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RESEARCH PAPER

A cohort study of the effects of multidisciplinary in-patient primary care in older adults

Martin Gronbech Jorgensen[1] · Maria Rodrigo-Domingo[2] · Stig Andersen[1,3] · Johannes Riis[1,3] · Dorthe Bruun Jakobsen[4] · Mikkel Lerche[4] · Hanne Hostrup[5] · Jane Andreasen[6,7]

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Key summary points

Aim To evaluate to the effects of a multifactorial, multidisciplinary in-patient municipality intervention on functioning, need-of-care, and quality of life in functionally declining older adults.

Findings Following the intervention, patients had increased quality of life, which remained at the post-intervention level even after 6 months. Further, participants had lower need-of-care and increased performance in physical function tests.

Message A well-structured multifactorial and multidisciplinary in-patient intervention may lead to long-term clinically relevant improvements in functionally declining older adults.

Abstract

Purpose To evaluate short and long-term effects of a multifactorial and multidisciplinary in-patient municipality intervention including training of activities of daily living, cardiovascular exercise, resistance training and social activities on quality-of-life, need-of-care, and physical function in older adults at risk of further functional decline.

Method A cohort study including data collected rigorously during 3.5 years at an in-patient municipality rehabilitation center in Aalborg, Denmark. Patients received a multifactorial and multidisciplinary intervention. Outcomes were quality-of-life (EQ5D), weekly need-of-care hours, and test of physical functioning (sit-to-stand, 6-min walking test, tandem balance).

Results Data was collected from 532 patients (63.3% women). The median [5; 95 percentiles] age was 79 [55; 92] years with a length-of-stay of 21 [8; 55] days. The mean (95% CI) EQ5D index score showed a clinically relevant improvement from admission 0.46 (0.44; 0.48) to discharge 0.69 (0.67; 0.71) and there was no decline 6-month postdischarge 0.67 (0.64; 0.70). The weekly need-of-care decreased significantly by 7.2 (6.6, 7.9) h from a mean of 9.8 h before admission to 2.6 h 6-month postdischarge. Sit-to-stand improved from 6.3 (6.0; 6.7) to 9.3 (8.9; 9.6) repetitions, 6-min walking test from 147 (138; 156) to 217 (207; 227) m, and tandem balance from 20.7 (19.8; 21.6) to 25.2 (24.8; 26.2) s.

Conclusion Our results were remarkable and highlight that a well-structured multifactorial and interdisciplinary intervention with a clear aim and inclusion criteria related to functional decline may lead to long-term clinically relevant improvements in functionally declining older adults. Future studies should, however, explore similar interventions in comparable populations preferably in randomized controlled designs.

✉ Johannes Riis
johannes0408@live.dk

1 Department of Geriatric and Internal Medicine, Aalborg University Hospital, Hobrovej 18, 9000 Aalborg, Denmark

2 Department of Psychiatry, Aalborg University Hospital, Aalborg, Denmark

3 Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

4 Unit of Quality and Innovation, Department of Care for the Elderly and Disabled, Aalborg Municipality, Aalborg, Denmark

5 Rehabilitation Center Aalborg (Mou), Aalborg, Denmark

6 Department of Physiotherapy and Occupational Therapy, Aalborg University Hospital, Aalborg, Denmark

7 Public Health and Epidemiology Group, Department of Health, Science and Technology, Aalborg University, Aalborg, Denmark

Keywords Need-of-care · Quality of life · Physical functioning · Frailty · Multidisciplinary rehabilitation intervention · In-patient care

Introduction

Loss of physical function among older adults is common and affects more than 25% of older adults after discharge from hospital care [1–3]. This functional decline may lead to inability of living an independent life and ultimately increased mortality [1, 2, 4]. This is a concer as loss of independence is rated the number-one concern for the majority of older adults (76%), while death is rated second (11%) [5].

Hence, it is essential to develop feasible, efficient, and cost-effective interventions to avoid slow down, or reversed functional decline in older adults. This has led to a number of primary health care interventions targeting older adults at risk of functional decline over the latest decades. Many of these interventions have focused on out-patient rather than in-patient interventions in community settings and they have often lacked either multidisciplinary, multifactorial, or exercise components [6–9]. This is unfortunate, as a growing body of evidence demonstrates the effect of exercise interventions as a key element in rehabilitation of functional decline and prevention of disability, although long-term effects are poorly reported [10, 11]. Besides, integrated care interventions vary considerably in intensity, duration, disciplines involved, and setting. Additionally, the effects reported on clinical outcomes have been absent, merely modest, or inconsistent [12–15]. A recent narrative review [16] on integrated primary care stresses the need for explorative and multicomponent studies combining key components in integrated primary care interventions. This led us to evaluate both short-term (at discharge) and long-term (3- and 6-month post-discharge) effects of a multidisciplinary in-patient intervention on health related quality-of-life (EQ5D), need-of-care (hours per week), and physical functioning (6-min walking test, sit-to-stand and balance) among community-dwelling older adults at further risk of functional decline.

Materials and methods

Study design and setting

This cohort study included data collected routinely and consecutively over a 3.5-year period from January 2014 to October 2017 from patients at a municipal in-patient rehabilitation center in Aalborg, Denmark. Data collection on health-related quality of life was initiated later at the rehabilitation center and, therefore, collected from January 2015 to October 2017, need-of-care was measured in a period from January 2014 to December 2015, and data on physical function tests were collected over the entire period. A stay at Aalborg Rehabilitation Center (from here on referred to as the "center") is free of charge for the patient. Furthermore, the center assesses and addresses the functional decline of the individual patient rather than having a disease-specific and specialized approach. The program at the center has a comprehensive approach to rehabilitation and uses a partnership between the course patient and the staff as a tool to support the course patient's contribution to rehabilitation. This extends to linguistic aspects with patients referred to as "course participants" and staff not wearing uniforms to support an informal and equal relationship with the patients. The staff comprises a multidisciplinary team of physiotherapists, occupational therapists, social care assistants, support worker, and nurses. The center is in close contact with the patients´ individual physicians during their stay; this may be by telephone, by email, or by visiting the doctor, or the physician's visit to the rehabilitation center.

The focus and intention are to create an environment that mirrors the patient's daily life and to create a sense of community, for example by morning gatherings, healthy breakfast, and other social activities. Patients have their own private apartment during the stay. In addition, each day takes its course with a healthy breakfast together with the rest of the course participants to facilitate social interaction.

Intervention

The needs and goals of the individual patient were the core determinants of the activities, and the occupational therapy and physiotherapy interventions were tailored to these. The daily interventions included training of routines necessary for daily living (ADL) and for instrumental activities of daily living (iADL). Physiotherapy training consisted of cardiovascular training aiming at 70% of maximal aerobe capacity and 70–80% of 1 repetition maximum in strength training [17–19]. Furthermore, patients were encouraged to participate in additional activities. These included lunch preparing teams, indoor car-entering and -exiting training, beauty-salon, and activity rooms. Outdoor activities such as fishing tours, walking, and shopping trips were planned at regular intervals. The length of stay at the center was typically between 2 and 12 weeks, with longer stay length offered to patients with greater needs of rehabilitation. If needed, a team would follow the patient home and help to reestablish daily routines. Participants were contacted regularly after the stay if they had provided consent.

Preadmission assessment and participants

Potential patients were referred from hospitals or the municipality by physicians, social care workers, the patient themselves, or relatives. Approximately 49% were referred from a hospital and 51% from the municipality. Formal inclusion criteria were: minimum 18 years of age, requiring at least 5 h of weekly need-of-care before the stay, or being at high risk of requiring care needs in the future (criteria assessed by the visitation authority at the municipality office). All patients were classified as being at risk of further functional decline and/or at increased risk of care. In addition, patients themselves should express interest in a stay at the center to be offered a stay. Furthermore, the patients should have a rehabilitation potential to benefit from the stay and it should be considered realistic that the required need-of-care hours per week would be reduced after the stay. Patients with neurological disorders, alcohol or drug abuse, severe pain conditions or patients with cognitive limitations were excluded as their conditions would require a more specialized rehabilitation. A trained occupational therapist performed all assessments.

Data sources and outcome measures

Data were obtained from self-reported measures, physical function measures and from the municipality registers, where all activities for each citizen in the municipality is registered. The flow of patients and outcomes is illustrated in Fig. 1. The center consecutively obtained outcome measures on all eligible patients regarding health related quality of life, need-of-care measured by hours per week, and basic functional capability at inclusion and post-rehabilitation, but only health related quality of life and need of care were recorded after 3- and 6-month post-rehabilitation. The patient-reported health related quality-of-life was assessed by EQ5D-5L. EQ5D-5L is a generic instrument with well-established psychometric properties [20] that consists of five dimensions: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression, which can be reported with a cumulative index score. The index score varies from 1 (full health) to 0 (death) and − 0.59 (conditions regarded worse than death). A Danish reference population is available [21]. At 3 and 6 months the questionnaire was mailed to the participants with an included response envelope with a stamp. One telephone reminder call was made to non-responding patients. Weekly hours of need-of-care were obtained from municipality registrations for all patients before the stay at the center, at discharge, and 3 and 6 months after the stay. The covariates gender, age, and marital status were registered at inclusion. The physical function was examined by three tests (sit-to-stand, 6-min walking test, tandem balance) at inclusion and at discharge from the center. All physical test have been tested for reproducibility and validity in older populations [22–25]. The primary outcome was the change in health-related quality of life (EQ5D-5L) measured by the EQ5D-index from discharge to 6 months. Secondary outcomes were changes in need-of-care from baseline to 6 months, the 6-min walk test, the sit-to-stand test and the tandem balance test from admission to discharge from the center.

Statistical methods

Summary statistics for the relevant variables are: number and percentage within categories for categorical variables

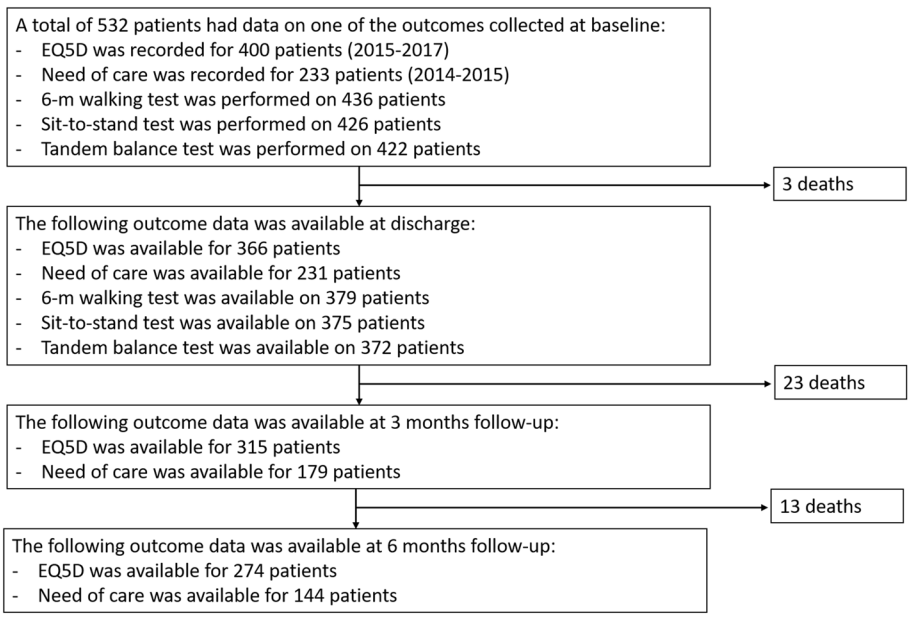

Fig. 1 Flowcharts showing the number of observations available for the different outcomes

and mean and standard deviation for continuous variables—unless visual inspection of histograms revealed a highly skewed variable, in which case the median and 5th and 95th percentiles are reported. Summary statistics are presented for the group as a whole as well as for males and females separately. The changes in EQD5 index with time are analyzed using a mixed effects model with time as fixed effect and course participant as random effect. A second model adjusted for sex and the interaction between time and sex as a fixed effect is used to produce a figure. For comparison purposes, we used the age- and sex-dependent EQ5D means reported [26] to compute a weighted EQ5D average for males and a weighted average for females. The weights are the percentage of our patients that fall in each of the age categories defined in [27] (20–29; 30–39; 40–49; 50–59; 60–69; and 70–79 years of age). The change in need-of-care was analyzed in a mixed-effects model with need-of-care as dependent variable, time as the fixed effect and patient as the random effect. Separate mixed-effects models were used to analyze the function scores with each function score as dependent variable, time as a fixed effect, and patient as random effect. All models were adjusted for possible confounders in two versions: (1) sex, age category (as defined above), and length of stay, or (2) sex, age category (as defined above), length of stay, and value at admission of the corresponding dependent variable. There was no imputation of data. The analyses were done in Stata SE 14.2. Results with p values below 0.05 are considered statistically significant.

Results

From January 2014 to October 2017 data was obtained from 532 consecutive patients, course participants. Within 6 months from the admission date, 7.5% ($N=40$) had died, 4 during admission and 26 within the first 3 months after discharge from the center. Among the admitted patients, 2/3 were women and they were markedly older than the men. Table 1 presents baseline characteristics at admission of the study-population by gender and in total. The mean health-related quality-of-life measured by EQ5D index improved markedly during the stay at the center. Indeed, from a mean EQ5D index at admission of 0.46 [95% CI (0.44; 0.49)] to 0.69 [95% CI (0.67; 0.71)] at discharge, and the index score was upheld when measured at three 0.66 [95% CI (0.63; 0.68)] and 6 months 0.67 [95% CI (0.65; 0.70)] after discharge (Fig. 2). Although there was no statistically significant difference between males and females regarding the improvement in EQ5D index, we have chosen to present the two genders separately to illustrate a slightly different pattern and to compare with a Danish reference population [21]. The mean weekly hours of need-of-care decreased from 9.8 h [95% CI (9.2; 10.4)] to 2.6 h [95% CI (1.9; 3.3)] 6 months after discharge (Fig. 3). From admission to discharge, sit-to-stand improved from 6.3 (6.0; 6.7) to 9.3 (8.9; 9.6) repetitions, 6-min walking test from 147.1 (137.9; 156.4) to 216.5 (206.5; 226.5) meters, and tandem balance from 20.7 (19.8; 21.6) to 25.2 (24.8; 26.2) seconds (Table 2). The estimates from the adjusted analyses did not differ by more than 3 decimal points from those reported, one centesimal point for EQ5D (data not shown). Besides, sensitivity analyses performed excluding patients who died in admission or within 3 months after discharge, or excluding those lost to follow-up but still alive showed no relevant differences with respect to the reported estimates. Furthermore, sensitivity analysis excluding patient under the age of 60 showed no relevant differences from the primary analysis (Table 3). No serious adverse effects were reported during the study period.

Discussion

This cohort study on a multidisciplinary in-patient municipality-based intervention aimed at older adults at risk of further functional decline showed that health related quality-of-life (EQ5D) and need-of-care improved significantly by 48% and 73% at discharge, respectively, and that these effects were maintained at 6-month postdischarge. Likewise, for the functional tests, statistically and clinically significant improvements were observed. Specifically, the improvements from admission to discharge in both the 6-min walk test and sit-to-stand test were 47%, and that of the tandem balance test was 22%.

EQ5D

The improvements in EQ5D were clearly clinically relevant even though our patients did not reached the level of the Danish background population [21]. In fact, the magnitude of the change from admission to discharge in the EQ5D index was 3 times that of the minimal important difference (0.074) reported by Walters and Brazier in 2005 [28]. Relevant and sustained increases in the EQ5D index, such as the ones seen in the current study, have not been seen in reviews [10, 27, 29–33], due to short term follow-up and because only few of the included studies used health related quality-of-life as an outcome. The marked improvements in EQ5D seen in the current study might be explained by three factors: (1) the comprehensive and rigorous multifactorial intervention, (2) the selected study population and (3) the patients lost to follow-up. First, the intervention was unique in the sense that it was an in-patient stay, where patients lived in their own private apartment during the stay. Second, this was a selected group of patients as they had to be self-motivated with rehabilitation potential to be admitted. These factors

Table 1 Clinical and demographic characteristics of patients at admission

	All	Males	Females
Total period			
Participants[a]	532	195 (36.75%)	337 (63.35%)
Age (years)[b]	79 [55; 92]	75 [52; 91]	81 [59; 92]
Living alone[a,d]	301 (76.4%)	87 (63.5%)	214 (83.3%)
EQ5D-5L			
Participants[a]	400	138 (34.5%)	262 (65.5%)
Score[b]	0.55 [− 0.01; 0.76]	0.55 [− 0.01; 0.77]	0.55 [− 0.06; 0.76]
Need of care			
Participants[a]	233	84 (36.05%)	149 (63.95%)
Hours[b]	9.3 [3.2; 18.1]	10.2 [3.2; 19.7]	8.7 [3.2; 18.1]
Six-min walking			
Participants[a]	436	156 (35.8%)	280 (64.2%)
Meters[c]	140.7 (90.0)	141.1 (92.8)	140.5 (88.5)
Sit-to-stand			
Participants[a]	426	148 (34.7%)	278 (65.3%)
Repetitions[c]	6.25 (3.1)	6.3 (3.2)	6.2 (3.0)
Tandem balance			
Participants[a]	422	147 (34.8%)	275 (65.2%)
Seconds[c]	20.6 (8.9)	21.0 (9.2)	20.3 (8.8)

[a]Count and percentage males/females of the total

[b]Median [Q05; Q95]

[c]Mean (SD)

[d]Data not available for all participants. Percentages computed based on available information

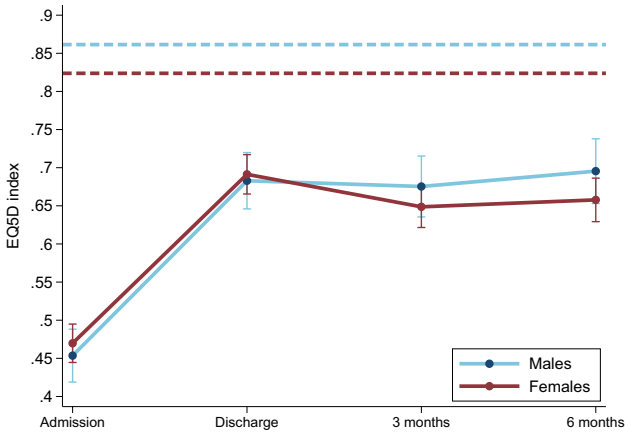

Fig. 2 Mean and 95% CI for EQ5D scores at the different time points for males and females separately. The dashed lines at the top represent the population norms

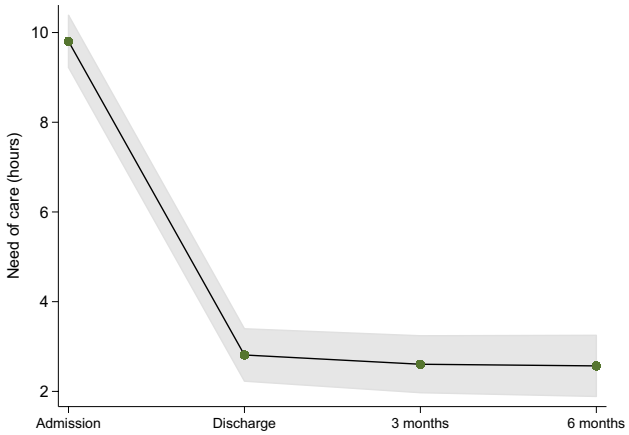

Fig. 3 Mean and 95% CI for need-of-care (hours) at the different time points

may be key for the successful long-term rehabilitation effects suggested by our data. By excluding the patients who were not motivated, our results might be pushed towards an optimistic view. Third, EQ5D data was missing for 125 participants 6-month postdischarge (40 of which died). These patients lost to follow-up might have been the patients with the worst outcomes and frailty status. In such case, we would probably have seen a reduction of the sustained effect on EQ5D at 3- and 6-month postdischarge.

Need-of-care

The need-of-care was reduced significantly at discharge, and 3- and 6-month postdischarge compared to admission.

Table 2 Change in scores for the different outcomes

	Initial value (mean)	Change at discharge	Change at 3 months	Change at 6 months
EQ5D-5L	0.46	0.22 [0.20, 0.25]	0.19 [0.16, 0.22]	0.20 [0.17, 0.24]
Need of care (h)	9.8	− 6.99 [− 7.63, − 6.36]	− 7.20 [− 7.92, − 6.48]	− 7.24 [− 8.01, − 6.46]
Six-min walking (meters)	141.0	71.48 [64.03, 78.93]		
Sit-to-stand (repetitions)	6.45	2.93 [2.65, 3.22]		
Tandem balance (score)	20.6	4.77 [4.03, 5.50]		

Difference from baseline (mean and 95% CI) using mixed effects linear models (unadjusted)

Table 3 Sensitivity analysis of change in scores for the different outcomes in patients 60 years or older

	Initial value (mean)	Change at discharge	Change at 3 months	Change at 6 months
EQ5D-5L	0.46	0.22 [0.19, 0.25]	0.19 [0.16, 0.22]	0.21 [0.18, 0.24]
Need of care (h)	9.8	− 6.95 [− 7.60, − 6.30]	− 7.11 [− 7.87, − 6.34]	− 7.14 [− 8.00, − 6.28]
Six-min walking (meters)	138.0	67.69 [60.73, 74.65]		
Sit-to-stand (repetitions)	6.45	3.55 [2.49, 4.62]		
Tandem balance (score)	20.6	5.08 [4.27, 5.89]		

Difference from baseline (mean and 95% CI) using mixed effects linear models (unadjusted)

The administration at Aalborg Municipality did an internal calculation showing a net saving per year of 9.20 million Danish kr. (€ 1.2 million on November 2018) in 2014 and 10.50 million Danish kr. (€ 1.4 million) in 2015, after the expenditures from the center were subtracted. The review by Apostolo (2018) included cost benefit calculations as a secondary outcome, and the two original studies included showed that group-based interventions provided better value for money compared to usual care [27]. Brusco et al. published a review in 2014 with an economic evaluation of adult rehabilitation in a variety of settings. Their findings were inconclusive due to lack of consistency in the results across different populations and no "in-patient" municipality-based rehabilitation center was evaluated [34].

Physical function tests

Data from the 6-min walking test showed an increase in mean walking distance of 69.4 m from baseline to discharge, which is well above the minimal important differences of 54 m previously defined [35]. In addition, a recent review [36] defined an improvement of 14–30.5 m as being the minimally clinically important difference for the 6-min walk test in adults with pathologies. The review by Verweij [10] included seven randomized controlled trials and showed that, compared to usual care, a multidisciplinary intervention consisting of advice on lifestyle, exercise, and follow-up visits in older people improved their 6-min walking test by 23 m (95% CI − 1.3; 48.3) at a 3-month follow-up. Compared to this, our finding were impressive considering that half of the included patients were referred to the center directly following hospitalization. Furthermore, the patients improved their sit-to-stand significantly and the mean of 9.3 repetitions from a starting point of 6.3 at inclusion for the patient is an important and clinically relevant improvement, as the threshold value in relation to loss of functional mobility within a year was set at 8 repetitions [23]. The balance test also improved significantly in the patients. However, based on practical considerations the center chose to perform only the static standing balance test part of the Short Physical Performance Battery, which originally consisted of three physical tests. Therefore, no clinically relevant difference can be defined for this part.

Strengths and limitations

The main strengths of the current study were the large size of the study population and the long-term follow-up for up to 6-months postdischarge. This observational cohort-study evaluated the implementation of an innovative practice inspired by the Danish Folk Highschools and used data obtained from registers, self-reported questionnaires, and standardized procedures for several functional tests.

A main limitation was that the current study was not a randomized controlled trial. Furthermore, we did not have a control group serving as a standard care group in our cohort study. This meant that confounders potentially

could influence our results. To accommodate these potential confounders, we adjusted for gender, age, admission values and length of stay in the mixed-effect model. This added no change in the effect sizes indicating that gender and age only played a minor role as confounders. Secondly, application of our results to other populations or settings should be performed with caution, as the center used specific inclusion criteria for the current patients.

Another limitation of our study was that included patients were motivated to have a stay and participate in activities at the rehabilitation center. Thus, the effectiveness of the intervention may be overestimated when compared to the general population. However, as this is an extensive intervention, it is reasonable to offer it only to motivated patients, for whom our results are applicable.

Finally, we did not have access to physical test at 3- and 6-month follow-up. Therefore, we could only report results for EQ5D and need of care, which are general and subjective measures.

Conclusion

The results of this cohort study were remarkable in that a well-structured multifactorial and interdisciplinary intervention with a clear mission and clear inclusion criteria can lead to long-term and clinically important sustained improvements. It is suggested that future studies should explore similar interventions in a randomized setup. Importantly, the approach of a comprehensive in-patient community-based rehabilitation center may be a path to addressing the challenges that a rapidly growing aging population presents to the community and to healthcare systems.

Data availability Upon reasonable request data from the current study can be made available.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflicts of interest.

Ethics approval This cohort study was assessed by the Danish Regional Ethics Committee who stated that no approval was required (mail correspondence on April 28, 2018).

Informed consent In Denmark, research consisting of retrospective analysis of data stored in registries of routine care does not require informed consent and as a result, participants were not aware they were being studied. All data were pseudo anonymized following the recommended procedures by the Danish Data Protection Agency.

References

1. Mudge AM, O'Rourke P, Denaro CP (2010) Timing and risk factors for functional changes associated with medical hospitalization in older patients. J Gerontol Ser A Biol Sci Med Sci 65A:866–872. https://doi.org/10.1093/gerona/glq069
2. Tanderup A, Lassen AT, Rosholm JU, Ryg J (2018) Disability and morbidity among older patients in the emergency department: a Danish population-based cohort study. BMJ Open. https://doi.org/10.1136/bmjopen-2018-023803
3. Matzen LE, Jepsen DB, Ryg J, Masud T (2012) Functional level at admission is a predictor of survival in older patients admitted to an acute geriatric unit. BMC Geriatr. https://doi.org/10.1186/1471-2318-12-32
4. De Buyser SL, Petrovic M, Taes YE, Toye KRC, Kaufman JM, Goemaere S (2013) Physical function measurements predict mortality in ambulatory older men. Eur J Clin Investig 43:379–386. https://doi.org/10.1111/eci.12056
5. Fried TR, Tinetti ME, Iannone L, O'Leary JR, Towle V, Van Ness PH (2011) Health outcome prioritization as a tool for decision making among older persons with multiple chronic conditions. Arch Intern Med 171:1854–1856. https://doi.org/10.1001/archinternmed.2011.424
6. Ruikes FGH, Zuidema SU, Akkermans RP, Assendelft WJJ, Schers HJ, Koopmans RTCM (2016) Multicomponent program to reduce functional decline in frail elderly people: a cluster controlled trial. J Am Board Fam Med 29:209–217. https://doi.org/10.3122/jabfm.2016.02.150214
7. Gill TM, Baker DI, Gottschalk M, Peduzzi PN, Allore H, Byers A (2002) A program to prevent functional decline in physically frail, elderly persons who live at home. N Engl J Med 347:1068–1074. https://doi.org/10.1056/NEJMoa020423
8. Moeldrupnielsen L (2018) effectiveness of the "elderly Activity Performance Intervention" on elderly patients' discharge from a short-stay unit at the emergency department: a quasi-experimental trial. Clin Interv Aging 13:737–747. https://doi.org/10.2147/CIA.S162623
9. Travers J, Romero-Ortuno R, Bailey J, Cooney M-T (2019) Delaying and reversing frailty: a systematic review of primary care interventions. Br J Gen Pract 69:e61–e69. https://doi.org/10.3399/bjgp18X700241
10. Verweij L, van de Korput E, Daams JG, ter Riet G, Peters RJG, Engelbert RHH et al (2018) Effects of post-acute multidisciplinary rehabilitation including exercise in out-of-hospital settings in the aged: systematic review and meta-analysis. Arch Phys Med Rehabil. https://doi.org/10.1016/j.apmr.2018.05.010
11. Marzetti E, Calvani R, Tosato M, Cesari M, Di Bari M, Cherubini A et al (2017) Physical activity and exercise as countermeasures to physical frailty and sarcopenia. Aging Clin Exp Res 29:35–42. https://doi.org/10.1007/s40520-016-0705-4
12. Ad B, Rees K, Dieppe P, Ayis S, Gooberman-Hill R, Horwood J et al (2008) Complex interventions to improve physical function and maintain independent living in elderly people: a systematic review and meta-analysis. Lancet. https://doi.org/10.1016/S0140-6736(08)60342-6
13. Eklund K, Wilhelmson K (2009) Outcomes of coordinated and integrated interventions targeting frail elderly people: a systematic review of randomised controlled trials. Health Soc Care Community. https://doi.org/10.1111/j.1365-2524.2009.00844.x
14. Low LL-F, Yap M, Brodaty H (2011) A systematic review of different models of home and community care services for older persons. BMC Health Serv Res. https://doi.org/10.1186/1472-6963-11-93
15. Sadler E, Potterton V, Anderson R, Khadjesari Z, Sheehan K, Butt F et al (2019) Service user, carer and provider perspectives

on integrated care for older people with frailty, and factors perceived to facilitate and hinder implementation: a systematic review and narrative synthesis. PLoS One 14:e0216488. https://doi.org/10.1371/journal.pone.0216488
16. Hoogendijk EO (2016) How effective is integrated care for community-dwelling frail older people? The case of the Netherlands. Age Ageing. https://doi.org/10.1093/ageing/afw081
17. Liu CJ, Latham N (2011) Can progressive resistance strength training reduce physical disability in older adults? A meta-analysis study. Disabil Rehabil. https://doi.org/10.3109/09638288.2010.487145
18. Bray NW, Smart RR, Jakobi JM, Jones GR (2016) Exercise prescription to reverse frailty. Appl Physiol Nutr Metab. https://doi.org/10.1139/apnm-2016-0226
19. Hart PD, Buck DJ (2019) The effect of resistance training on health-related quality of life in older adults: systematic review and meta-analysis. Heal Promot Perspect 9:1–12. https://doi.org/10.15171/hpp.2019.01
20. Hurst NP, Kind P, Ruta D, Hunter M, Stubbings A (1997) Measuring health-related quality of life in rheumatoid arthritis: validity, responsiveness and reliability of EuroQol (EQ-5D). Rheumatology. https://doi.org/10.1093/rheumatology/36.5.551
21. Juel K, Sorensen J, Bronnum-Hansen H (2008) Supplement: Risk factors and public health in Denmark. Scand J Public Health. https://doi.org/10.1177/1403494800801101
22. Steffen TM, Hacker TA, Mollinger L (2002) Age- and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go Test, and gait speeds. Phys Ther. https://doi.org/10.1093/ptj/82.2.128
23. Rikli RE, Jones CJ (2013) Development and validation of criterion-referenced clinically relevant fitness standards for maintaining physical independence in later years. Gerontologist. https://doi.org/10.1093/geront/gns071
24. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG et al (1994) A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol. https://doi.org/10.1093/geronj/49.2.M85
25. Zou H, Zhang J, Chen X, Wang Y, Lin W, Lin J et al (2017) Reference equations for the six-minute walk distance in the healthy Chinese Han Population, aged 18–30 years. BMC Pulm Med 17:1–10. https://doi.org/10.1186/s12890-017-0461-z
26. Sørensen J, Gudex C, Davidsen M, Brønnum-Hansen H, Pedersen KM (2009) Danish EQ-5D population norms. Scand J Public Health. https://doi.org/10.1177/1403494809105286
27. Apóstolo J, Cooke R, Bobrowicz-Campos E, Santana S, Marcucci M, Cano A et al (2018) Effectiveness of interventions to prevent pre-frailty and frailty progression in older adults. JBI Database Syst Rev Implement Rep. https://doi.org/10.11124/JBISRIR-2017-003382
28. Walters SJ, Brazier JE (2005) Comparison of the minimally important difference for two health state utility measures: EQ-5D and SF-6D. Qual Life Res. https://doi.org/10.1007/s11136-004-7713-0
29. De Labra C, Guimaraes-Pinheiro C, Maseda A, Lorenzo T, Millán-Calenti JC (2015) Effects of physical exercise interventions in frail older adults: a systematic review of randomized controlled trials physical functioning, physical health and activity. BMC Geriatr. https://doi.org/10.1186/s12877-015-0155-4
30. Lozano-Montoya I, Correa-Pérez A, Abraha I, Soiza RL, Cherubini A, O'Mahony D et al (2017) Nonpharmacological interventions to treat physical frailty and sarcopenia in older patients: a systematic overview—the SENATOR project ONTOP series. Clin Interv Aging. https://doi.org/10.2147/CIA.S132496
31. Dedeyne L, Deschodt M, Verschueren S, Tournoy J, Gielen E (2017) Effects of multi-domain interventions in (pre)frail elderly on frailty, functional, and cognitive status: a systematic review. Clin Interv Aging 12:873–896. https://doi.org/10.2147/CIA.S130794
32. Silva RBB, Aldoradin-Cabeza H, Eslick GDD, Phu S, Duque G (2017) The effect of physical exercise on frail older persons: a systematic review. J Frailty Aging. https://doi.org/10.14283/jfa.2017.7
33. Lopez P, Pinto RS, Radaelli R, Rech A, Grazioli R, Izquierdo M et al (2018) Benefits of resistance training in physically frail elderly: a systematic review. Aging Clin Exp Res. https://doi.org/10.1007/s40520-017-0863-z
34. Brusco NK, Taylor NF, Watts JJ, Shields N (2014) Economic evaluation of adult rehabilitation: a systematic review and meta-analysis of randomized controlled trials in a variety of settings. Arch Phys Med Rehabil 95(94–116):e4. https://doi.org/10.1016/j.apmr.2013.03.017
35. Crapo RO, Casaburi R, Coates AL, Enright PL, MacIntyre NR, McKay RT et al (2002) ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. https://doi.org/10.1164/ajrccm.166.1.at1102
36. Bohannon RW, Crouch R (2017) Minimal clinically important difference for change in 6-minute walk test distance of adults with pathology: a systematic review. J Eval Clin Pract 23:377–381. https://doi.org/10.1111/jep.12629