status

There was no difference in the institutionalization rates between the groups (28% in both groups, OR 1.02, 95% CI: 0.6–1.7, *P* = 0.94). In total, 46 of 170 survivors in the IG versus 48 of 166 survivors in the CG had moved to a nursing home at the 90-day follow-up.

7.3.1.6 Mortality *(Paper II [158])*

The mortality rates were not significantly different between the groups: 5.4% and 8.1% in the IG and 7.1% and 9.3% in the CG, at 30 and 90 days, respectively. Unadjusted HRs of time to death within 30 and 90 days for the IG compared with the CG were 0.49, 95% CI: 0.15–1.63, *P* = 0.25, and 0.87, 95% CI: 0.43–1.7, *P* = 0.68, respectively (Figure 3). Adjustment for gender, age, and place of referral in a Cox proportional hazards model had no effect on the HRs: the adjusted HR during the 30-day follow-up was 0.49, 95% CI: 0.15–1.6, *P* = 0.25, and the adjusted HR for the 90-day follow-up was 0.85, 95% CI: 0.42–1.7, *P* = 0.65.

Figure 5. Kaplan–Meier survival estimates for older people referred to the rehabilitation units.



7.3.2 Medication use, cognitive function, ADL function, and OQoL (Hypothesis 2)

7.3.2.1 Medication use

Number of medications, and hyperpolypharmacy prevalence *(Paper III* [160]*)*

The numbers of medications were non-significantly reduced in survivors in both groups. After 90 days, a median of 7, range 0–22 [IQR 5–9] medications were used in the IG versus a median of 8, range 0–17, [IQR 6–10] medications in the CG, $P = 0.09$ (Table 9)[160].

Adjusted for baseline values, the number of persons using ≥10 medications daily at day 90 was lower in the IG than in the CG, OR 0.5, 95% CI, 0.3–0.9, $P = 0.02$ (Table 9)[160].

Medication profile *(Paper III)*[160]

Fewer persons used proton pump inhibitors, loop diuretics, and anti-asthmatic inhalers, while more persons used cholecalciferol in the IG than in the CG. No differences were found for the prevalence of other drugs use (Table 9).

Table 9. Regular medication in the Intervention group versus the Control group at the 90-day follow-up (*Paper III* [160]).

Drug users exposed for, n	Intervention group (n=170)[2]	Control group (n=166)[2]	OR (95% CI)[2]	*P*-value[3]
Total number of drugs per person,				
median	7	8		
range (IQR)	0-22 (5-9)	0-17 (6-10)		0.09
<5 drugs/day	26	26	0.9 (0.4-1.8)	0.78
5-9 drugs/day	106	82	1.7 (1.1-2.8)	0.03
≥10 drugs/day	38	58	0.5 (0.3-0.9)	0.02
ATC classification system[1] class				
Gastrointestinal system	164	153	3.1 (0.1-9.1)	0.06
Cholecalciferol	45	10	9.6 (3.5-26.8)	<0.001
Proton pump inhibitors	64	73	0.4 (0.2-0.9)	0.02
Blood and blood-building organs	110	117	0.9 (0.5-1.8)	0.80
Cardiovascular system	124	128	1.2 (0.5-2.6)	0.71
Loop-diuretics	33	61	0.2 (0.1-0.5)	0.001
Antihypertensives, excl. loop-diuretics	102	102	1.5 (0.6-3.3)	0.36
Urogenital system	11	20	0.5 (0.2-1.3)	0.16
Drugs for urinary frequency and incontinence	1	7	0.5 (0.2-1.4)	0.17
Endocrine system	24	30	0.9 (0.3-2.1)	0.73
Corticosteroids for systemic use	15	14	0.9 (0.4-2.6)	0.95
Systemic infections	6	12	0.5 (0.2-1.5)	0.22
Musculoskeletal system	38	31	1.0 (0.4-2.5)	0.98
Central nervous system	126	131	0.6 (0.3-1)	0.09
Opioids	26	26	1.1 (0.5-2.2)	0.83
Hypnotics and sedatives	5	15	0.5 (0.2-1.6)	0.23
Anxiolytics	3	3	1.0 (0.2-5.9)	0.98
Selective serotonin reuptake inhibitors	46	47	1.3 (0.6-3.2)	0.51
Tricyclic antidepressants	11	2	4.6 (0.9-20.9)	0.05
Other antidepressants	32	28	1.1 (0.4-2.9)	0.92
Antipsychotics	8	6	1.8 (0.5-6.9)	0.41
Antiepileptics	26	23	1.4 (0.3-7.3)	0.68
Respiratory system	21	29	0.2 (0.04-0.7)	0.01
Anti-asthmatic inhalers	11	21	0.2 (0.04-0.7)	0.02
Antiparasitic products, quinine	0	5	0.1 (0.001-3.2)	0.16
Dermatologicals	5	3	1.5 (0.4-5.7)	0.59
Antineoplastic and immunomodulators	3	7	1.2 (0.2-7.3)	0.85
Sensory organs	14	9	1.3 (0.4-4.2)	0.68
Various	3	3	0.2 (0.01-4.0)	0.29

[1]Anatomical Therapeutic Chemical classification system

[2] Drugs are presented in survivors

[3] ORs and *P*-values were adjusted for baseline medication values

In both groups, medication discontinuation was the most prevalent medication change followed by dosage decrease, dosage initiation, and dosage increase[160]. Dosage decrease was observed within the gastrointestinal, cardiovascular, and central nervous system drugs (Appendix 2. F)[160].

The medication changes in the IG during the individualized rehabilitation stay persisted during the post-rehabilitation period (Table 10).

Information on medication changes during the rehabilitation stay was not available for the CG.

Table 10. Regular medication changes in the Intervention group during the rehabilitation stay and up to 90-day follow-up *(Paper III [160])*

	From the beginning to the end of the rehabilitation stay[1]			From the end of the rehabilitation stay to the end of the 90-day follow-up				
Drug users[2] with any medication change within	Stopped	Dosage decrease	Started	Re-started	Re-increased dosage	Stopped	Further dosage decrease	Started
All ATC classes[3]	144	97	115	27	23	28	5	48
Gastrointestinal system*, n	83	37	89	7	8	17	1	22
Cholecalciferol	2	2	9	0	1	6	0	1
Proton pump inhibitors	22	11	9	2	2	1	0	3
Cardiovascular system*, n	46	54	21	6	7	4	2	5
Furosemide	17	15	6	1	3	2	1	1
Respiratory system*, n	18	4	3	1	0	1	0	3
Anti-asthmatic inhalers	8	1	2	0	0	1	0	1

[1] The rehabilitation stay and the post-rehabilitation period were of individual length

[2] Dosage increase was observed in 41 participants (all ATC classes) during the individualized rehabilitation stay

[3] Drugs are presented in survivors (n = 170)

*ATC classes and certain drugs were chosen based on the observed significant differences between the Intervention group and the Control group at 90-day follow-up

7.3.2.2 Cognitive function *(Paper III [160])*

Complete case analysis (n = 231)

The within-group change:

The mean MMSE significantly improved within both groups after 90 days. In the IG, MMSE increased from a mean of 21.3 (SD ± 6.1) to 23.6 (SD ± 6.4) points. The mean improvement was 1.6 points (95% CI: 0.8–2.4, $P < 0.001$). In the CG, MMSE increased from a mean of 21 (SD ± 6.1) to 24.3 (SD ± 5.2). The mean improvement was 2.3 points (95% CI: 1.6–2.9, $P < 0.001$). The mean improvement for both groups pooled was 1.9 points (95% CI: 1.4–2.4, $P < 0.001$).

The between-group change:

The mean difference in the MMSE sum-scores did not differ between the groups. It was −0.41 points (95% CI: −1.58–0.78, $P = 0.72$) in the IG versus the CG at day 90. In total, 70 of 120 persons improved their MMSE sum-score in the IG, and 72 of 111 persons improved their MMSE sum-score in the CG during the follow-up (OR 0.76, 95% CI: 0.44–1.29, $P = 0.31$).

Worst value imputation (n=351)

For MMSE, we imputed 208 (14%) missing values of the total 1472 possible MMSE measurements. The reason for missing values was lack of cooperation (171 measurements) or death (37 measurements). For these values, we imputed the worst possible MMSE value. Seventeen persons (eight persons in the IG and nine persons in CG were excluded from the analysis as all four possible measurements were missing, 68 (5%) of the total of 1472 possible measurements. The MMSE values and curves for each participant (n = 351), and the mean difference in the MMSE sum-scores for each group can be found in Appendix 2. G.

The within-group change:

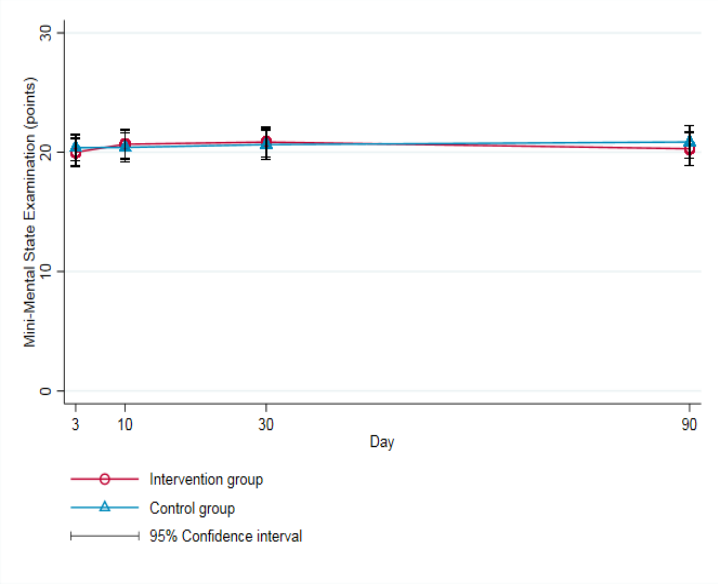
The mean MMSE improved within both groups after 90 days. In the IG, MMSE increased from a mean of 20.9 (SD ± 6.9) to 21.2 (SD ± 8.9) points. The mean increase was 0.3 (95% CI: −0.6–1.2, $P = 0.48$) points. In the CG, MMSE improved from a mean of 21.4 (SD ± 6.1) to 21.9 (SD ± 8.3). The mean improvement was 0.5 points (95% CI: −0.5–1.5, $P = 0.24$). The mean improvement for both groups pooled was 0.4 (95% CI: −0.3–1.1, $P = 0.2$).

The between-group change:

The mean difference in the MMSE sum-scores did not differ between the groups (Figure 6). It was −0.27 points (95% CI: −1.7–1.2, *P* = 0.71) in the IG versus the CG at day 90.

In total, 82 (46%) of 177 persons improved their MMSE sum-score in the geriatrician-performed CGC group, and 93 (53%) of 174 persons improved their MMSE sum-score in the CG (OR 0.75, 95% CI: 0.49–1.14, *P* = 0.18) during the follow-up (Figure 7).

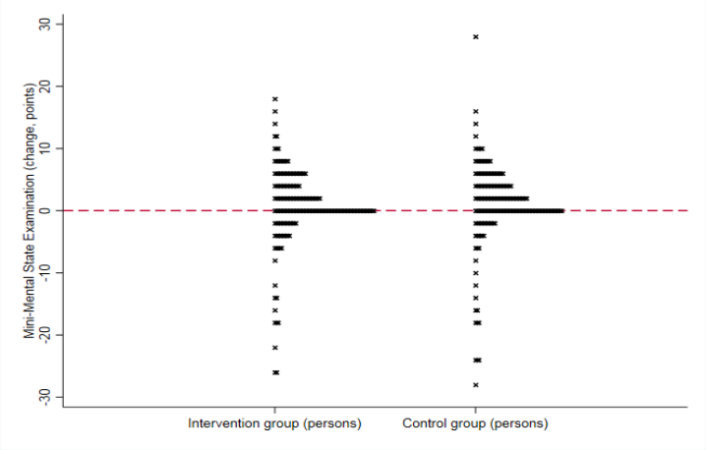
Figure 6. The mean between-group differences in the MMSE sum scores at day 3, 10, 30, and 90.



The dots represent mean MMSE sum-scores in the IG (open red circles) and in the CG (open blue triangles); the bars represent 95% CIs.

The MMSE measures were analyzed using the repeated measurements mixed model; the analyses included 351 participants with at least one MMSE measurement available.

Figure 7. The individual changes in cognitive function measured by MMSE change between day 3 and day 90.



Each dot represents the cognitive function change for every one of the 177 participants in the IG and for the 174 participants in the CG from the MMSE score at baseline to MMSE score on day 90.

The positive value represents the MMSE improvement; zero value represents no MMSE change; the negative value represents the MMSE worsening. The missing MMSE values in non-survivors were set to zero points (meaning the worst possible MMSE). The worst value imputation method was used in all other cases of missing values.

7.3.2.3 ADL function *(Paper II [158])*

Complete case analysis (n = 303)

The within-group change:

The mean MBI significantly improved within the both groups after 90 days. In the IG, MBI increased from a mean of 61.6 (SD ± 25.2) to 76.6 (SD ± 25.0) points. The mean improvement was 13.4 points (95% CI: 10.3–16.4, $P < 0.001$). In the CG, MBI increased from a mean of 63.1 (SD ± 24.4) to 78.1 (SD ± 22.7). The mean improvement was 13.7 points (95% CI: 10.5–16.9, $P < .001$). The mean improvement for both groups pooled was 13.5 points (95% CI: 11.3–15.7, $P < 0.001$).

The between-group change:

The mean difference in the MBI sum-scores did not differ between the groups. It was -1.86 points (95% CI: −6.44–2.7, $P = 0.43$) in the IG compared with the CG at day 90. In total, 128 of 156 persons' MBI sum-scores in the IG and 114 of 147 persons' MBI sum-score in the CG improved during the follow-up period (OR 1.32, 95% CI: 0.75–2.32, $P = 0.33$).

Worst value imputation (n = 368)

For MBI, we imputed 126 (8.6%) missing values of the 1472 possible MBI measurements. The reason for missing data was lack of cooperation (82 measurements, we imputed the worst MBI value) or death (44 measurements, we imputed MBI zero points). The MBI values and curves for each participant (n = 368), and the mean difference in the MBI sum-scores for each group can be found in Appendix 2. H.

The within-group change:

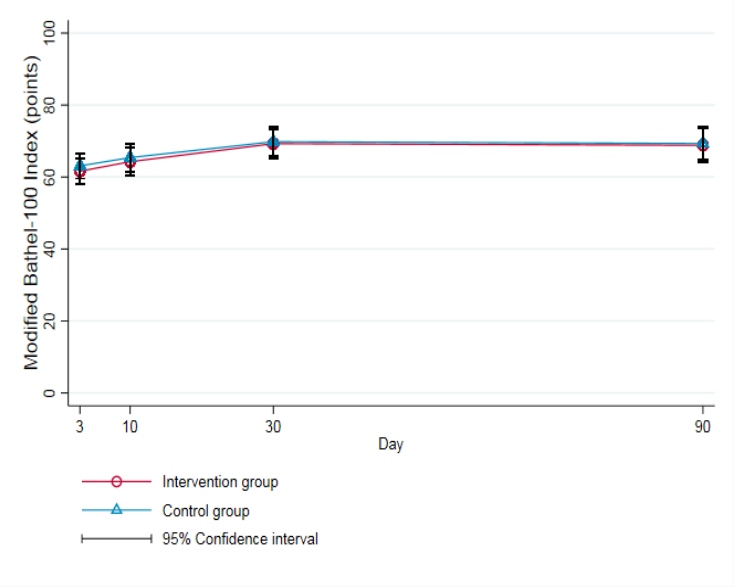
The mean MBI significantly improved within the both groups after 90 days. In the IG, MBI increased from a mean of 61.6 (SD ± 25.2) to 68.8 (SD ± 32.2) points. The mean improvement was 7.2 points (95% CI: 3.7–10.7, $P < 0.001$). In the CG, MBI increased from a mean of 63.1 (SD ± 24.4) to 69.3 (SD ± 31.5 points). The mean improvement was 6.2 points (95% CI: 2.8–9.6, $P < .001$). The mean improvement for both groups pooled was 6.7 points (95% CI: 4.3–9.1, $P < 0.001$).

The between-group change:

The mean difference in the MBI sum-scores did not differ between the groups (Figure 8). It was −0.82 points (95% CI: −6.03–4.38, *P* = 0.76) in the IG compared with the CG at day 90.

In total, 128 of 185 persons improved their MBI sum-scores in the IG, and 114 of 183 persons improved their MBI sum-score in the CG (OR 1.36, 95% CI: 0.9–2.1, *P* = 0.16) during the follow-up period (Figure 9).

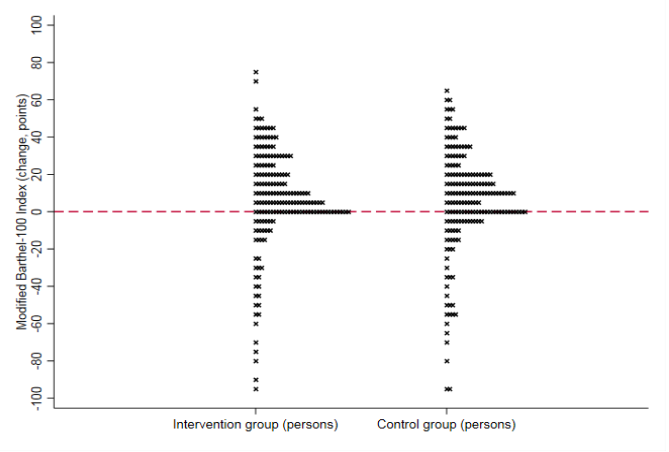
Figure 8. The mean between-group differences in the MBI sum-scores at day 3, 10, 30, and 90.



The dots represent mean MBI sum-scores in the IG (open red circles) and in the CG (open blue triangles); the bars represent 95% CIs.

The MBI measures were analyzed using the repeated measurements mixed model; the analyses included 368 participants with at least one MMSE measurement available.

Figure 9. Individual changes in ADL function measured by MBI change between day 3 and day 90.



Each dot represents the ADL function change for every one of the 185 participants in the IG and for the 183 participants in the CG from MBI-score at baseline to MBI-score at day 90.

The positive value represents the ADL function improvement; zero value represents no ADL function change; the negative value represents the ADL function worsening. The missing MBI values in non-survivors were set to zero points (meaning the worst possible ADL). The worst value imputation method was used in all other cases of missing values.

7.3.2.4 Overall quality of life *(Paper II [158])*

Complete case analysis (n=227)

The within-group change:

The mean DL improved significantly in both groups after 90 days. In the IG, DL decreased from a mean of 9.9 (SD ± 5.6) to 6.9 (SD ± 5.3) points. The mean improvement was −2.9 points (95% CI: −3.7 to −2.2, *P* < .001). In the CG, DL decreased from a mean of 9.3 (SD ± 5.4) to 7.6 (SD ± 5.3) points. The mean improvement was −1.8 points (95% CI: −2.6 to −0.97, *P* < .001). The mean improvement for both groups pooled was -2.4 points (95% CI: −2.9 to −1.8, *P* < .001).

The between-group change:

The mean difference in the DL sum-scores did not differ between the groups. It was −0.21 points (95% CI: −1.22–0.8, *P* = 0.69) in the IG compared with the CG at day 90. However, more persons improved their OQoL in the IG (78 of 117) than in the CG (64 of 110) during the follow-up period (OR 1.44, 95% CI: 0.84–2.47, *P* = 0.19).

Worst value imputation (n = 355)

We excluded 13 participants with an MMSE < 5 (n = 9 in the IG, n = 4 in the CG) and imputed 233 (16.4%) missing DL values of the in total 1420 possible DL measurements. The reason for missing data was lack of cooperation (194 measurements, we imputed the worst DL value) or death (39 measurements, we imputed DL 30 points). The DL values and curves for each participant (n = 355), and the mean difference in the DL sum-scores for each group can be found in Appendix 2. I.

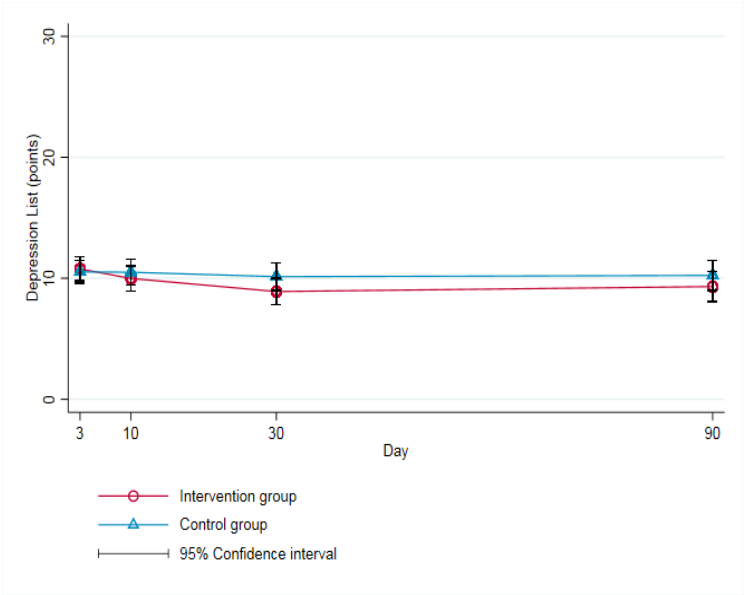
The within-group change:

The mean DL improved within the both groups after 90 days. In the IG, DL decreased significantly from a mean of 10.3 (SD ± 6.2) to 8.3 (SD ± 7.9) points. The mean improvement was −1.5 points (95% CI: −2.4 to −0.6, *P* = 0.001). In the CG, DL non-significantly decreased from a mean of 9.97 (SD ± 5.6) to 9.67 (SD ± 7.9) points. The mean improvement was −0.3 (95% CI: −1.2–0.6, *P* = 0.5). The mean improvement for both groups pooled was −0.89 points (95% CI: −1.5 to −0.3, *P* = 0.004).

The between-group change:

The mean difference in the DL sum-scores did not differ between the groups (Figure 10). It was −0.59 points (95% CI: −1.9–0.7, *P* = 0.37) in the IG compared with the CG at day 90. Significantly more persons improved their OQoL in the IG (99 of 176) than in the CG (79 of 179) during the follow-up period (OR 1.63, 95% CI: 1.07–2.48, *P* = 0.023) (Figure 11).

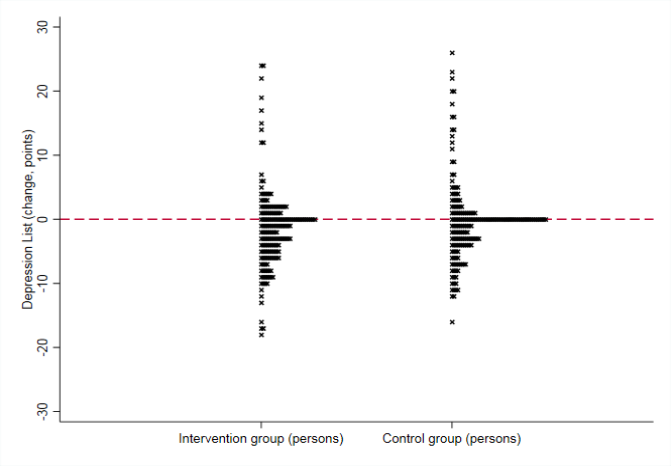
Figure 10. The between-group difference in OQoL measured by DL sum-scores mean differences at day 3, 10, 30, and 90.



The dots represent mean DL sum-scores in the IG (open red circles) and in the CG (open blue triangles); the bars represent 95% CIs.

The MMSE measures were analyzed using the repeated measurements mixed model; the analyses included 355 participants with at least one DL measurement available.

Figure 11. Individual changes in OQoL measured by DL change between day 3 and day 90.



Each dot represents the OQoL change for every one of the 176 participants in the Intervention group and the 179 participants in the Control group from the DL-score at baseline to the DL-score at day 90.

The negative value represents the OQoL improvement; the zero value represents no OQoL change; the positive value represents the OQoL worsening. The missing DL values in non-survivors were set to 30 points (meaning the worst possible OQoL). The worst value imputation method was used in all other cases of missing values.

7.3.3 Post hoc analyses

7.3.3.1 Sensitivity analyses of the secondary healthcare contacts

In order to investigate whether the hospital contacts were planned or acute, and as a sensitivity analysis, the research nurse retrospectively obtained data on the hospital admissions and ED visits through the Electronic Patient Record. Planned hospital contacts were defined as planned hospital admissions or ambulatory contacts including dialysis treatments and chemo- or radiation therapy. Acute hospital contacts were defined as unplanned hospital admissions or unplanned ambulatory contacts or ED visits. The sensitivity analysis did not change the results. We observed no significant differences between the IG and the CG as far as the overall rate ratios of the acute or planned contacts for the all three periods were concerned (Appendix 2. D).

7.3.3.2 Exploratory analyses of the participants with missing measurements

Analysis of participants with missing baseline MMSE, MBI, and DL measurements was conducted to explore how the participants differed from participants without any missing measurements with regard to their age, gender, place of referral, comorbidity burden, and exposure to hyperpolypharmacy at baseline.

In all, 155 of the 368 (42%) participants who lacked at least one MMSE measurement had a significantly higher baseline-comorbidity burden (median CCI score 2 [IQR 1-3] versus median 1 [IQR 1–3], $P = 0.01$) than the participants for whom all MMSE measurements were available.

A total of 88 of the 368 (24%) participants who lacked at least one MBI measurement had a significantly higher baseline-comorbidity burden (median CCI score 2 [IQR 1–3] versus median 2 [IQR 1–3], $P = 0.02$) than the participants for whom all MBI measurements were available.

In all, 146 of the 355 (41%) participants who lacked at least one DL measurement had a significantly higher baseline-comorbidity burden (median CCI score 2 [IQR 1–3] versus median 1 [IQR 1–3], $P = 0.03$) than the participants for whom all DL measurements were available.

In the analyses of the participants with missing baseline MMSE, MBI, and DL measurements, age, gender, place of referral, or exposure for hyperpolypharmacy at baseline did not differ compared with the participants who completed all the measurements.

The mean reason for missing measurements was the lack of cooperation. The main reasons for the lack of cooperation (noted by the assessors) were (1) physical or mental fatigue; (2) delirium; (3) some well-functioning persons were offended by the questions and declined to answer selected items; (4) language barriers for non-Danish speakers if assistance from relatives or translators was not available[160].

7.3.3.3 Subgroup analyses with the baseline comorbidity as predictor

Subgroup analyses were conducted to explore whether the effects of intervention were dependent on the baseline comorbidity burden being low/moderate or high. These analyses were conducted separately for the outcome measures of hospital admissions and ED visits, cognitive function, ADL function, and OQoL.

We found no difference in the number of the hospital admissions and ED visits between the IG and the CG for the participants with a low/moderate comorbidity burden (n = 261) compared with the participants with a high comorbidity burden (n = 107) (Table 11).

The low/moderate comorbidity burden (n = 261) in the IG versus the CG was as follows:
62 of 134 persons improved their cognitive function versus 65 of 127 persons, 99 of 134 persons improved their ADL function versus 78 of 127 persons, and 75 of 129 persons improved their OQoL versus 56 of 124 persons (Table 11).
The high comorbidity burden (n = 107) in the IG versus the CG was as follows:
20 of 51 persons improved their cognitive function in the IG versus 28 of 56 persons in the CG, 29 of 51 persons improved their ADL function in the IG versus 36 of 56 persons in the CG, and 24 of 47 persons improved their OQoL in the IG versus 23 of 55 persons in the CG (Table 11).

Table 11. Effects of the geriatrician-performed CGC on number of hospital admissions and ED visits, cognitive function, ADL function, and OQoL during the 90-day follow-up with baseline comorbidity burden as predictor*.

At baseline / At 90-day	Participants with low/moderate comorbidity (n=261)	Participants with high comorbidity (n=107)
Hospital admissions and ED visits IRR (95% CI) *P*-value	0.98 (0.58-1.66) 0.94	1.44 (0.78-2.64) 0.24
Cognitive function OR (95% CI) *P*-value	0.82 (0.5-1.3) 0.43	0.65 (0.3-1.4) 0.26
ADL function OR (95% CI) *P*-value	1.78 (1.05-3.0) 0.03	0.73 (0.3-1.6) 0.43
OQoL OR (95% CI) *P*-value	1.68 (1.03-2.8) 0.04	1.45 (0.66-3.18) 0.35

*Control group as reference.

8 DISCUSSION

In this section, the main findings of the PhD project are merged through a joint discussion in the context of the existing literature. Furthermore, ethical and methodological considerations related to the trial are addressed in line with the CONSORT recommendations[161].

8.1 MAIN FINDINGS

8.1.1 Study population

8.1.1.1 Recruitment

The 69% recruitment rate observed in the present study is in line with recruitment rates reported in other RCTs with vulnerable older people[162,163,164]. Much effort was devoted to track data on non-entry into our study to identify refusal reasons and factors affecting recruitment. Eligible elderly who are frail and cognitively impaired as well as their family members are usually more reluctant to give their consent to research due to increased fatigue or anxiety on their part[165].

The recruitment rates were slightly different between the two involved rehabilitation units, with higher rates at the rehabilitation unit Thorsgården, where the participants had a more severe comorbidity burden (Appendix 2. C).
It is known from previous research that participants are more likely to consent for a study if they expect a potential benefit in relation to a current medical problem[166].

An increase in willingness to participate in the study was noticed when the geriatrician rather than the research nurse sought the informed consent (Appendix 3. E).

In this trial, transferal to the community rehabilitation units was used as an inclusion criterion to target frail older home-dwelling people with a critical functional decline. However, nearly half of the population screened for trial eligibility was excluded due to having been seen by a geriatrician within the past month. Application of this criterion might lead to exclusion of older persons coping with multiple diseases and disabilities and complicated medical and social problems that cause considerable impairment and frailty. Accordingly, these persons were most likely the ones who would benefit from the geriatric care in the study because of their persistent need for rehabilitation even though they had recently had been seen by a geriatrician.

8.1.1.2 Participants

The final population recruited was more heterogeneous in terms of health and extent of disabilities than expected. Possible explanations for this could be the shift toward broader criterial for transfer to Danish rehabilitation units in recent years and exclusion of persons with recent contact with a geriatrician during the month leading up to the study.

When claiming that an intervention is effective or not effective, it is essential to describe the type of participants in whom the intervention was tested[167]. A striking baseline finding in our study was the high baseline prevalence of hyperpolypharmacy[160]. The prevalence was higher than in populations of home-dwelling or hospitalized older people[52,55] and was close to the prevalence recorded in the population of adults taking ≥10 drugs in the last year of their lives[57].

This high baseline prevalence of psychotropic drugs use (52%) at the beginning of the rehabilitation stay is in line with evidence that older people use psychotropic drugs more frequently than the general population[168]. Moreover, at baseline, most of the study participants were living alone[158,160]. There is evidence that approximately one-third of people aged ≥65 years will experience loneliness late in life[169]. Loneliness is associated with the use of psychotropic drugs even after adjustment for somatic and psychological comorbidities and psychosocial variables[170].

8.1.1.3 Setting

Comparing the study population and settings with those in other CGA/CGC trials done in different countries across the world is difficult. The closest equivalent to a Danish non-hospital-based community rehabilitation unit may be the 'intermediate care facility' in the UK[171]. These UK facilities provide health-related care and services to individuals who do not require the degree of care provided by hospitals or skilled nursing facilities, but who do require care and services above the level of room and board[172]. In Europe, the term intermediate care facilities is often use to describe any alternative to hospital inpatient care and does not imply a specific, well defined type of health care[171].

8.1.2 Outcomes related to Hypothesis 1

8.1.2.1 Hospital admissions and ED visits

The number of hospital admissions and ED visits was chosen as the primary outcome in our study because of prior knowledge that for older people, hospital admission is associated with a risk of rapid decline in functional ability and cognitive impairment[8,9]. We have previously observed a significant number of hospital contacts in older Danes who are referred to the community rehabilitation unit[7]. Reducing hospital contacts seems beneficial.

The trial's main result was that geriatrician-performed CGC had no influence on the total number of hospital admissions and ED visits during the 90-day follow-up period. This finding is in line with that of several recent studies showing that complex interventions (including CGAs) in older people with functional decline in community settings have little or no effect on the number of hospital contacts[173]. Neither the recent Cochrane review[105] on the effectiveness of inpatient CGA nor an older meta-analysis (including outpatient CGAs)[108] showed a benefit of CGA on this outcome.

The main finding in our study was somewhat unexpected as the geriatrician had multiple contacts with the rehabilitation units' staff regarding clinical judgments and treatments/care advice related to the acute medical conditions that occurred in the IG during the rehabilitation stay[158]. In the absence of an on-site geriatrician, such questions would normally result in a hospital being contacted. A post-hoc retrospective recording of hospital contacts and ED visits was therefore done by a blinded project nurse through the Electronic Patient Record. Sensitivity analysis confirmed that the intervention had no effect on the primary outcome.

The number of hospital admissions and ED visits can be affected by multiple factors. Not all of them may be quality-of-care related. In particular, readmissions could indicate something else than the need for acute care because of a sudden change in health status. Evidence suggests that readmissions of older persons comprise the course of care rather than specific illnesses episodes[174]. Hospital readmissions are associated with the individual's medical history and underlying comorbidities rather than a single medical condition[175]. Older people who are at increased risk of future readmissions are generally frequent users of in- as well as out-patient health services[174]. We did not evaluate 'unnecessary' or 'potentially avoidable' hospital admissions or ED visits due to the risk of detection bias if such subjective and imprecise evaluations are used. On the other hand, information on data regarding the participants' hospital admissions and ED visits prior to randomization would have been of high value and might have been of aid in interpreting the findings.

8.1.2.2 Hospital contacts and days in hospital

We found no effect of the intervention on the number of hospital contacts and the number of days spent in hospital.

Neither the recent Cochrane review[105] on effectiveness of inpatient CGA nor the meta-analysis including outpatient CGAs[108] showed a benefit of CGA on number of days spent in hospital. However, in a recent study, comparable to our study, the long-term outpatient CGA model in an ambulatory setting in Sweden resulted in fewer days in hospital compared with usual care[113]. As it was pointed out in the editorial by Rubenstein in the *Journal of the American Medical Directors Association*[176] in reference to this study, the targeting of high utilizers with multiple hospitalizations was a crucial factor in that model of outpatient CGA and contributed to its success.

The extremely skewed data reflect a high degree of heterogeneity in the study population. In both groups, only 7% of the persons generated more than half of the in-hospital days. On the other hand, the geriatrician-performed CGC

could have worked as a disease-screening process in the 'too healthy' participants who had no comorbidity at baseline (19% in IG). Screening carries a risk of side-effects such as increased anxiousness and sickness[177] and introduces an opportunity for 'doctor-shopping', which could have led to a higher use of healthcare services[178].
It cannot be ruled out that the lack of an effect of geriatrician-performed CGCs may be explained as a dilution effect, where the possible beneficial effect of the intervention occurred only in participants who were neither 'too healthy' nor 'too ill' to benefit from the intervention.

Moreover, CGC interventions are usually aimed at primary and secondary prevention as well as tertiary[179]. The post-interventional follow-up in our study was only 55 days. Thus, we cannot rule out that the geriatrician-performed CGC may lower the number of hospital contacts and days in hospital in the long run.

8.1.2.3 GP contacts

A highly significant reduction of the number of GP contacts in the IG was seen during the rehabilitation stay. This was an expected finding since the presence of the geriatrician in the rehabilitation unit may ensure redirection of many GP tasks. A higher number of evening and night GP contacts after the end of the rehabilitation stay in the IG compared with the CG [158] is in agreement with other studies[100]. More focus on health combined with a lower threshold for contact to the GP may explain part of it.

8.1.2.4 Residential status and mortality

The study showed no difference between the groups in regard to residential status or mortality at 90-day follow-up. This result is in line with the earlier meta-analyses on outpatient CGA[107,108]. Also, a good-quality, large, cluster-randomized trial of multidimensional CGA followed by either a geriatric team or the primary care clinician alone showed no differences between the groups with regard to institutionalization and mortality[180]. That trial recruited participants from 106 general practices, the participants mean age was 81 years, the mean number of medications at baseline was 2.6 (SD ± 2), the follow-up was 3 years. The higher baseline medication use and a shorter follow-up period in our study make the comparison of trials difficult.

8.1.3 Outcomes related to Hypothesis 2

8.1.3.1 Medication use

The geriatrician-performed CGC significantly reduced the number of persons using ≥10 regular medications compared with usual care at the 90-day follow-up. To our knowledge, no RCTs have addressed the effect of intervention on the prevalence of hyperpolypharmacy. In our study, this outcome measure was deliberately chosen as a proxy indicator for medication burden and potentially inappropriate medicine use[181-183]. A recent observational longitudinal multicenter study in older patients who had been discharged from acute care hospitals showed that hyperpolypharmacy predicted functional decline after adjusting for potential confounders[81].

Polypharmacy is often unavoidable if the patient suffers from several conditions that require drug treatment. This can be appropriate in certain clinical situations. However, whereas the risk of an adverse drug event is 13% with the use of two medications, it reaches up to 58% when five medications are used[46]. Prescription of seven or more medications further increases the incidence of adverse events to 82%[184]. Older people are especially defenseless with regard to hyperpolypharmacy, which leads to a heightened risk of the adverse effects of many drugs even at doses that are well tolerated by middle-aged individuals. When more than four medications are prescribed simultaneously, it becomes difficult to identify potential health problems as it is difficult to differentiate between possible adverse effects and symptoms related to the patients' disorders and the effects of normal aging processes[185]. The observed reduction in the prevalence of hyperpolypharmacy in the IG in our study may be valuable as it could reduce the risk of adverse drug effects, noncompliance, as well as costs in long term[45].

The intervention resulted in a significant reduction in the use of proton pump inhibitors, loop diuretics, and anti-asthmatic inhalers – the indications for which should be carefully considered in older people[186]. The study results on mortality show that the discontinuation of these medications was safe[158,160].

However, the total number of drugs used did not significantly differ between the groups[160]. Our results are comparable with those of a study from Norway in which geriatric inpatient care optimized the medication profile but did not reduce the median number of drugs used per person[84]. Our trial was not designed as a medication withdrawal trial aimed at reducing the number of drugs. Instead of using a pre-defined checklist of inappropriate medications, we intended to optimize medication use based on the CGC. Clinicians should focus on personalized decision-making rather than the systematic discontinuation of medications according to a one-size-fits-all set of criteria[57]. In our study, discontinuation of unnecessary therapy was in accordance with a geriatric approach because an assessment was made regarding whether a drug was truly necessary for a given patient[187].

The intervention in the present study also involved initiation of medication. The proportion of persons using tricyclic antidepressant amitriptyline rose in the IG due to the relatively high proportion of persons suffering from

neuropathic pain caused by a previous stroke, where initiation of a treatment with small dose tricyclic antidepressants is recommended as first-line treatment[188].

Medication adjustment by a geriatrician was a synergistic part of the provision of personalized care within the context of the complex CGC intervention. The adjustment of medication was active rather than being reliant on indirect medication review methods such as recommendations to the doctors who prescribe medications. This approach might conflict with established guidelines addressing the care of people with a single chronic disease but seldom explicitly concern older people with multiple conditions[31]. Other physicians who were involved in patient care during the post-interventional period could have modified patient medication according to the given clinical situation. In only a few cases were drugs re-stared or increased in dosage (Appendix 2. F). The medication changes in the IG seem to have remained unchanged throughout the post-rehabilitation period (Table 10).

8.1.3.2 Cognitive function

The improvement of cognitive function in survivors in both groups at 90 days after beginning the rehabilitation stay may reflect the overall beneficial effect of rehabilitation. However, the improvement did not differ between the groups. The observed lack of intervention effect on cognitive function is in line with evidence from a meta-analysis on the effectiveness of outpatient geriatric assessment consultation[108]. Furthermore, recent RCTs aiming to reduce polypharmacy have failed to show a positive effect on cognitive functions in spite of a reduction of unnecessary prescribing[32,47].

The absent intervention effect on MMSE may have been be affected by missing values, as 42% of the participants lacked at least one out of four possible MMSE measurements. The exploratory analysis showed that the participants with missing MMSE measurements had a significantly higher comorbidity burden. It is likely that the outcomes measured by the performance-based test MMSE were underestimated because the group of participants in whom the geriatrician-performed CGC could have made a difference was excluded from the analyses.

The observed 52% baseline prevalence of regular psychotropic medication use among our study participants was higher than previously described in non-institutionalized elderly populations, 35% and 38% in New Zealand[189] and Finland[190], respectively, but lower than the prevalence of 70% in a nursing home population in Finland[191]. The long-term use of benzodiazepines, antidepressants, and antipsychotics in older people should be avoided[77], as many such drugs have sedative and anticholinergic properties[78]. Evidence suggests that withdrawal of psychotropics is associated with improved cognition[69]**.** Therefore, the geriatrician often initiated a dosage reduction of the psychotropic drugs as the first step of drug withdrawal in the IG (Appendix 2. F). The gradual dosage reduction was initiated to avoid withdrawal symptoms[192]. However, long-term use of benzodiazepines by older people is related to prolonged impairment of attentional and psychomotor cognitive functioning that persists for at least 6 months after withdrawal[193]. With respect to drugs with anticholinergic effects, it has been reported that cognitive dysfunction

improved 1–4 years after their withdrawal[194,195]. On the other hand, the effect of the initialized treatment of vitamin D-insufficiency may also be achieved only in the long term[113]. Thus, many effects of the optimization of the medication profile may only become manifest at a later point in time.

It should be mentioned that CNS drugs use, in particular the use of opioids, was optimized in the participants in the CG, which may be a reflection of GPs' growing attention to the use of these drugs[196,186].

It was not possible to follow the change in medication dosage on the level of defined daily dose. We also lack data on the participants' PNR medication, which ought to be taken into account when considering their medication burden.

8.1.3.3 ADL function

As is the case for cognitive function, improvement of ADL function in survivors in both groups at 90 days after initiation of the rehabilitation stay may reflect the overall beneficial effect of rehabilitation. The findings of no effect of the intervention on ADL function in the IG compared with the CG should be interpreted with caution. First, the ADL assessment may be influenced by false-negative results arising in the absence of change due to 'floor' and 'ceiling' effects on the assessment instrument, rendering subtle changes impossible to detect[147]. Second, the difference between statistical significance and clinical importance should always be kept in mind[161]. Thus, type II errors should be avoided when interpreting a non-significant result as indicating equivalence between two interventions.

To date, none of the meta-analyses of the effectiveness of outpatient CGA[107,108] have addressed ADL function. However, a recent systematic review and meta-analysis of complex interventions showed that the geriatricians' involvement maintained independent living of elderly people[118]. Also, CGAs conducted in inpatient rehabilitation settings[5] and as home visits[109] have shown that the interventions were instrumental in reducing functional decline and nursing home admission. The contrast to our findings can probably be explained by different target populations.

Our exploratory analyses showed that the subgroup of participants with low and moderate comorbidity tended to achieve a greater improvement in their ADL functions *(Paper II).* We have speculated that the less sick persons might have more potential for improvement of their ADL function if properly treated. The sub-group results of our *Paper II* were expounded in the Editorial by Palmer and Onder to underline the need for a better definition of the ideal target population that may benefit from the geriatrician-performed CGC[25]. However, the post-hoc subgroup analysis should always be interpreted with caution due to a lack of power in the subgroups and the increased risk of type I error due to multiple analyses. Further studies designed to examine the effect of treatment in subgroups are necessary to confirm the findings from these exploratory analyses.

8.1.3.4 Overall quality of life

Assessment of quality of life is important in the evaluation of interventions and when making treatment decisions[197], but is a challenge in geriatric research. When quality of life is applied as a subjective concept regarding experience of well-being and life-satisfaction[198], self-rating is the gold standard method for measurement[199]. However, most questionnaires used to measure quality of life require prolonged attention and concentration from respondents and are therefore hardly suitable for older people with cognitive impairment. In our study, we used the less used DL[154,155] to measure quality of life. We decided in favor of this instrument because of the advantages of this interview-based questionnaire; it is easy to use, has an acceptable reproducibility, and can detect a clinically relevant change over time in frail elderly people[156].

More participants improved their OQoL measured by the DL in the IG than in the CG at the 90-day follow-up *(Paper II)*. However, the between-group mean differences in the DL sum-scores were not significantly affected along the study timeline. The DL scale showed no 'floor' and 'ceiling' effects in our study (Appendix 2. I), and the DL scale seems therefore to be a realistic tool for measuring the quality of life in a heterogeneous population of older people. On the other hand, we would argue that in a heterogeneous population of older people, it makes more sense to assess the improvement or worsening on a personal level rather than to use average group changes.

No RCT has evaluated the effectiveness of CGA or CGC on the quality of life measured by DL. The study that is most similar to our study is an RCT in ≥70-year-old home-dwelling Norwegians with hip fractures in inpatient geriatric care in which a positive effect of CGC intervention on quality of life was observed[103]. Quality of life was measured by comparing mean differences in the EuroQoL-5 dimension-3L questionnaire[200], and a significant improvement in quality was observed at 4 and 12 months. However, their study population was less heterogeneous than the one enrolled in our study and included cognitively and physically well-functioning patients.

Another RCT[112] showed a positive effect of outpatient CGA coupled with an adherence intervention on health-related quality-of-life measures captured by the SF-36[201] at 15-month follow-up. The community-dwelling older persons needed to have at least one of four specific geriatric conditions (falls, urinary incontinence, depressive symptoms, or functional impairment) to be included in the study. However, the 363 participants were less cognitively impaired, with a baseline mean of 28 (SD ± 1.5) MMSE point versus the baseline mean of 21.3 (SD ± 6.1) points in our study population. Substantial differences in study populations makes the comparison between the studies difficult despite methodological similarities.

Various previous interventions reducing inappropriate prescribing in older people addressed but had no effect on quality of life[47]. A recent randomized study in home-dwelling elderly people from Finland showed that medication assessment as part of CGA resulted in an increased self-perceived health experience 1 year later[202].
The observed optimized medication use in our study could also have contributed to the increase in the OQoL in the IG.

8.2 ETHICAL CONSIDERATIONS

Damage to the participants

A planned interim analysis was performed on mortality when 185 participants had been randomized and had completed the 90-day follow-up. The interim analysis was performed by an independent statistician blinded to treatment allocation. The findings were evaluated by an independent researcher in order to stop the study prematurely if significant mortality differences were found. Mortality was not increased in any of the groups, and the study inclusion therefore continued as planned.

We had no predefined checklist for registration of any adverse outcomes of drug discontinuation or dosage reduction, but the geriatrician monitored the participants in the IG with regard to change in symptoms, signs, or results of relevant blood tests that might indicate the need to restart a discontinued medication.

8.3 METHODOLOGICAL CONSIDERATIONS

8.3.1 Subgroups analyses with *comorbidity* as predictor

Subgroup analyses can help better identify the ideal target population who may benefit from an intervention[203]. We intended to explore whether treatment effects of geriatrician-performed CGC as compared with usual care depended on a low and moderate comorbidity versus a high comorbidity burden. Comorbidity was expected to predict the functional rehabilitation outcome, because several competing chronic diseases may impede physical, occupational, and rehabilitation therapy[204]. Especially in older patients, it is essential to know to what extent the comorbidity burden influences functional outcome.

However, use of the CCI index as a predictor of functional outcomes in older people was shown to have substantial limitations. A systematic review and meta-analysis explored the associations between four comorbidity indexes, including the CCI, and functional outcomes after inpatient stroke or hip fracture rehabilitation. Paradoxically, the authors found insufficient evidence that assessing comorbidity helps predict functional prognosis[205]. Use of CCI is considered especially controversial in older people as the comorbidity index was originally developed and validated in a younger population of female cancer patients[140].

A targeting of high-risk populations is a crucial factor in assessing outpatient CGA effectiveness[176]. Because disability emphasizes the biological domain, psychological factors, and social factors, a frailty index rather than a comorbidity index is probably a better tool to identify a high-risk population.

8.3.2 Statistical notes on the choice of analysis methods

Deviations from the original protocol are not uncommon as it is often impossible to predict every possible change in circumstances during the course of a trial[161]. Especially, internal validity can be compromised by the choice of statistical methods[206]. We have done our best in this area. However, our statistical analysis plan was not predefined in detail before the data were acquired[136] as we did not foresee what kind of data we would be collecting. During the data analysis period, we made efforts to comply with current standards relating to the statistical methods used, and the advanced analyses were therefore performed under the guidance of the experienced statisticians.

8.3.2.1 Dealing with count-data of hospital contacts

While most outcomes were normally or close to being normally distributed, the data on hospital contacts were over-dispersed due to a highly heterogeneous study population. When more events are studied for each individual, the models have to account for the extra variability between persons, as some persons will tend to have experienced many and others only a few or no events. Therefore, we considered IRRs to be the most appropriate way to compare the number of hospital contacts[207]. IRRs were calculated using a Poisson regression model and compared using negative binominal regression.

8.3.2.2 Dealing with missing data

Up to 42% of the study participants lacked at least one measurement of cognitive function, ADL function, or OQoL despite considerable efforts made by data assessors (research occupational therapists) during the data collection period. The prevalence of missing data on cognitive function, ADL function, and OQoL was higher in participants with a high comorbidity burden in both the IG and the CG. This may mean that the missing data were not completely random. However, the missing data were balanced between the IG and the CG owing to the use of an appropriate randomization method in our study. Thus, we have no reason to suspect that the comorbidity burden or any unknown confounder caused selection bias.

Missing data is a challenge in all clinical trials, but they are especially important in studies focusing on older people with functional decline[208]. Many investigators exclude patients without an observed outcome. Whereas a few missing outcomes will not cause a problem; in half of trials conducted more than 10% of randomized patients may have missing outcomes[209]. Thus, investigators must choose between omitting the participants without final outcome data and imputing any missing outcome data[210]. In our study, we chose the last solution.

A mixed model is an appropriate method when data are missing[211]. We used a preplanned mixed model method to analyze the effect of the intervention in three different ways: complete case analyses, last value carried forward, and worst value imputation in case of missing values. A ‘complete case’ analysis includes only those whose outcome is

known. A widely used method is 'last observation carried forward', but this method has been extensively criticized in recent years[212]. We therefore chose to use the worst value imputation method[213]. However, both approaches have drawbacks: (1) complete cases are usually not a random subsample of the whole sample; (2) worst-case imputation is usually biased by no randomness in the imputation, as the lowest value is taken among the data for the same person who has both missing and observed values. We therefore reported both the complete case analyses and the worst-case imputation analyses to give the full picture of our results.

8.3.2.3 Dealing with data on medication use

In *Paper III*, we had pointed out that the analysis on medication use and cognitive function was a secondary analysis of the previously published study *(Paper II)*[158]. There were three ways to analyze the results: (1) differences between outcome and baseline values; (2) adjustment for baseline values in the logistic regression model; (3) repeated measurements analysis[214]. The logistic regression model with penalized maximum likelihood estimation[159] was chosen as this is the only regression model that could handle the issue that the baseline values (explanatory variable) did not vary much and therefore were perfect predictors of the outcome medication values.

8.3.3 Internal validity

One of definitions of internal validity is the degree to which the results are compromised by systematic errors (bias). Thirty-five types of bias may distort the design, execution, analysis, and interpretation of research[215]. In this section, the four main types of bias that might compromise a study result will be briefly discussed: selection bias, performance bias, detection bias, and attrition bias[216].

8.3.3.1 Selection bias

Selection bias occurs to a limited extent in our study. No participants left the study, and the data on the participants' hospital and GP contacts and their medication use were complete. When properly implemented, randomization eliminates selection bias, balancing both known and unknown prognostic factors in the assignment of treatments[217]. In our study, the blinded computer-based and stratified randomization ensured that the participants' baseline characteristics were duly balanced. We used randomization with unknown block size to eliminate the possibility of manipulation of the results. Although proper random assignment prevents selection bias, it does not guarantee that the groups are totally equivalent at baseline. However, any differences in baseline characteristics are the result of chance rather than bias[218]. The functional outcomes could be influenced by exclusion from the analyses of the participants with missing values. We discussed this issue in Section 8.3.2 *Statistics notes on the choice of analysis models: Dealing with missing data.*

8.3.3.2 Performance bias

The overall risk of performance bias in our study seems limited because allocation was concealed in the groups in which data were collected. However, assessments of cognitive function, ADL function, and OQoL were potentially subject to performance bias. The functional tests assessors were theoretically blinded to treatment allocation, but it could not be ruled out that the participants might have mentioned their allocation during the assessment and thereby introduced detection bias. Allocation to the active treatment group might medicalize the participants. This medicalization might potentially result in underperforming and lead to performance bias in participants suffering from functional decline and loneliness.

8.3.3.3 Detection bias

Detection, or ascertainment, bias occurs when the results or conclusions of a trial are systematically distorted by knowledge about which intervention each participant is receiving. Blinding helps prevent detection bias but cannot always be implemented[219].

In our study, data on the primary outcome were obtained from national Danish registers. The validity of the following registers is high: the Danish National Hospital Register[220], the Danish Psychiatric Central Register[221], and the National Health Insurance Service Register[222]. The datasets were generated by register staff who were blinded to our patients' allocation. The project manager was blinded to the study outcomes, which were collected from the registers. Furthermore, the research nurse who retrospectively obtained outcome data on medication use through the Aarhus Community Care Record was blinded to participant allocation.

Owning to the nature of the study, it was impossible to blind the participants, their relatives, the geriatrician, and the rehabilitation units' staff to the allocation group. The study research occupational therapist was blinded to treatment allocation, but patients might have mentioned their allocation during the assessment. Blinding is particularly important when outcome measures involve some subjectivity. Thus, the performance-based measure of physical and cognitive functioning could be biased.

8.3.3.4 Attrition bias

Participation in our study was voluntary. There were no drop-outs during the study. The healthcare utilization and medication data were complete because they were collected from national registers or from electronic patient records. The functional and quality-of-life outcomes data contain some missing values at different assessment time points. We have done our best to deal with missing data and have described our considerations concerning this effect in Section 8.3.2 *Statistics notes on the choice of analysis models: Dealing with missing data.*

8.3.4 External validity

External validity, or generalizability of the trial findings, means the degree to which the results are valid not only in the present study but in other different settings as well[223]. That can only be evaluated if the internal validity is good[223].

We conducted an RCT including older people with cognitive impairment who are often excluded from RCTs[224-226]. The trial had an appropriately large sample size, successful randomization, and a 100% retention rate. The intervention was based in a 'real-world' non-academic setting of a community rehabilitation unit. We believe that the recruited participants adequately represent the real picture of the growing population of elderly needing community rehabilitation unit services.

However, we should mention some trial limitations with regard to external validity. First, the external validity of our study is limited to the Danish setting of Aarhus Municipality**.** Second, our study results cannot be extrapolated to even older people who were excluded due to the study's exclusion criteria. Whereas eligibility criteria do not affect the internal validity of a trial, they are central to its external validity[161]. The proportion of eligible participants who refused to enter the trial is also important for its generalizability as it may indicate patient preferences and reveal information about the acceptability of an intervention[161]. We cannot extrapolate our study results to cover either the non-consenters or the potentially eligible older people who did not enter for other reasons. We obtained information on age, gender, place of referral, and comorbidity burden for participants as well as for non-consenters and other non-participants prior to randomization. However, we were unable to control the non-enterer's other potentially important characteristics, e.g. current medication use.

Third, a single specialist physician in geriatric medicine performed the intervention. When the intervention depends on one physician, the results are less generalizable.

Finally, the CGC intervention in our study was not and could not be standardized. Successful interventions for geriatric patients have often been of a complex type[227]. The older peoples' individual needs are often complicated by medical, functional, psychological, and social problems[228]. This may lead to an atypical clinical presentation requiring flexibility and variation of the treatment. Therefore, any CGC intervention is unique for everyone.

9 CONCLUSIONS

The geriatrician-performed CGC was established in a non-hospital-based rehabilitation unit and compared with a standard rehabilitation stay with the GP as back-up.

The results of the intervention were as follows:

1) The intervention did not reduce the total number of hospital admissions and ED visits during the 90-day period after the participants initiated their individualized rehabilitation stay. No effect was found with regard to the number of days in hospital, ambulatory contacts, institutionalization, and mortality at the 90-day follow-up. The observed effect in the form of a reduction in the total number of GP contacts during the rehabilitation stay did not persist.

2) The intervention group had a slightly reduced proportion of persons taking 10 and more regular medications/day and proportion of persons taking proton pump inhibitors, loop diuretics, and anti-asthmatic inhalers (medications for which the indication should be reconsidered in older people). The medication changes in the IG during the individualized rehabilitation stay persisted at the 90-day follow-up. The intervention did not improve cognitive function nor ADL function, but seems to have improved OQoL during the 90-day follow-up.

10 FUTURE PERSPECTIVES

This PhD project evaluated effects of geriatrician-performed CGC on several healthcare and patient-relevant outcomes in older people referred to a community rehabilitation unit. No difference was found in the effectiveness of the geriatrician-performed CGC intervention and usual care with regard to the primary outcome. The project has a number of important learning points for research and clinical practice.

10.1 IN RESEARCH

We should be careful not to conclude that the intervention does not work. As it discussed above, the common error of interpreting a non-significant result as indicating equivalence of interventions should be avoided[161]. On the other hand, the lack of effect of the complex CGC intervention in our trial is not surprising in the light of the possible spill-over effect and the increasing quality of care in the rehabilitation units. Both the IG and CG were treated by the same staff at the rehabilitation units. The geriatrician provided education and support to the staff of the rehabilitation units during the project data collection period. Cooperation between the geriatric department and the rehabilitation units strengthened care continuity and improved communication with patients, their relatives, and rehabilitation unit staff. We have no data, but believe that the better cooperation will likely improve compliance and make care more cost-effective in the long run.

RCTs performed in real-life community settings are important whether they produce positive, mixed, or negative findings because these findings may help guide future research into interventions targeting the growing and heterogeneous population of older people[36]. Such research is important, irrespective of what appears to be positive discrimination favoring publication of manuscript producing statistically significant results over those reporting non-significant results[229]. However, a larger sample size than that in our trial could have been preferable as the population of older people generally displays more heterogeneity than younger populations[215].

Future research should move away from conducting studies insufficiently powered to evaluate patient outcomes but primarily designed to test feasibility and effectiveness of process-of-care outcomes. It is well known that patients are more concerned about mental health, emotional wellbeing, general health, and vitality, which are only rarely measured in RCTs[230]. Remembering to evaluate participants and providers' satisfaction with the proposed model of care is an important consideration. The role of carers in the rehabilitation process is important, as outcomes are usually better if carers are fully involved and engaged[231].

In a time of the demographic change, increasing economic scrutiny, and hyperpolypharmacy in all resource-rich countries, CGC should be directed at patients with the highest needs. A future long-term follow-up RCT evaluating CGC performed by a geriatrician or another generalist physician may include frailty assessment at baseline or a

validated frailty index as part of the inclusion criteria. A pragmatic approach to target the study population could be to focus on functionally impaired older people with hyperpolypharmacy.

10.2 IN CLINICAL PRACTICE

The present PhD project was not able to prove that the presence of *a geriatrician* providing 'on site' medical expertise at a community rehabilitation unit should be a standard of care in Danish healthcare. However, the presence of a generalist physician on site at the community-based units could be recommended. The physician's role in rehabilitation and care of community-dwelling disabled older people remains critical for underpinning all subsequent actions[231]. Common for the successful CGA/CGC interventions was that they were usually coordinated by specialists in geriatrics or primary care physicians with an interest in older people[118].

Geriatricians are trained in the management of complex health conditions and polypharmacy and have firm knowledge about age-related changes in physiology and pharmacology[84], but typically see patients over only a short period. GPs have a unique knowledge about their patients. Since most of patients in the future will have chronic diseases or disabilities or have frailty-related problems, all generalists will have to incorporate their specific knowledge about frail older people into their clinical practice.

At present in the UK, 118 'geriatric' GPs are members of the British Geriatrics Society. Creation of a subspecialty of community geriatric medicine[39] in Denmark in line with that in UK could bridge the gap between hospital and the community and help break down some of the existing barriers between geriatricians and GPs. For many of the residents of community rehabilitation units, an effective rehabilitation in a non-hospital-based unit may be their last chance to return to a dignified life. Closer cooperation between geriatricians and GPs should be established. Effective communication, rather than 'passing the buck', especially regarding the responsibility of medication adjustment[232], is required.

11 ENGLISH SUMMARY

Background: Patients' length of stay in hospital is declining and therefore rehabilitation of frail older persons must be provided in the community outside hospitals. During the past decades, community-based rehabilitation units in Denmark have offered older persons an opportunity to improve their level of functioning. The goal has been to reduce re-hospitalization and restore functional ability during a 3- to 5-week rehabilitation stay.

Data from the National Patient Registry in older adults referred to a community rehabilitation unit in Denmark showed a significant number of hospital admissions and emergency department (ED) visits within 3 months of start of the rehabilitation stay. Suboptimally treated subacute medical conditions and inappropriate medication may result in visits to the ED or re-hospitalization.

An integrated model of care such as comprehensive geriatric assessment (CGA) can address and prioritize older people's complex health needs. Core components of CGA include evaluation of functional capacity, fall risk, cognition, polypharmacy, social support, goals of care, and advanced care preferences[102].

The recently suggested concept of comprehensive geriatric care (CGC) covers the combined assessment and interventional follow-up process. However, we do not know whether CGC provided by a geriatrician will make standard rehabilitation more effective and reduce hospital contacts.

Aim: The aim of this randomized controlled trial was to examine the effectiveness of geriatrician-performed CGC in older people referred to a non-hospital-based rehabilitation unit. We wanted to examine whether it was possible: (1) to reduce hospital admissions and ED visits without increasing mortality and institutionalization; (2) to optimize medication use and to increase functional ability as well as quality of life.

Methods: The 368 participants were 65 years of age or older and were referred to two Danish community-based rehabilitation units from home or hospital. The exclusion criteria were assessment by a geriatrician during the past month or receiving palliative care.

The intervention was CGC performed by a geriatrician in collaboration with the staff of the rehabilitation units. The medication adjustment based on clinical judgment was the key element of the geriatric intervention. The control group received standard rehabilitation with GPs as back-up.

The primary outcome was the number of hospital admissions and ED visits in the first 90 days following admission to the rehabilitation units. The secondary outcomes included the number of days spent in hospital, number of ambulatory contacts, number of GP contacts, medication use, cognitive function, activity of daily living (ADL) function, overall quality of life, residential status, and mortality.

Results: No difference in the number of hospital admissions and ED visits was found. The number of days in hospital, ambulatory contacts, and out-of-hour GP visits or phone calls did not differ between the groups. The number of daytime GP consultations and visits or phone and email consultations was lower in the Intervention group compared to the Control group. Use of day-time GP services was lower in the Intervention group during the rehabilitation stay, but not afterwards. Institutionalization and mortality rates were similar in the two groups. The intervention reduced the prevalence of hyperpolypharmacy (≥10 regular medications prescribed concurrently) and the use of proton pump inhibitors, loop diuretics, and anti-asthmatic inhalers. No difference between the groups regarding changes of cognitive function and ADL function was found. More participants in the Intervention group than in the Control group improved their overall quality of life during the 90-day follow-up.

Conclusions: The geriatrician-performed CGC did not reduce the number of hospital admissions and ED visits during the 90-day period after the participants initiated their individualized rehabilitation stay. No effect was found with regard to the number of days in hospital, ambulatory contacts, institutionalization, and mortality. The observed effect in the form of a reduction in the total number of GP contacts during the rehabilitation stay did not persist. The intervention slightly reduced the hyperpolypharmacy and optimized medication profile. The intervention did not improve cognitive function or ADL function, but seemed to improve overall quality of life during the 90-day follow-up.

Perspectives: The present PhD project was unable to prove that the presence of *a geriatrician* providing 'on site' medical expertise at a community rehabilitation unit should be standard in Danish healthcare. The target group for CGC may be more selected. A future long-term follow-up RCT evaluating CGC performed by a geriatrician or a primary care physician with an interest in older people in a community-based rehabilitation unit should include frailty assessment at baseline or a validated frailty index as part of the inclusion criteria. A pragmatic approach to target the study population could be to focus on functionally impaired older people with hyperpolypharmacy.

12 DANISH SUMMARY/ DANSK RESUMÉ

Baggrund: Indlæggelsesvarigheden er faldende på hospitalerne verden over, hvorfor rehabilitering af svækkede ældre mennesker må finde sted udenfor hospitalerne. Gennem de seneste årtier har kommunale rehabiliterings- og aflastningsenheder i Danmark givet ældre mennesker en mulighed for at forbedre deres funktionsevne. Målet har været at reducere genindlæggelser og at genvinde den tabte funktion under et 3-5 ugers rehabiliterings- og aflastningsophold.

Data fra Landspatientregistret viser et stort antal af hospitalsindlæggelser og skadestuebesøg hos de ældre fra starten af deres rehabiliterings- og aflastningsophold og tre måneder frem. Suboptimalt behandlede subakutte medicinske tilstande og uhensigtsmæssig medicinering kan resultere i et besøg på skadestuen eller i en akut indlæggelse.

En integreret behandlingsmodel, såsom Comprehensive Geriatric Assessment (CGA) kan identificere, adressere og prioritere ældre menneskers komplekse medicinske behov. Kerneelementerne inden for CGA inkluderer evaluering af funktionsevne, faldrisiko, kognition, polyfarmaci og målopsætning for behandling.

Comprehensive Geriatric Care (CGC) dækker både over den geriatriske vurdering og en indgribende interventions- og opfølgningsproces. Dog ved vi ikke, om CGC foretaget af en speciallæge i geriatri (geriater) vil gøre standardrehabiliteringen på en kommunal rehabiliterings- og aflastningsenhed mere effektiv og reducere antallet af hospitalskontakter.

Mål: Målet med dette lodtrækningsstudie var at undersøge effekten af CGC udført af geriater på ældre mennesker, som er henvist til et rehabiliterings- og aflastningsophold. Vi ville undersøge, om det er muligt at: 1) reducere antal af hospitalsindlæggelser og skadestuebesøg uden at øge dødelighed og plejehjemsanbringelse; 2) optimere medicinforbrug og øge kognitive og fysiske funktioner såvel som livskvalitet.

Metode: De 368 projektdeltagere var 65 år eller derover og var overflyttet til én af to danske kommunale rehabiliteringsenheder enten fra eget hjem eller fra hospitalet. Eksklusionskriterier var vurdering af en geriater inden for den sidste måned eller et palliativt forløb. Interventionen bestod i CGC udført af en geriater i samarbejde med personalet på rehabiliteringsenheden. Justeringen i medicin, baseret på en klinisk vurdering og patientens præferencer, var nøgleelementet i den geriatriske intervention. Kontrolgruppen modtog standard rehabilitering med praktiserende læger som backup.

Den primære effektparameter var det samlede antal af hospitalsindlæggelser og skadestuebesøg i de første 90 dage efter indlæggelse på rehabiliterings- og aflastningsenheden. De sekundære effektparametre inkluderede antal dage tilbragt på hospitalet, antal ambulante hospitalskontakter, antal kontakter til praktiserende læge/vagtlæge, medicinforbrug, kognitiv funktion, ADL-funktion, overordnet livskvalitet, boligsituation og dødelighed.

Resultater: Der var ikke signifikant forskel på det samlede antal hospitalsindlæggelser og skadestuebesøg mellem interventions- og kontrolgruppen. Der var ikke signifikant forskel på antallet af dage på hospitalet, ambulante kontakter og lægebesøg af praktiserende læge eller telefonsamtaler med praktiserende læge udenfor normal åbningstid mellem grupperne. Antallet af besøg hos praktiserende læge eller telefonsamtaler og e-mail konsultationer var signifikant lavere i interventionsgruppen end i kontrolgruppen. Brug af praktiserende læge i åbningstiden var signifikant lavere i interventionsgruppen under rehabiliteringsopholdet, men ikke bagefter. Hyppighed af plejehjemsanbringelse og dødelighed var ikke signifikant forskellige i de to grupper. Interventionen reducerede antallet af personer med hyperpolyfarmaci (brug af 10 eller flere forskellige lægemidler dagligt), samt brugen af protonpumpehæmmere (mavesårsmedicin), loop-diuretika (vanddrivende) og midler til obstruktive luftvejssygdomme. Der blev ikke fundet signifikant forskel mellem grupperne i kognitiv funktion eller ADL-funktion. Flere deltagere i interventionsgruppen end i kontrolgruppen forbedrede deres overordnede livskvalitet under den 90-dages opfølgning.

Konklusion: CGC udført ved geriater reducerede ikke antallet af hospitalsindlæggelser og skadestuebesøg under 90-dages perioden. Der blev ikke fundet nogen effekt i henhold til antal af dage på hospitalet, ambulante kontakter, hyppighed af plejehjemsanbringelse eller dødelighed. Reduktionen i det totale antal kontakter til praktiserende læge under rehabiliterings- og aflastningsopholdet fortsatte ikke efter opholdet. Interventionen reducerede antallet af personer med hyperpolyfarmaci. Det samlede medicinforbrug blev kun beskedent optimeret. Interventionen forbedrede ikke kognitiv funktion eller ADL-funktion, men ser ud til at have forbedret livskvaliteten 90 dage efter starten af rehabiliterings- og aflastningsopholdet.

Perspektiver: Dette ph.d.-projekt kunne ikke vise, at tilstedeværelsen af en geriater i en kommunal rehabiliterings- og aflastningsenhed skal være en standard behandling. Et eventuelt fremtidigt lodtrækningsstudie, der evaluerer effekten af CGC udført af en geriater eller en alment praktiserende læge med interesse for geriatri på en kommunal rehabiliterings- og aflastningsenhed, kunne med fordel inkludere en valideret skrøbelighedsvurdering som en del af inklusionskriterierne. En pragmatisk tilgang kunne være at fokusere på ældre mennesker med funktionsnedsættelse og hyperpolyfarmaci.

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"If she cannot herself obtain access to the Snow Queen, and remove the glass fragments from little Kay,

we can do nothing to help her" (H. C. Andersen, Snow Queen)

14 APPENDICES

Appendix 1.The published papers in relation to the PhD dissertation

Paper I

Comprehensive geriatric care versus standard care for elderly referred to a rehabilitation unit – a randomized controlled trial. Zintchouk D, Lauritzen T, Damsgaard EM

Journal of Aging Research and Clinical Practice, 2017; 6:40-47

DOI: https://doi.org/10.14283/jarcp.2016.126.


SYGEHUS
VIKÆRGÅRDEN

Paper II

Geriatrician-performed comprehensive geriatric care in older adults referred to a community rehabilitation unit: A randomized controlled trial.

Zintchouk D, Gregersen M, Lauritzen T, Damsgaard EM

European Journal of Internal Medicine, 2018; 51:18-24

DOI: https://doi.org/10.1016/j.ejim.2018.01.022


MANDIA

Paper III

Impact of Geriatrician-performed Comprehensive Geriatric Care on Medication Use and Cognitive Function in Older Adults Referred to a Non-Hospital-Based Rehabilitation Unit.

Zintchouk D, Gregersen M, Lauritzen T, Damsgaard EM

The American Journal of Medicine, 2019; 132 (1): 93–102.e2

DOI: https://doi.org/10.1016/j.amjmed.2018.09.030

Appendix 2. Materials that related to the PhD study

Appendix 2. A

Search strategy

We searched for systematic reviews, meta-analyses and randomized trials in PubMed and the Cochrane Database of Systematic Reviews. The relevant publications were identified using two separate search strategies for the outpatient geriatrician-led CGA/ CGC and the interventions to reduce polypharmacy. The searches were performed using standard search terms back to 1985. Additional citations were identified from reference lists and hand searching. Only studies published in English were included. Systematic reviews were used as the primary source of evidence. The studies which were included in the systematic reviews were not considered separately. The review process was conducted in line with the PRISMA guidelines[133].

Types of studies (Search 1 and search 2):

Randomized controlled trials, meta-analyses or systematic reviews.

Types of participants (Search 1 and search 2):

People aged ≥65 years received a non-hospital based/outpatient CGA or CGC in order to manage physical deterioration due to medical, psychological, functional or social problems or other similar conditions referred to as 'frailty', 'functional decline', 'risk of hospitalization', 'post-acute period', 'risk of readmission', 'risk of rehospitalization/institutionalization' or 'unable to live in own home'.

Additional terms for the search 2: Polypharmacy and inappropriate prescribing.

Types of interventions and settings:

Search 1: Studies addressing outpatient geriatrician-lead/physician-led CGA or CGC in non-hospital bed-based community rehabilitation settings, intermediate care or in primary care. Studies of condition specific organized care (e.g. stroke rehabilitation units, hip-fracture rehabilitation units) or in-hospital rehabilitation units will not be included and evaluated. For the medication review studies the interventions performed by other health care providers will also be considered and evaluated.

Search 2: Studies addressing electronic and non-electronic strategies to reduce polypharmacy: hospital Information Systems, Decision Support Systems, Clinical Pharmacy Information Systems, Medical Order Entry Systems, drug Therapy, Electronic Prescribing, Adverse Drug Reaction Reporting Systems, medication errors, Potentially Inappropriate Medication List, medication reconciliation, medication therapy management, drug utilization review.

Outcome measures (Search 1 and search 2):

Hospital admissions and ED visits, medication (safety-based drug withdrawals, medication errors, drug interactions, prescription drugs, drug-related side effects and adverse reactions, drug therapy), cognitive function, ADL function, quality of life, mortality.

Search strategy 1. The outpatient geriatrician-led CGA/CGC. MEDLINE (PubMed) searched 27/11/2018.

Concept	Search#	Search string	Results	Notes
Geriatrics	#1	“Geriatrics”[Mesh]	28973	
	#2	"Aged"[Mesh]	2878418	*Aged, and aged 80 and over retrieved too many irrelevant hits to include*
	#3	#1 AND #2	11275	
Care models	#4	(((((((“Geriatric Assessment”[Mesh]) OR “Personnel Staffing and Scheduling”[Mesh]) OR “Health Services for the Aged”[Mesh]) OR “Referral and Consultation”[Mesh]) OR “Patient-Centered Care”[Mesh]) OR (“Patient Care”[Mesh] OR “Patient Care Team”[Mesh])) OR “Case Management”[Mesh]) OR “Program Evaluation”[Mesh]) OR “Interdisciplinary Communication”[Mesh]	1119811	
Non-geriatricians	#5	(((((“Medical Staff”[Mesh]) OR “Physicians”[Mesh]) OR “Primary Health Care”[Mesh]) OR “Internal Medicine”[Mesh]) OR “General Practice”[Mesh]) OR "Intermediate Care Facilities"[Mesh]	422106	
	#6	#3 AND #5	1308	
	#7	#4 AND #6	785	
	#8	#7	657	*Filters activated: Publication date from 1985/01/01*

Search strategy 2. The medication optimization interventions in older people. MEDLINE (PubMed) searched 27/11/2018.

Concept	Search#	Search string	Results	Notes
Population	#1	(("Geriatrics"[Mesh]) OR "Aged"[Mesh]) OR "Frail Elderly"[Mesh]	2895585	*Too many irrelevant hits to include*
	#2	("Polypharmacy"[Mesh]) OR "Inappropriate Prescribing"[Mesh]	6194	
	#3	#6 AND #7	3597	
Intervention, electronic strategies	#4	((((((("Hospital Information Systems"[Mesh]) OR (("Decision Support Systems, Management"[Mesh]) OR "Decision Support Systems, Clinical"[Mesh])) OR (("Clinical Pharmacy Information Systems"[Mesh]) OR "Medical Order Entry Systems"[Mesh])) OR "Electronic Prescribing"[Mesh]) OR "Adverse Drug Reaction Reporting Systems"[Mesh]) OR "Medication Errors"[Mesh]) OR "Drug Therapy, Computer-Assisted"[Mesh])	54394	
Intervention, non-electronic strategies	#5	((("Potentially Inappropriate Medication List"[Mesh]) OR "Medication Reconciliation"[Mesh]) OR "Medication Therapy Management"[Mesh]) OR "Drug Utilization Review"[Mesh]	6676	
	#6	#4 OR #5	59429	
Outcome	#7	((((("Mortality"[Mesh] OR "Morbidity"[Mesh])) OR "Hospitalization"[Mesh])) OR "Quality of Life"[Mesh]	1143578	
	#8	(("Prescription Drugs"[Mesh]) OR ("Drug-Related Side Effects and Adverse Reactions"[Mesh])) OR "Drug Therapy"[Mesh]	1360998	
	#9	#7 OR #8	2417766	
	#10	#3 AND #6 AND #9	4845	*Publication date from 1985/01/01.*
	#11	#10	538	*Meta-Analysis, Randomized Controlled Trial, Systematic Review*

Appendix 2. B

Baseline characteristics of participants versus non-concenters and other non-enters.

Baseline characteristics (n=1326)	**Concenters** (n=368)	**Non-concenters** (n=164)	**Did not met inclusion criteria** (n=638)[1]	**Did not entered due to other reasons** (n=156)
Age, mean (SD)	78.6 ± 8.1	78.5 ± 8.3	81.5 ± 8.6*	76.1 ± 8.7*
Gender, women %	51	52	56*	40*
CCI score, median, [IQR], (range)	2, [1-3], (0-7)	1, [1-2], (0-8)	NR[2]	2, [1-2], (0-6)
Place of referral, hospital %	63.4	62.8	85.6*	62.2

[1] <65 years old persons referred to the rehabilitation units (n=316) are not included.
[2] Not recorded
**P*-value <0.05

Appendix 2. C

Characteristics of the participants recruited from rehabilitation units Vikærgården versus Thorsgården.

Parameter	Vikærgården	Thorsgården
Screened for eligibility, n	1455	187
Referred from hospital, %	71	76
Age <65 years old, %	21	11
Geriatric assessment during past month, %	38	44
Receiving palliative treatment, %	3	7
Declined to participate, % of eligible population	31	21
Included in the study, n	348	20
CCI participants, median, [IQR], (range)	2, [1-3], (0-7)	2, [1-3], (0-5)
CCI non-participants, median, [IQR], (range)	2, [1-2], (0-8)	2, [1-2], (0-5)

Appendix 2. D

Hospital admissions and ED visits obtained retrospectively though Electronic Patient Record by the project nurse.

	Intervention group (n=185)	**Control group** (n=183)	**Incidence Rate Ratio (IRR)#** (95% CI)	***P*-value***
During 90-day follow-up				
Acute contacts ¤				
Number	143	118	1.3 (0.8-2.1)	0.3
Median (IQR)	0 (0-1)	0 (0-1)		0.3
Persons without any contact (%)	124 (67)	130 (71)		0.5
Persons with 1-3 contacts (%)	48 (26)	43 (23)		
Persons with ≥ 4 contacts (%)	13 (7)	10 (6)		
Planned contacts §				
Number	460	454	1 (0.7-1.4)	0.8
Median (IQR)	1 (0-2)	1 (0-3)		0.8
Persons without any contact (%)	59 (32)	62 (34)		0.3
Persons with 1-3 contacts (%)	97 (52)	95 (52)		
Persons with ≥ 4 contacts (%)	29 (16)	26 (14)		
During rehabilitation stay				
Acute contacts ¤				
Number	76	64	1.3 (0.7-2.3)	0.4
Median (IQR)	0 (0-0)	0 (0-0)		0.6
Persons without any contact (%)	145 (79)	147 (80)		0.8
Persons with 1-3 contacts (%)	34 (18)	32 (18)		
Persons with ≥ 4 contacts (%)	6 (3)	4 (2)		
Planned contacts §				
Number	256	224	1.2 (0.8-1.7)	0.4
Median (IQR)	0 (0-2)	0 (0-1)		0.6
Persons without any contact (%)	95 (51)	98 (53)		0.8
Persons with 1-3 contacts (%)	71 (39)	71 (39)		
Persons with ≥ 4 contacts (%)	19 (10)	14 (8)		
After rehabilitation stay to day 90				
Acute contacts ¤				
Number	67	54	1.3 (0.7-2.2)	0.4
Median (IQR)	0 (0-0)	0 (0-0)		0.5
Persons without any contact (%)	150 (81)	152 (83)		0.2
Persons with 1-3 contacts (%)	33 (18)	28 (15)		
Persons with ≥ 4 contacts (%)	2 (1)	3 (2)		
Planned contacts §				
Number	204	230	0.9 (0.6-1.3)	0.5
Median (IQR)	0 (0-1)	0 (0-2)		0.1
Persons without any contact (%)	107 (58)	92 (50)		0.4
Persons with 1-3 contacts (%)	67 (36)	79 (43)		
Persons with ≥ 4 contacts (%)	11 (6)	12 (7)		

Abbreviations: IQR, 25% interquartile range; IRR, Incidence Rate Ratios; CI, confidence intervals.

* Number of contacts was compared using two-sample Wilcoxon rank-sum (Mann-Whitney) test, IRR was compared using negative binominal regression, number of persons with contacts was compared using Chi2 test

IRR was adjusted for mortality by including the risk time as an exposure variable

¤ Acute contacts were defined as acute hospitals admissions or acute ambulatory contacts or ED contacts

§ Planned contacts were defined as planned hospitals admissions or planned ambulatory contacts inclusive dialyze treatments and chemo-/radioactive therapy

Appendix 2. E Primary healthcare contacts (GPs) obtained from the National Health Insurance Service Register (*Paper II*)[158].

	During 90-day follow-up				*During rehabilitation stay*				*After rehabilitation stay to day 90*			
Primary healthcare contacts	**Intervention group** (n=185)	**Control group** (n=183)	**Incidence rate ratio (IRR)**[1] (95% CI)	*P*-value[2]	**Intervention group** (n=185)	**Control group** (n=183)	**Incidence rate ratio (IRR)**[1] (95% CI)	*P*-value[2]	**Intervention group** (n=185)	**Control group** (n=183)	**Incidence rate ratio (IRR)**[1] (95% CI)	*P*-value[2]
Daytime consultations and visits												
Number	318	433	0.7 (0.6-0-9)	<0.001	81	190	0.4 (0.3-0-6)	<0.001	237	243	1 (0.8-1.2)	0.71
Median (IQR)[3]	1 (0-3)	2 (1-3)		0.001	0 (0-1)	1 (0-1)		<0.001	1 (0-2)	1 (0-2)		0.56
Persons without any contact (%)[4]	52 (28)	28 (15)		0.009	127 (68)	78 (43)		<0.001	71 (39)	63 (35)		0.7
Persons with 1-3 contacts (%)	104 (56)	115 (63)			57 (31)	96 (52)			97 (52)	103 (56)		
Persons with ≥4 contacts (%)	29 (16)	40 (22)			1 (1)	9 (5)			17 (9)	17 (9)		
Daytime phone and email												
Number	919	1455	0.6 (0.5-0-7)	<0.001	315	771	0.4 (0.3-0-5)	<0.001	604	684	0.9 (0.7-1.1)	0.17
Median (IQR)[3]	5 (2-7)	8 (4-11)		<0.001	1 (0-2)	4 (2-6)		<0.001	3 (1-5)	3 (1-6)		0.09
Persons without any contact (%)[4]	13 (7)	9 (5)		<0.001	51 (28)	20 (11)		<0.001	37 (20)	28 (15)		0.54
Persons with 1-3 contacts (%)	58 (31)	23 (13)			107 (58)	71 (39)			75 (41)	66 (36)		
Persons with ≥4 contacts (%)	113 (61)	151 (83)			27 (16)	92 (50)			73 (39)	89 (49)		
Evening and night visits												
Number	91	63	1.4 (0.9-2.2)	0.14	48	41	1.1 (0.6-2.1)	0.65	43	22	1.9 (1.0-3.6)	0.045
Median (IQR)[3]	0 (0-1)	0 (0-1)		0.40	0 (0-0)	0 (0-0)		0.36	0 (0-0)	0 (0-0)		0.37
Persons without any contact (%)[4]	133 (72)	137 (75)		0.37	150 (81)	155 (84)		0.52	159 (86)	162 (89)		0.09
Persons with 1-3 contacts (%)	47 (25)	45 (24)			34 (18)	27 (15)			24 (13)	162 (89)		
Persons with 4 contacts (%)	5 (3)	1 (1)			1 (1)	1 (1)			2 (1)	0		
Evening and night phone												
Number	102	119	0.8 (0.6-1.3)	0.39	64	65	1 (0.5-1-7)	0.89	38	54	0.7 (0.4-1.2)	0.19
Median (IQR)[3]	0 (0-1)	0 (0-1)		0.31	0 (0-0)	0 (0-0)		0.47	0 (0-0)	0 (0-0)		0.29
Persons without any contact (%)[4]	127 (69)	118 (64)		0.74	150 (81)	142 (77)		0.61	158 (85)	150 (82)		0.12
Persons with 1-3 contacts (%)	62 (34)	58 (32)			33 (18)	38 (21)			25 (14)	32 (17)		
Persons with ≥4 contacts (%)	6 (3)	7 (4)			2 (1)	3 (2)			2 (1)	1 (1)		
Other GPs services												
Number	425	737	0.5 (0.4-0.7)	<0.001	111	341	0.3 (0.2-0.5)	<0.001	314	396	0.8 (0.6-1.1)	0.107
Median (IQR)[3]	1 (0-4)	3 (1-5)		<0.001	0 (0-1)	1 (0-3)		<0.001	0 (0-3)	1 (0-3)		0.07
Persons without any contact (%)[4]	70 (38)	38 (21)		<0.001	131 (71)	88 (48)		<0.001	95 (51)	75 (41)		0.56
Persons with 1-3 contacts (%)	63 (34)	69 (38)			46 (25)	67 (37)			53 (29)	63 (34)		
Persons with ≥4 contacts (%)	52 (28)	76 (41)			8 (4)	28 (15)			37 (20)	45 (25)		

Abbreviations: IQR, 25% interquartile range; IRR, incidence rate ratios; CI, confidence interval.

[1] IRR compared using negative binominal regression

[2] IRR adjusted for mortality by including the risk time as an exposure variable

[3] Number of contacts compared using the Mann-Whitney U test

[4] Number of persons with contacts compared using the chi-squared test

Appendix 2. F

Changes in regular medication in the Intervention group (IG, n=170) vs. the Control group (CG, n=166) at 90-day *(Paper III)*[160].

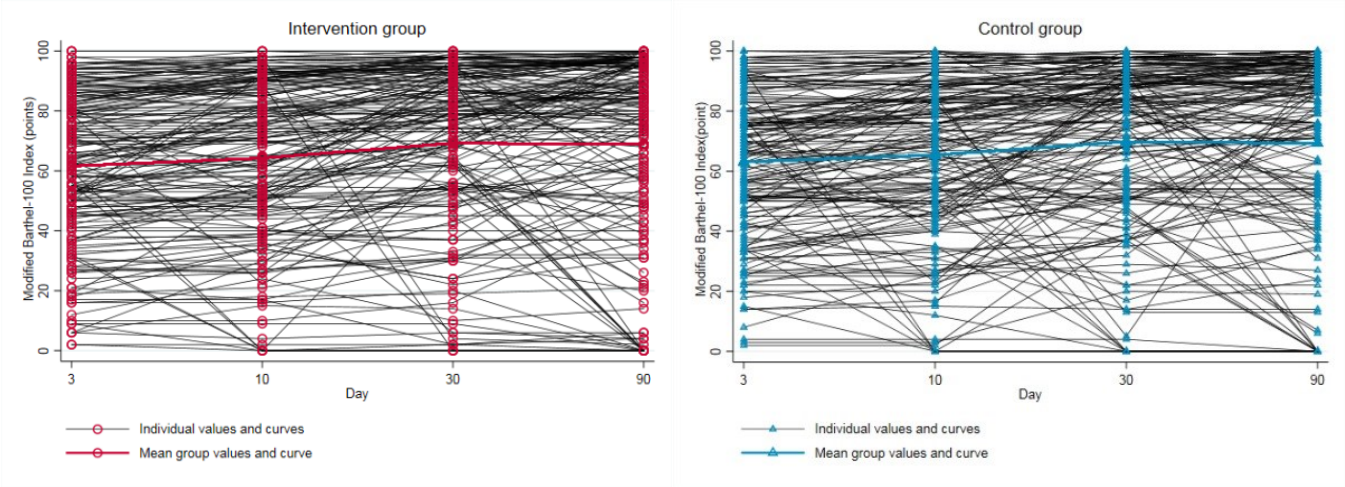
	Stopped			**Started**			**Dosage decrease**[2]			**Dosage increase**		
	IG	**CG**	*P*-value	**IG**	**CG**	*P*-value	**IG**	**CG**	*P*-value	**IG**	**CG**	*P*-value
Number of any drugs changed per person, median (range)	2 (0-12)	1 (0-11)	<0.001	1 (0-7)	0 (0-11)	<0.001	0 (0-7)	0 (0-2)	<0.001	0 (0-3)	0 (0-2)	0.06
Drug users with at least one medication changed within the ATC classes[1], (n)	134	100	<0.001	124	71	<0.001	80	31	<0.001	46	31	0.07
Gastrointestinal system	77	38	<0.001	85	34	<0.001	33	11	<0.001	18	13	0.38
Cholecalciferol	3	2	0.67	29	1	<0.001	1	0	.32	2	0	0.16
Proton pump inhibitors	25	3	<0.001	11	3	0.053	11	2	.02	0	2	0.015
Blood and blood-building organs	38	30	0.33	16	17	0.79	2	1	.58	3	3	0.98
Cardiovascular system	40	24	0.03	19	23	0.46	45	7	<0.001	12	11	0.88
Loop-diuretics	17	3	0.002	5	6	0.73	12	1	0.003	6	7	0.74
Antihypertensives, excl. furosemide	18	17	0.97	13	13	0.95	27	6	<0.001	9	4	0.17
Urogenital system	8	2	0.06	5	4	0.76	1	0	0.32	0	0	-
Urinary frequency/ incontinence	8	3	0.14	3	4	0.68	3	0	0.09	0	0	-
Endocrine system	9	6	0.46	6	4	0.55	5	3	0.49	4	3	0.73
Corticosteroids for systemic use	8	6	0.62	4	3	0.73	5	2	0.27	3	1	0.33
Systemic infections	38	39	0.80	2	3	0.63	0	2	0.15	0	0	-
Musculoskeletal system	7	2	0.17	8	6	0.62	1	0	0.32	2	1	0.58
Central nervous system	55	43	0.19	40	33	0.42	29	10	0.002	15	3	0.006
Opioids	20	19	0.92	10	6	0.33	10	3	0.09	0	1	0.32
Hypnotics and sedatives	6	6	0.97	3	3	0.98	0	0	-	0	0	-
Anxiolytics	1	0	0.32	2	1	0.58	1	0	0.32	0	0	-
Selective serotonin reuptake inhibitors	1	4	0.17	10	9	0.86	3	0	0.25	7	1	0.07
Tricyclic antidepressants	3	1	0.33	7	0	0.02	0	0	-	1	0	0.32
Other antidepressants	0	0	-	0	0	-	1	0	0.32	0	0	-
Antipsychotics	2	5	0.24	2	2	0.98	1	0	0.32	1	0	0.32
Antiepileptics	3	0	0.12	2	3	0.63	5	0	0.06	0	2	0.15
Respiratory system	16	1	<0.001	5	2	0.27	3	0	0.25	0	0	-
Anti-asthmatic inhalers	9	0	0.004	2	1	1.00	1	0	1.00	0	0	-
Antiparasitic products (quinine)	1	0	0.32	0	1	0.31	0	0	-	0	0	-
Dermatologicals	9	6	0.46	4	2	0.43	1	0	0.31	0	0	-
Antineoplastics/immunomodulators	1	6	0.052	0	1	0.31	0	0	-	1	0	0.32
Sensory organs	4	3	0.73	3	3	0.98	0	0	-	1	0	0.32
Various	4	0	0.047	0	1	0.31	0	0	-	1	0	0.32

[1] Drugs are presented in survivors with at least one medication changed within the Anatomical Therapeutic Chemical (ATC) classification system classes

[2] Dosage reduction was the first step of the drug withdrawal for benzodiazepines, opioids and antidepressants due to the risk of withdrawal symptoms, and for loop-diuretics, antihypertensive, proton pump inhibitors, and anti-asthmatic inhalers, due to the rebound phenomena

Appendix 2. G

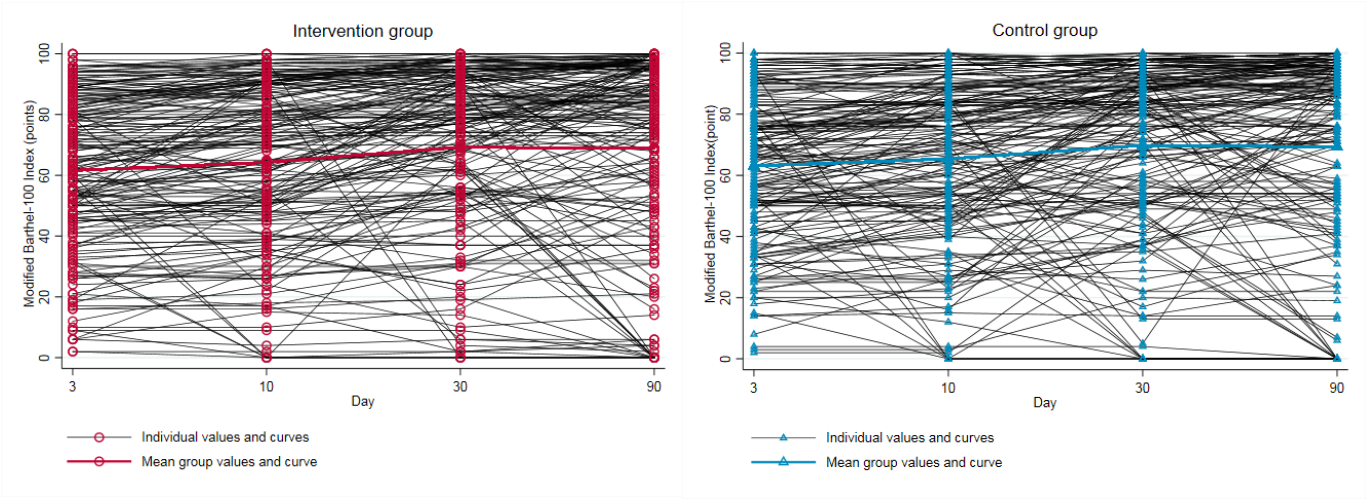
The MMSE sum-score values and curves for each participant (n = 351), the mean difference in the MMSE sum-scores for each group.



Each black line represents the individual curves of MMSE sum-score points for the 177 participants in the IG and the 174 participants in the CG.
The missing MMSE values in non-survivors were set to zero points (meaning worst possible MMSE).
The worst value imputation method was used in all other cases of missing values.

Appendix 2. H

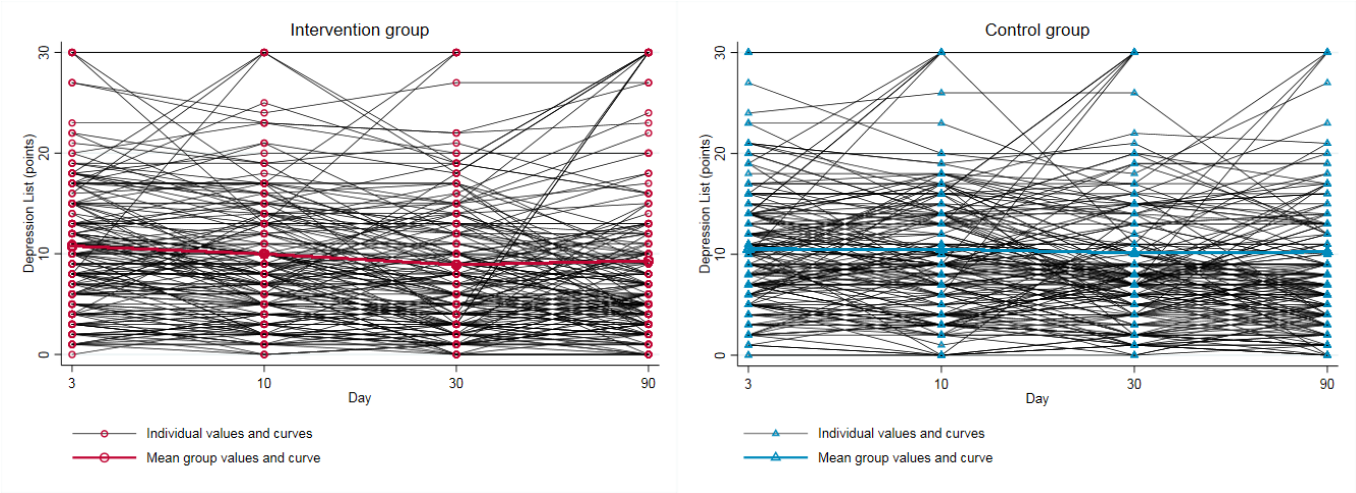
The MBI values and curves for each participant (n = 368), and the mean difference in the MBI sum-scores for each group.



Each black line represents the individual curves of MBI sum-score points for the 185 participants in the IG and the 183 participants in the CG.
The missing MBI values in non-survivors were set to zero points (meaning the worst possible ADL).
The worst value imputation method was used in all other cases of missing values.

Appendix 2. I

The DL values and curves for each participant (n = 355), and the mean difference in the DL sum-scores for each group.



Each black line represents the individual curves of DL sum-score points for the 176 participants in the IG and the 179 participants in the CG.
The missing DL values in non-survivors were set to 30 points (meaning the worst possible DL).
The worst value imputation method was used in all other cases of missing values.

Appendix 3. Other relevant materials related to the PhD project

Appendix 3. A The standard care description in detail *(by research nurse Else Shneider, 2015).*

The typical standard course of rehabilitation at Rehabilitation Unit Vikaergaarden has a duration of five weeks.
The course consists of the following elements:

1) Visitation.
Applications from resident/whether resident is received by the resident consultant or Visitation-line, which inspects the course. Residents are put on a waiting list in the short term database with a recommendation of either a one-day rehabilitation or a short term placement.

2) Course coordination.
The course coordinator assigns a one-day rehabilitation and contacts the resident/relevant relative/hospital department to plan the transfer.

3) Reception - moving in, and expectation interview.
Reception comprises a period of approximately three days. Before arrival the resident is assigned a contact person and a staff member who will be responsible for the course. The moving in interview is a general introduction. The expectation interview compares the resident's expectations of the residency to the staff's expectations of the resident.

4) Planning - assessment, goal setting and agreements.
The assessment phase is approximately the first 1.5 weeks, during which all the professional groups contribute to the identification of the resident's wants/needs, current health condition and ability to function. Necessary information, i.e. Care testament, Terminal declaration, allergy, Pacemaker, etc. Upon permission from the resident, information about diagnoses relevant to care and treatment can be obtained. Caregivers (Nurses and health care assistants) observe and evaluate the resident's problem areas. Nutrition: The first morning, the resident is weighed, and a nutrition screening is done, as well as evaluation of the need for nutritionist intervention. The resident is weighed again at the end of the course, and an evaluation is done regarding the possible need for specific actions after the course. Skin and mucous membranes: Skin and mucous membranes are observed. Respiration and circulation: BT and pulse are measured the first morning. Pain and sensory impressions: The resident is observed for possible pains or problems with sight and hearing. Sleep and rest: Factors that ease or hinder sleep and rest are observed. Waste elimination: Incontinence, constipation, diarrhea, possible catheter and stomy are observed. These observations are documented in focus areas, resident's daily plan and function evaluation. Physical therapists observe and evaluate the resident's ability to function in relation to transfers and create a transfer description on the arrival day. In the first week and at the end of the stay, the physical therapist does a DEMMI test (De Morton Mobility Index test). With current residents a Time up and go test and a stand/sit test. Occupational therapists observe and evaluate the resident's wants and needs. Tools used are COPM (Canadian Occupational Performance Measure) and/or interview. PADL Evaluation (Personal Activities of Daily Living) is done the first morning, after which the Resident's Daily Plan and Function Evaluation are started. The PADL Evaluation is repeated at the end of the course. With current residents the occupational therapist administers a Dysphagia screening on the arrival day. Likewise, the occupational therapist administers a MOCA test (Montreal Cognitive Assessment) to current residents. The complete picture of the resident's health status and the current problems are the starting point for the subsequent goal setting interview. At the goal setting interview, which is held approximately 1 - 1.5 weeks before, the course determines "Resident's Goal" and related agreements and the overall direction for the rehabilitation course.

5) Execution.
Implementation of the professional actions in practice: There are various tools and technologies available in the execution phase, i.e. bathroom technology and transfer assistive devices. During the weekly interdisciplinary meetings the professional effort is coordinated, evaluated and adjusted. Return home and delivery: In the last part of "execution" an interview is done regarding the planning of the return home, including the consistency in the transition to the citizen's own home or other unit. The resident consultant participates in these including relevant relatives, if the patient wishes. As an end to the course and as a part of the information relayed to the next unit a COPM and DEMMI are done. Finally, the interdisciplinary personnel update the Resident's Daily Plan and Function Evaluation.

Appendix 3. B

Deltager information, habil person *(samtykke form S1),* Vikærgården.

Information

om deltagelse i videnskabelig undersøgelse af

Effekt af geriatrisk lægelig intervention overfor ældre med behov for rehabiliterings- eller aflastningsophold

Videnskabelig undersøgelse:
Vi beder Dem venligst om at deltage i en videnskabelig undersøgelse.

Formål:
Undersøgelsen skal vise om ældre mennesker, der skal på et midlertidigt genoptrænings- eller aflastningsophold kan have glæde af at blive undersøgt af en læge, der er specialist i ældres sygdomme (en geriatrisk læge).
Vi vil gerne vide, om en sådan undersøgelse vil ændre en række væsentlige forhold for ældre såsom behov for kontakter til sygehuset, til egen læge og til hjemmeplejen. For Deres eget vedkommende Deres evne til at klare den daglige tilværelse, Deres livskvalitet, behov for boligskift og Deres forbrug af medicin.

Før De beslutter, om De vil deltage i undersøgelsen, skal De fuldt ud forstå, hvad undersøgelsen går ud på, og hvorfor vi gennemfører den. Vi vil derfor bede Dem om at læse denne deltagerinformation grundigt.
De vil desuden blive inviteret til en samtale, hvor denne information vil blive uddybet, og hvor De har mulighed for at stille spørgsmål. De må gerne tage en pårørende med til samtalen.

Hvis De beslutter Dem for at deltage i forsøget, vil vi bede Dem om at underskrive en samtykkeerklæring.

Selve undersøgelsen:
De personer, der vælger at deltage i undersøgelsen, inddeles i to grupper ved lodtrækning:
Den ene gruppe undersøges af speciallæge i ældres sygdomme og får desuden samme behandling og optræning, som hidtil er brugt på Vikærgården.
Den anden gruppe får den samme behandling og optræning, som hidtil er blevet brugt på Vikærgården.

Hvis De kommer med i den gruppe, der skal lægeundersøges, vil De blive tilknyttet Geriatrisk Afdeling, som ambulant patient i 30 dage eller indtil De har fået svar på gennemførte undersøgelser. De vil blive undersøgt af en geriatrisk speciallæge inden for to døgn. Lægen vil tale med Dem om Deres sygehistorie og foretage en almindelig lægelig undersøgelse af Dem. De vil få taget blodtryk og nogle almindelige blodprøver, der viser Deres blodprocent, blodsukker, stofskifte, nyrefunktion, mulige betændelse i kroppen og hvor meget D-vitamin De har i blodet. Deres medicin vil blive gennemgået og justeret, hvis nødvendigt. De vil blive grundigt orienteret om resultatet af disse undersøgelser. Hvis der er grund til det, vil De få tilbudt røntgenundersøgelse og hjertediagram. Hele den lægelige undersøgelse vil vare en times tid.

Blodprøve analyseres og opbevares på Klinisk Biokemisk Afdeling, Aarhus Universitetshospital på samme måde som prøver taget på Geriatrisk Afdeling. Det samme gælder evt. røntgenundersøgelser eller hjertediagram.
Til brug for forskningsprojektet tastes alle undersøgelsesresultater ind i en database, som kun projektlederen har adgang til, og alle data bliver slettet efter projektets ophør.
Ingen prøver skal gemmes i biobank til senere forskning.
Der tages heller ikke andet biologisk materiale fra til opbevaring for senere undersøgelse.

Uanset hvilken gruppe, De tilhører, vil De blive undersøgt af en terapeut, som vil se på Deres evne til at klare hverdagen og vurdere Deres livskvalitet. Det varer også omkring en time.
Ti dage samt en og tre måneder efter starten af Deres ophold på Vikærgården vil De få besøg af terapeuten, som vil undersøge Dem på samme måde, som i begyndelsen af Deres ophold på Vikærgården. Disse besøg vil også vare ca. en time.

Vi vil indhente oplysninger om Deres kontakter til sygehus, til Deres egen læge og til hjemmeplejen fra offentlige registre og fra Deres omsorgsjournal i kommunen.
Deres egen læge vil få besked om, at de indgår i denne videnskabelige undersøgelse. Såfremt De er med i den gruppe, der bliver undersøgt af speciallæge, vil resultatet af Deres undersøgelser også blive sendt til Deres egen læge, hvis De er indforstået dermed.

Nytte:
Ved at deltage i forskningsprojektet kan De bidrage med ny viden om, hvorvidt en undersøgelse ved en specialist i ældresygdomme kan gavne ældre, der skal starte på et aflastnings- eller træningsophold. Hvis De kommer i den gruppe, som undersøges af speciallæge, kan De formentlig opnå en bedre funktionsevne, en bedre livskvalitet og en længere levetid.

Ulemper:
Hvis De kommer med i den gruppe, der skal undersøges af speciallæge, vil de anvendte undersøgelsesmetoder være almindeligt anvendte og anerkendte. Der er ingen alvorlige bivirkninger i forbindelse med blodprøvetagning. Der kan dog opstå en mindre blødning eller blodansamling. I meget sjældne tilfælde kan opstå en lokal betændelse ved indstiksstedet. Skulle der mod forventning ske skader som følge af undersøgelsen, har De mulighed for erstatning efter Lov om klage- og erstatningsadgang.

Deltagelse:
Det er frivilligt at deltage.
De har ret til 24 timers betænkningstid, før De eventuelt giver Deres samtykke. De kan på ethvert tidspunkt, og uden begrundelse trække Deres samtykke om Deres deltagelse tilbage. Det vil ikke få konsekvenser for Deres videre behandling.

Økonomi:
Der gives ikke honorar for deltagelse i forsøget. Projektet modtager økonomisk støtte fra Folkesundhed i Midten og fra Helsefonden.

Adgang til resultater:
Alle oplysninger behandles fortroligt og opbevares i et midlertidigt register, som er beskyttet og kun få har kendskab til. Projektets forventede samlede varighed er 4 år. Resultaterne offentliggøres i en foreløbig rapport og senere i relevante internationale tidsskrifter uden Deres navn eller andre personlige oplysninger.

Yderligere information:
I den vedlagte folder ”Dine rettigheder som forsøgsperson i et biomedicinsk forskningsprojekt” kan De læse mere om deltagelse i videnskabelige undersøgelser - blandt andet om tavshedspligt, aktindsigt og klagemuligheder.

De er også altid velkommen til at kontakte undertegnede, hvis De har behov for yderligere informationer.

Appendix 3. C

Skabelon af brev til egen læge (Vikærgården).

Kære _____

Deres patient _____ _____er i øjeblikket tilknyttet Rehabiliterings- og kortidspladsenhederne på Vikærgården.

_____ vil gerne deltage i et forsøg, der skal vurdere effekten af en geriatrisk udredning af 65+ årige ældre i Århus Kommune, når borgerne henvises til et rehabiliterings- eller aflastningsophold.

Formålet er at afgøre, om en geriatrisk vurdering forud for et rehabiliterings- eller aflastningsophold kan påvise behandlelige sygdomme eller tilstande, og om en relevant intervention kan reducere antallet af boligskift til plejebolig, indlæggelser og genindlæggelser, samt om borgeren kan opnå et højere funktionsniveau, en bedre livskvalitet og en længere levetid.

Alle projektdeltagere i interventionsgruppen behandles som tilknyttet Geriatrisk Afdeling, Aarhus Universitetshospital. De er dækket af de samme patientsikkerhedsregler, hvad angår alle undersøgelser og eventuelt behandling, som afdelingens øvrige patienter.

Projektet er godkendt af Datatilsynet og De Videnskabsetiske Komiteer for Region Midtjylland.

Deltagerinformation er vedhæftet.

Ved spørgsmål er De velkommen til at kontakte mig.

Med venlig hilsen

Dmitri Zintchouk, projektleder, speciallæge i geriatri,
Forskningsenheden,
Geriatrisk Afdeling G,
Aarhus Universitetshospital.
Telefon: 29 12 06 75 eller 26 70 09 03
e-mail: dmizin@rm.dk

Appendix 3. D

Geriaterens tjekliste for hver ny projektdeltager på inkluderings dag.

- ❑ Den nye projektdeltager er markeret på Vikærgården kontors tavle og i Omsorgsjournalen som G-Vik-P1 (intervention) eller G-Vik-P2 (kontrol)

- ❑ Lægens kontaktkort er udleveret til G-Vik-P1 og/eller de pårørende samt Vikærgårdens kontakt personale

- ❑ Hos G-Vik-P1 har orienteret pt. og evt. de pårørende og altid Vikærgårdens personale (kontaktpersonen) om medicinændringer og behandlingsplan og lavet et tilsvarende kort og fordansket notat i Omsorgsjournalen

- ❑ Den nye G-Vik-P1 er oprettet i EPJ under ”Geriatrisk Funktion Vikærgården” og blodprøver er bestilt

- ❑ Medicinstatus ved ankomsten til Vik. fra Omsorgsjournalen (hvis deltager kommer hjemmefra) eller fra epikrise (deltager fra hospitalet) er printet ud og sat ind i Geriaterens Dataindsamlingsmappe

- ❑ Medicin status efter intervention og svar på blodrøver er printet ud og sat ind i Geriaterens Mappe

- ❑ Den opdaterede medicinstatus er udleveret til kontaktpersonale

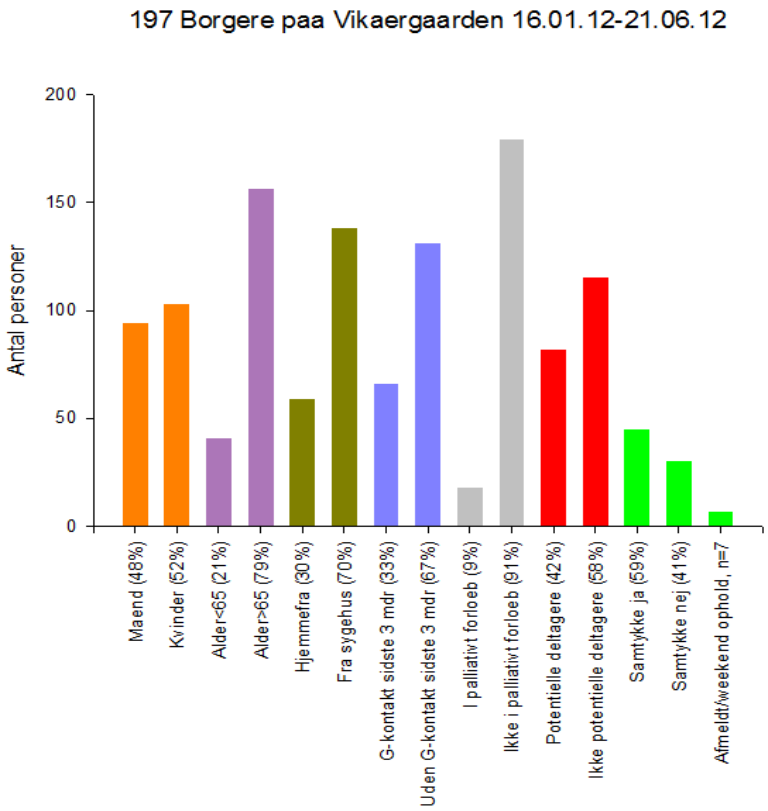
- ❑ Notat på G-Vik-P1 er skrevet i EPJ (koder ZZ0150D og ZZ9030A) som ”hjemmebesøg” med kopi af planen til e.l.

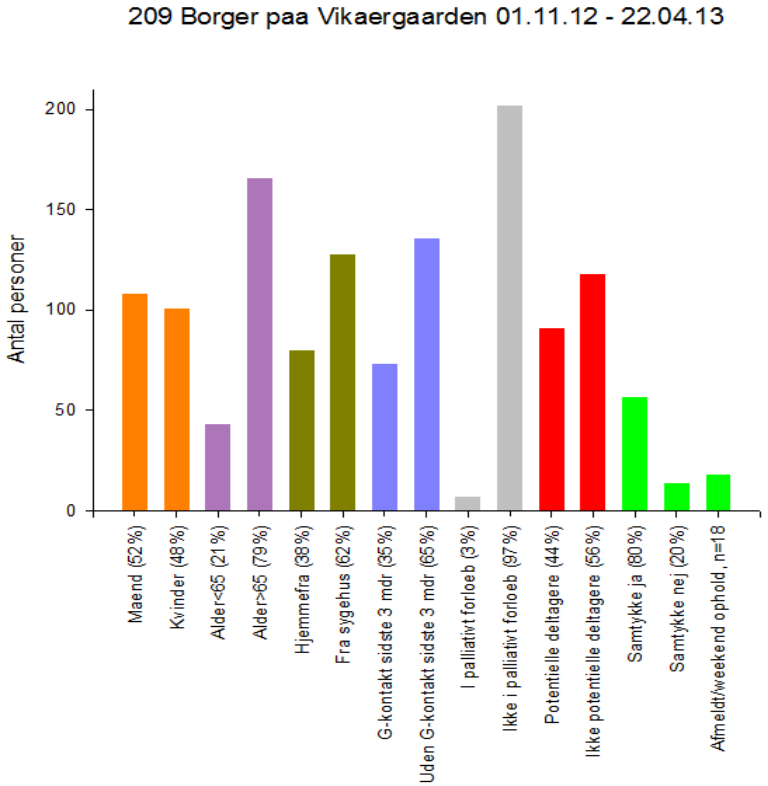
- ❑ Orienterende om projektet brev til egen læge er afsendt med intern post

- ❑ Projektterapeut er orienteret om den nye projektdeltager (navn, cpr, id-nr., ophold starts dato, stuenummer)

- ❑ Dataindsamlingsmapperne er udfyldt og låst inde i skabet

Appendix 3. E_Changes in the population referred to the rehabilitation unit Vikaergaarden observed during the study first 15 months enrollment's period.





Appendix 3. F

Instruks til afløser.

Kære kollega,
Jeg vil bede dig om hjælp til en ”geriatrisk intervention” i vores projekt, dvs. en geriatrisk gennemgang af en interventionsgruppe projektdeltager (G-Vik-P1) inden for de første 3 dage efter start af opholdet her på Vikærgården.

Efter selve interventionen skal du naturligvis orientere pt-s kontakt personale fra Vikærgården om planen (fuldstændig som G-Teams læge gør) og oprette forløbet i EPJ under ”G – funktion - Vikærgården” med en forsimplet GO-Teams standardplan i EPJ. Kontrol-gruppe deltagere (”P-2”) skal naturligvis ikke ses af dig. Det er vores projektsygeplejerske, der vil inkludere projektdeltagere. Projektsygeplejersken er på arbejde fra 7.30 til 13.30 hver hverdag og hendes arbejdstelefon nr. er 51 57 60 11. Projektsygeplejersken er oplært i og står for både inklusionsfilter og samtykke procedure. Endvidere for alt andet praktisk inklusiv afsendelse af orienterende brev til egen læge (du skal bare tage brevet med og sende det gratis med intern post fra afd. G2 inden for 1 døgn).

Du skal selv printe PDB sedler ud til en G-Vik-P1 og labels til både P1- og P2- deltagere på GO-Teams printer. Jeg opretter dataindsamlings mapperne, får styr på dem og taster data i min elektroniske database, når jeg kigger forbi Vikærgården 2 gange ugentligt (mandag og torsdag kl. 9 – 11).

Du er altid velkommen til at få sparring og feedback hos mig ved at kontakte mig per mail eller telefonisk, hvis du er i tvivl om noget. Hvis der er noget, der kræver akut konf. med mig, må du gerne sende mig en sms eller ringe på min mobil 26 70 09 03.

Som reminder:
* alle interventionsgruppes projektdeltagere er kodet som ”G-Vik-P1” og det VED alle Vikærgårdens personale
* kontrolgruppes deltagere (”G-Vik-P2”) må du ikke give et godt råd til, da de må klares af deres egen læge
* både G-Vik-P1 og G-Vik-P2 behandles af vagtlægen udenfor den normale arbejdstid

Jeg håber, at du får en god oplevelse ved at medvirke i vores, nok et af Danmarks vigtigste inden for sundhedsvidenskaben, projekt.

Med venlig hilsen,
Dmitri Zintchouk,
projektleder, speciallæge i geriatri.

Appendix 3. G

Charlsons Comorbidity Index (CCI) |__| (sum score)

Sygdom	Værdi	ICD-8	ICD-10
Akut myokardie infarkt	1	410	I21;I22;I23
Hjerteinsufficiens	1	427.09; 427.10; 427.11; 427.19; 428.99; 782.49	I50; I11.0; I13.0;I13.2
Karsygdomme	1	440; 441; 442; 443; 444; 445	I70; I71; I72; I73; I74; I77
Cerebrovaskulære sygdomme	1	430-438	I60-I69; G45; G46
Demens	1	290.09-290.19; 293.09	F00-F03; F05.1; G30
Kronisk lungesygdomme	1	490-493; 515-518	J40-J47; J60-J67; J68.4; J70.1; J70.3; J84.1; J92.0; J96.1; J98.2; J98.3
Bindevævssygdomme	1	712; 716; 734; 446; 135.99	M05; M06; M08; M09;M30;M31; M32; M33; M34; M35; M36; D86
Ulcussygdomme	1	530.91; 530.98; 531-534	K22.1; K25-K28
Milde leversygdomme	1	571; 573.01; 573.04	B18; K70.0-K70.3; K70.9; K71; K73; K74; K76.0
Diabetes type1 Diabetes type2	1 1	249.00; 249.06; 249.07; 249.09 250.00; 250.06; 250.07; 250.09	E10.0, E10.1; E10.9 E11.0; E11.1; E11.9
Hemiplegi	2	344	G81; G82
Nyresygdomme	2	403; 404; 580-583; 584; 590.09; 593.19; 753.10-753.19; 792	I12; I13; N00-N05; N07; N11; N14; N17-N19; Q61
Diabetes med komplikationer type1 type2	 2 2	 249.01-249.05; 249.08 250.01-250.05; 250.08	 E10.2-E10.8 E11.2-E11.8
Solide kræftformer	2	140-194	C00-C75
Leukæmi	2	204-207	C91-C95
Lymfomer	2	200-203; 275.59	C81-C85; C88; C90; C96
Moderate til svære lever-sygdomme	3	070.00; 070.02; 070.04; 070.06; 070.08; 573.00; 456.00-456.09	B15.0; B16.0; B16.2; B19.0; K70.4; K72; K76.6; I85
Metastaserende cancer	6	195-198; 199	C76-C80
AIDS	6	079.83	B21-B24

Confusion Assessment Method (CAM)

1. *Akut* opstående og fluktuerende forløb*

Denne oplysning opnås ofte fra en pårørende eller en sygeplejerske ved at udspørge om følgende: Er der tegn på akut ændring i patientens mentale status i forhold til det, der er normalt for patienten?

A: Ja |_| Nej |_|

Fluktuerede den abnorme adfærd i løbet af dage, dvs. havde den tendens til at komme og gå, eller tiltog eller aftog den i styrke?

B: Ja |_| Nej |_|

---

2. *Uopmærksomhed*

Denne egenskab blev opdaget ved positivt svar på følgende spørgsmål:

Havde patienten svært ved at fastholde opmærksomheden, f.eks. ved let at blive distraheret, eller havde patienten svært ved at holde fast i, hvad der blev sagt?

Ja |_| Nej |_|

---

3. *Usammenhængende tankegang*

Denne egenskab blev opdaget ved positivt svar på følgende spørgsmål:

Var patientens tankegang usammenhængende eller uorganiseret, var der irrelevant eller usammenhængende tale, uklar eller ulogisk strøm af ideer eller uforudsigelige skrift fra det ene emne til det andet?

Ja |_| Nej |_|

---

4. *Ændret bevidsthedsniveau*

Hvordan vil du overordnet vurdere patientens bevidsthedsniveau?

1. Normalt? (vågen) |_|
2. Agiteret? (hyperaktiv) |_|
3. Døsig? (sløv, vækkes let) |_|
4. Stuporøs (vanskelig at vække) |_|
5. Koma (kan ikke vækkes) |_|

Denne egenskab blev opdaget ved et hvilket som helst andet svar end vågen på overstående spørgsmål.

---

5. Diagnosen *akut konfusion* ved hjælp af CAM kræver tilstedeværelse af "ja" i mindst punkt 1 og 2 og enten punkt 3 eller 4

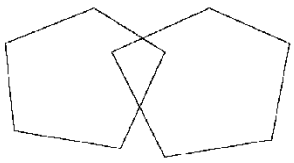
Akut konfusion ifølge CAM: Ja |_| Nej |_|

---

*) Ved akut forstår vi, at forvirringstilstanden kan vare fra timer til få dage eller længere tid.

Mini Mental State Examination (MMSE)

Orientering	**Score**	**Max. point**
1. Hvilket/n årstal, årstid, dato, ugedag, måned (1 point for hvert rigtigt svar)	_____	5
2. Hvor er vi? Land, by, amt, hospital/adresse, etage (1 point for hvert rigtigt svar)	_____	5
3. Registrering Nævn 3 genstande (nøgle, lygte, bog - 1 pr. sekund). Bed patienten gentage de 3 ord (1 point for hver korrekt svar).	_____	3
4. Opmærksomhed og regning 100-7 prøven. 1 point for hvert korrekt svar. Alternativt: stav ordet "trold" bagfra	_____	5
5. Genkaldelse Spørg igen om de 3 tidligere nævnte genstande. 1 point for hvert korrekt svar.	_____	3
6. Sprog Benævn 2 foreviste genstande F.eks. blyant, ur - 1 point for hvert rigtigt svar.	_____	2
7. Gentag: "Hvis - såfremt - ifald"	_____	1
8. 3-leddet kommando: "Tag papiret i Deres højre hånd, fold det på midten, og læg det på gulvet".	_____	3
9. Læs dette, og gør, hvad der står (se bilag: "luk øjnene")	_____	1
10. Skriv en sætning (1 point, hvis sætningen er meningsfuld og har både udsagnsord og navneord)	_____	1



11. Kopiering Bed patienten kopiere figuren på bilaget.	_____	1

Skriv en sætning: _____

SAMLET SCORE 30 **____**

Modificeret Barthel Index (MBI)

Aktivitet:	Point max.	
1. Spisning	10	
2. Forflytning stol/seng	15	
3. Pers. hygiejne	5	
4. Toiletbesøg	10	
5. Tage bad	5	
6. Gangfunktion Kørestol	15 5	
7. Trappegang	10	
8. Påklædning	10	
9. Tarmkontrol	10	
10. Blærekontrol	10	
MBI score	100	

The 30-second Chair Stand Test (30s-CST)

Anvend en højrygget stol (43-44 cm), placeret mod en væg.

Antal gange personen kan rejse sig fra siddende til fuldt oprejst stilling i løbet af 30 sekunder med armene foldet mod brystet.

Antal oprejsninger	
Uden armstøtte	
Med armstøtte	

Depressions List (DL)

Selv-vurdering af livskvalitet *(ved hvert spørgsmål vises et skilt med tilhørende overskrift i magnumprint)*

Spørgsmål:	**Svarkategorier:**	**Score:**
1. Er du tilfreds?	Tilfreds = 0 Ikke helt tilfreds = 1 Utilfreds = 2	
2. Sover du godt?	Godt = 0 Ikke så godt = 1 Dårligt = 2	
3. Spiser du godt?	God appetit = 0 Ikke så god appetit = 1 Dårlig appetit =2	
4. Føler du dig sund?	Sund = 0 Ikke så sund = 1 Syg = 2	
5. Er du nogensinde træt?	Ikke træt = 0 Indimellem træt = 1 Hele tiden træt = 2	
6. Føler du dig gammel?	Ikke gammel = 0 Lidt gammel = 1 Gammel = 2	
7. Føler du dig ensom?	Ikke ensom = 0 Indimellem ensom = 1 Ofte ensom = 2	
8. Har du venner?	Nogle eller mange venner og/eller bekendte = 0 Lidt tiltale = 1 Ingen venner eller bekendte = 2	
9. Får du nok besøg?	Tilfreds med besøg, der kommer nok = 0 Kunne ønske flere besøg = 1 Utilfreds med manglende besøg = 2	
10. Er du sørgmodig?	Sjældent = 0 Nogle gange = 1 Ofte = 2	
11. Keder du dig nogensinde?	Sjældent = 0 Nogle gange = 1 Ofte = 2	
12. Er du livlig?	Er livlig = 0 Er ikke helt så livlig = 1 Er slet ikke livlig = 2	
13. Føler du dig hjælpeløs?	Føler sig ikke hjælpeløs = 0 Føler sig lidt hjælpeløs = 1 Føler sig hjælpeløs = 2	
14. Føler du dig svag?	Føler sig ikke svag = 0 Føler sig nogle gange svag = 1 Føler sig svag = 2	
15. Forventer du stadig at få noget ud af livet?	Forventer stadigvæk noget af livet = 0 Forventer ikke så meget mere af livet = 1 Forventer intet eller en smule af livet = 2	

Samlet score:

AARHUS UNIVERSITY

Declaration of co-authorship concerning article for PhD dissertations

Full name of the PhD student: Dmitri Zintchouk

This declaration concerns the following article/manuscript:

Title:	Comprehensive geriatric care versus standard care for elderly referred to a rehabilitation unit – a randomized controlled trial.
Authors:	Zintchouk D, Lauritzen T, Damsgaard EM

The article/manuscript is: Published **x** Accepted ☐ Submitted ☐ In preparation ☐

If published, state full reference: Comprehensive geriatric care versus standard care for elderly referred to a rehabilitation unit – a randomized controlled trial. Zintchouk D, Lauritzen T, Damsgaard EM. Journal of Aging Research and Clinical Practice, 2017; 6:40-47.

Has the article/manuscript previously been used in other PhD or doctoral dissertations?

No **x** Yes ☐ If yes, give details:

The PhD student has contributed to the elements of this article/manuscript as follows:

A. Has essentially done all the work
B. Has done most of the work (67-90 %)
C. Has contributed considerably (34-66 %)
D. Has contributed (10-33 %)
E. No or little contribution
F. N/A

Element	Extent (A-F)
1. Formulation/identification of the scientific problem	B
2. Development of the method	B
3. Planning of the experiments and methodology design and development	C
4. Involvement in the experimental work/clinical studies/data collection/obtaining access to data	A
5. Development of analysis plan and preparation of data for analysis	B
6. Planning and conducting the analysis of data	B
7. Interpretation of the results	B
8. Writing of the first draft of the manuscript	A
9. Finalization of the manuscript and submission	B

Signatures of first- and last author, and main supervisor

Date	Name	Signature
20/12-18	Dmitri Zintchouk	Dmitri Zintchouk
20/12-18	Else Marie Damsgaard	Else Marie Damsgaard

Date: 20/12-18 Dmitri Zintchouk

Signature of the PhD student

AARHUS
UNIVERSITY

Declaration of co-authorship concerning article for PhD dissertations

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1. Formulation/identification of the scientific problem	B
2. Development of the method	B
3. Planning of the experiments and methodology design and development	C
4. Involvement in the experimental work/clinical studies/data collection/obtaining access to data	A
5. Development of analysis plan and preparation of data for analysis	B
6. Planning and conducting the analysis of data	B
7. Interpretation of the results	B
8. Writing of the first draft of the manuscript	A
9. Finalization of the manuscript and submission	B

Signatures of first- and last author, and main supervisor

Date	Name	Signature
20/12-18	Dmitri Zintchouk	Dmitri Zintchouk
20/12-18	Else Marie Damsgaard	Else Marie Damsgaard

Date: 20/12-18 Dmitri Zintchouk

Signature of the PhD student

AARHUS UNIVERSITY

Declaration of co-authorship concerning article for PhD dissertations

Full name of the PhD student: Dmitri Zintchouk

This declaration concerns the following article/manuscript:

Title:	Impact of Geriatrician-performed Comprehensive Geriatric Care on Medication Use and Cognitive Function in Older Adults Referred to a Non-Hospital-Based Rehabilitation Unit.
Authors:	Zintchouk D, Gregersen M, Lauritzen T, Damsgaard EM

The article/manuscript is: Published **x** Accepted ☐ Submitted ☐ In preparation ☐

If published, state full reference: Impact of Geriatrician-performed Comprehensive Geriatric Care on Medication Use and Cognitive Function in Older Adults Referred to a Non-Hospital-Based Rehabilitation Unit. Zintchouk D, Gregersen M, Lauritzen T, Damsgaard EM. The American Journal of Medicine, 2019; 132 (1): 93–102.e2

Has the article/manuscript previously been used in other PhD or doctoral dissertations?
No **x** Yes ☐ If yes, give details:

The PhD student has contributed to the elements of this article/manuscript as follows:

A. Has essentially done all the work
B. Has done most of the work (67-90 %)
C. Has contributed considerably (34-66 %)
D. Has contributed (10-33 %)
E. No or little contribution
F. N/A

Element	Extent (A-F)
1. Formulation/identification of the scientific problem	B
2. Development of the method	B
3. Planning of the experiments and methodology design and development	B
4. Involvement in the experimental work/clinical studies/data collection/obtaining access to data	A
5. Development of analysis plan and preparation of data for analysis	B
6. Planning and conducting the analysis of data	B
7. Interpretation of the results	B
8. Writing of the first draft of the manuscript	A
9. Finalization of the manuscript and submission	B

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