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Effects of home-based physical exercise on days at home and cost-effectiveness in pre-frail and frail persons – RCT

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Running title: Days at home and cost-effectiveness of exercise

Brief Summary: Twelve-month supervised home-based exercise had no effect on days lived at home vs. usual care in cases of frailty. It prevented decline in quality-of-life. The first years' increased healthcare costs were regained over the next year.

ABSTRACT

Objectives Frailty increases the risks of hospitalization, institutionalization and death. Our objective was to study the effects of home-based physical exercise on the number of days spent at home among pre-frail and frail persons, vs. usual care. In addition, utilization and costs of healthcare and social services, cost-effectiveness and health-related quality-of-life (HRQoL) were explored.

Design: Randomized controlled trial, with yearlong supervised exercise for 60 minutes twice a week vs. usual care. Follow-up for 24 months after randomization.

Setting and participants: A sample of 299 home-dwelling persons in South Karelia, Finland. Main inclusion criteria: ≥65 years, meeting at least one of the frailty phenotype criteria, Mini-Mental State Examination score ≥17.

Methods: Primary outcome, days spent at home over 24 months, was calculated deducting days in inpatient care, in nursing homes, and days after death. HRQoL was assessed (15D questionnaire) at baseline, and at 3, 6 and 12 months. Utilization data were retrieved from medical records.

Results: The participants' mean age was 82.5 (SD 6.3), 75% were women, 61% were pre-frail and 39% frail. After 24 months, there was no difference between groups in days spent at home (incidence rate ratio, IRR 1.03 [95% CI 0.98–1.09]). After 12 months, the costs per person-year were 1.60-fold in the exercise group (95% CI 1.23–1.98), and after 24 months, 1.23-fold (95% CI 0.95–1.50) vs. usual care. Over 12 months, the exercise group gained 0.04 quality-adjusted life-years and maintained the baseline 15D level, while the score in the usual-care group deteriorated (p for group <0.001, time 0.002, interaction 0.004).

Conclusions and implications: Physical exercise did not increase the number of days spent at home. Exercise prevented deterioration of HRQoL, and in the frail subgroup, all intervention

costs were compensated with decreased utilization of other healthcare and social services over 24 months.

INTRODUCTION

Frailty is a medical condition caused by deterioration of the physiological capacity of the organ systems, predisposing a person to stressors such as infections.[1,2,3] Recovery from illnesses is slow, and the person may not recuperate to their previous functional level.[1] Frailty is an extreme consequence of the normal ageing process, being multidimensional and dynamic,[4,5] and is more prevalent in women than in men.[6,7] Physical frailty is defined by frailty phenotype criteria, which include weight loss, weakness, low physical activity, slowness and exhaustion.[8] By meeting three or more of the criteria, a person is considered as frail and by meeting one or two, as pre-frail.[8]

When compared with robust persons, frail persons experience more hospitalizations[9,10,11,12] and longer stays at hospital;[13] they have lower health-related quality-of-life (HRQoL)[14] and a higher risk of mortality.[2,15] Both frailty and pre-frailty states are predictors of nursing home placement.[16] The severity of frailty is associated with greater healthcare and social services costs, as they can be 2.6 times higher for frail persons, and 1.7 times higher for pre-frail persons when compared with robust persons.[17,18]

Treatment of frailty is nonpharmacological, and progressive, individualized multicomponent physical exercise with resistance training is one option.[3] Whether exercise regimens can decrease inpatient hospital stays and postpone nursing-home admission, and whether the period of living at home could thus be lengthened, are open questions when considering frail and pre-frail older adults. Furthermore, there is a scarcity of studies on home-based training,[3] and there is inconsistent evidence on whether or not physical exercise can improve HRQoL among frail and pre-frail older adults[19,20] and whether exercise interventions are cost-effective.

The primary aim of this randomized controlled trial was to study the effects of a 12-month physiotherapist-supervised home-based physical exercise program on the number of days spent at home over 24 months in pre-frail and frail persons, compared with usual care. In addition, the utilization and costs of healthcare and social services over 24 months, and HRQoL over 12 months were assessed. We also calculated quality-adjusted life-years (QALYs) and cost-effectiveness of the intervention by using incremental cost-effectiveness ratio (ICER).

METHODS

Design and settings

The methods and protocol of this randomized controlled trial have been previously presented in detail.[21] Three hundred voluntary participants were recruited between December 2014 and August 2016. Prior to the start of recruitment, the study was registered at ClinicalTrials.gov (NCT02305433), and ethics approval was received in November 2014 from the relevant coordinating ethics committee. All participants signed a written informed consent document.

Participants

To be eligible, a person needed to score at least one point in the FRAIL questionnaire[22] and fulfill at least one of the frailty phenotype criteria.[8] Two of the phenotype criteria were slightly modified.[23] To define "low physical activity" we used 30 minutes per week as a cut-off value. For the slowness criterion, we used a common gait speed cutoff-value of 0.46 m/s for both genders, which was based on the lowest quartile in the Short Physical Performance Battery.[24,25] Participants were classified as pre-frail if they met 1–2 phenotype criteria and frail if they met 3–5. Other eligibility criteria were: age ≥65 years, home-dwelling (with or

without homecare services), able to walk with or without aid when indoors, a Mini-Mental State Examination (MMSE)[26] score of ≥17 and no severe illnesses that prevented them taking part in exercise training. Eligible persons were randomized to physical-exercise (n=150) and usual-care groups (n=150). Randomization was performed after the baseline assessments in consecutive order by using a computer program with varying block sizes, without stratification.

Outcomes

The primary outcome was the number of days spent at home during the 24-month period (730 days), beginning at the date of randomization. The outcome was considered relevant as the national policy in our country is focused on supporting the older people's abilities to live at home, and postponing a possible nursing home placement. Overnight stays in hospital wards, long-term wards, nursing homes, and days after death up to the end of the two-year period were summed up, and defined as days not lived at home. Information was gathered from the medical records of the social and healthcare district, which is responsible for primary and secondary healthcare and social services.

For secondary outcomes, data on the utilization and costs of healthcare and social services were gathered and analyzed over the 24-month period starting from the day of randomization. Business intelligence (BI) analysts, blinded to allocation, retrieved information on used services from the participants' medical records. We also retrieved information from the social-insurance registers, which provided information on the number of used healthcare services in the private sector. Both datasets were merged by our statistician and included in our analyses.

All contacts between the patients and professionals in healthcare and social services, days in inpatient care and nursing homes, and the physiotherapy sessions of our intervention were included in the analyses. Costs were calculated by multiplying the number of service-utilization units by the price of each unit. National mean unit costs in 2011 were used,[27] and the prices were corrected to the 2018 level according the inflation rate based on the cost-of-living index. For our intervention the mean cost of one physiotherapist visit (86.50€) was used and multiplied by the number of completed visits, and included in the rehabilitation costs of the exercise group. Used services and costs are calculated per person-year, and all costs are presented in euros (€).

HRQoL was assessed via the 15D questionnaire[28] at baseline and after three, six and 12 months. 15D has fifteen items, each having five answer options. The questionnaire was sent to the participants prior to the assessor's home visits. Each person completed the questionnaire by themselves or with the help of their relatives. If needed, the research physiotherapist or nurse helped the participant to complete the form. A weighted HRQoL index ranging from one (full health) to zero (death) was calculated.

Cost-effectiveness of the intervention was assessed with incremental cost-effectiveness ratio, based on the 12-month data of total costs (€) of used healthcare and social services and changes in QALYs.

At baseline, background information on marital status, living arrangements, illnesses and medication were gathered by interview and were completed by using electronic medical records.

Intervention

Participants in the physical-exercise group performed physiotherapist-supervised home-based physical exercises for 60 minutes, twice a week over 12 months. Exercises included 10 minutes of warm-up, 30–40 minutes of strength exercises mainly for the lower limbs, and 10 minutes of balance, flexibility and functional exercises combined with other exercises. The physiotherapists tailored the exercises according to the participants' health status and condition. The main strength and balance exercises were based on the exercises of the Otago program.[29,30] Ankle weights, weight vests, dumbbells, kettlebells and elastic bands were used to add resistance. Over the 12 months, exercise periods of power, force and endurance were cycled every eight to 12 weeks.

Therapists used dynamic, static and dual-task exercises, different surfaces at home and various types of equipment to add difficulty to the balance exercises. The goal was to include balance exercises as part of the functional exercises used to aid everyday tasks that a person needs to be able to live independently at home. Flexibility exercises were predominantly targeted at the larger joints to improve range of motion. Physiotherapists also gave counseling on nutrition. The participants could use all healthcare or social services they may have needed over 24 months. The usual-care group continued to live their lives as usual, without restrictions.

Statistical analysis

Concerning power calculations in connection with frail patients, there were no previous data on the duration of living at home. Therefore, we used data on Finnish patients with hip fractures in the PERFECT (PERFormance, Effectiveness and Cost of Treatment episodes) study,[31] in which data are available on the proportion of patients living at home one year after

the fracture. To detect a difference (α=0.05, power=80%) from the hypothesized difference of 180 days between the physical-exercise and usual-care groups, a sample size of 91 persons in each group would be needed. To allow for discontinuation (estimated as 15%) and death (20%) of participants during 24 months, our targeted sample size was 300 participants.

Descriptive statistics are presented as means with SDs or as counts with percentages. The primary outcome (days spent at home), and outpatient and inpatient visits to healthcare and social services were analyzed by using Poisson's model and reported as days and incidence rate ratios (IRRs) with 95% confidence intervals (CIs). Repeated measures in HRQoL between the groups were analyzed by using mixed-effects models, with unstructured covariance structure (Kenward–Roger method to the calculate degrees of freedom). Fixed effects were group, time, and group-time interactions. Cost analyses were performed using a generalized linear regression model with log link and gamma variance functions. The variance function was selected based on the Park test and Akaike's information criterion.

Cost-utility analyses in relation to QALYs were based on areas under the curve of 15D scores from baseline to the last measurement point. All participants who completed the baseline assessment and had at least one other measurement point were included in the analyses of HRQoL and QALYs. All costs were presented per person-year. The cost-effectiveness of home-based physical exercise was compared with usual care by using the incremental cost-effectiveness ratio (ICER). The bootstrapping technique was used in connection with incremental cost-effectiveness planes for costs and QALYs (5,000 replicates). The normality of variables was evaluated graphically and by using the Shapiro–Wilk W-test. Statistical analyses were performed by using the Stata 16.0, StataCorp LP (College Station, TX, USA) statistical package.

RESULTS

Eligibility was tested in 520 persons and recruitment was completed when the targeted 300 persons were reached. After randomization, one person in the usual-care group withdrew his/her consent to participate and declined the use of his/her data. The flowchart is shown in Figure 1. The mean age of the 299 participants was 82.5 years, 75% were female, 39% were frail, 61% were pre-frail, and 58% lived alone. Baseline characteristics are shown in Table 1.

Primary outcome

At 24 months, the primary outcome was analyzed in 299 participants. Over the 24 months (730 days) the mean number of days spent at home was 659 (95% CI 635 to 683) in the exercise group and 638 (95% CI 611 to 665) in the usual-care group (IRR 1.03 [95% CI 0.98 to 1.09], p=0.26). In addition, there was no difference in the days at home between the exercise and usual care groups by the frailty subgroups, for frail IRR 1.04 (0.96 to 1.12) and pre-frail IRR 1.03 (0.96 to 1.11). Eleven persons (7%) in the exercise group and 13 persons (9%) in usual care were permanently placed in nursing homes (p=0.66). In the exercise group 18 persons and in usual care 19 persons died within the 24-month study period; of these five and 10 persons died during the first 12 months, respectively (Figure 1). Sixty-one persons (41%) in the exercise group and 57 persons (38%) in usual care lived at home for the full 730 days without temporary inpatient care.

Secondary outcomes

Data on utilization of healthcare and social services (outpatient visits and inpatient days) and related costs are presented in Table 2. Mean total costs incurred by healthcare and social services per person-year during the first 12 months were 1.60-fold (95% CI 1.23 to 1.98) in

the exercise group (33,839 €) when compared with those in usual care (21,115 €). Over the 24-month period, mean costs per person-year were 1.23-fold (95% CI 0.95 to 1.50) in the exercise group (29,428 €) compared with those in usual care (23,961 €). Over the 24 months, in the exercise frail subgroup the mean costs were 1.02 times (95% CI 0.75 to 1.38) higher [32,507€ (SE 3,625) vs. 31,979€ (SE 3,597)] and in the exercise pre-frail subgroup 1.46 times (95% CI 1.03 to 2.06) higher [27,431 € (SE 3,348) vs. 18,851€ (SE 2,301)] when compared with the corresponding subgroups in the usual care.

We analyzed the effects of the intervention on HRQoL over 12 months, covering 96% (n=144) of the participants in the exercise group and 95% (n=141) of those in usual care. In the usual-care group the mean HRQoL score decreased significantly by 0.037 compared with the exercise group, which maintained the baseline level (p for group <0.001, time p=0.002, interaction p=0.002) (Figure 2). The difference in HRQoL is also seen in the subgroups of frail (p for group 0.002, time p=0.001, interaction p=0.084) and pre-frail (p for group 0.064, time p=0.078, interaction p=0.004) (Figure 2).

When HRQoL was converted to QALYs, the exercise group gained 0.040 QALYs more compared with the usual-care group over the 12 months (mean QALYs 0.723 and 0.683, respectively). In the incremental cost-effectiveness ratio plane, all participants lay in the northeast quadrant, implying that the intervention was more effective but more costly than usual care.

The intervention group completed in total 12,981 physical-exercise sessions and the mean number of sessions per participant was 87, median 96, with range of 3–104. Of the participants 58 % reported exercise-related mild transient muscle soreness, and 71% reported mild joint pain at some point during the year; 17 falls occurred during exercise sessions, with

one fall leading to an injury that needed medical care, and 18 persons took nitroglycerin during or after one exercise session. On five occasions, a participant needed acute medical care because of health problems at the time of the physiotherapist visit.

DISCUSSION

The primary aim of this trial was to explore the effects of a 12-month supervised home-based physical-exercise regimen on the number of days lived at home among pre-frail and frail persons within 24 months. Our intervention did not significantly increase the number of days spent at home compared with usual care.

In previous studies, interventions including exercise training have not decreased the rates of permanent nursing-home placements or acute hospitalizations in community-living frail persons,[32] or hospitalizations in persons living in nursing homes.[33] Frail persons are at a higher risk of nursing-home placement than pre-frail ones, and pre-frail persons are at a higher risk when compared with robust ones.[34] In our trial, a majority of participants were pre-frail (61%), which might reflect the low number of persons transferred to nursing homes. In addition, there was no difference between the groups in the 24-month mortality rate.

Our secondary aim was to study if costs of healthcare and social services can be reduced by way of the physical-exercise regimen. Frailty is associated with higher rates of hospitalization,[35] longer hospital stays[13] and higher healthcare costs[36] and clinical guidelines recommend physical exercise as a treatment option for frailty.[3] Over intervention year the costs per person-year in the exercise group were found to be increased vs. usual care, but the difference decreased over the next 12 months., The total costs over 24 months in the frail subgroup were the same between the exercise and usual-care, but the pre-frail exercise subgroup remained higher vs. usual care. Thus, targeting the intervention to those who are

273 frail seems to be the most cost-beneficial. In another study, an intervention with physical
274 exercise was considered as the most likely cost saving among the very frail[37].

275 Over the 12-month intervention period, those in the exercise group maintained their HRQoL
276 score at the baseline level, whereas the score in the usual-care group deteriorated by 0.037.
277 This deterioration can be considered as considerable and clinically meaningful. Regarding the
278 15D measure, a minimal important change has been proposed to be +/-0.015 and a change
279 of +/-0.035 can be considered large.[38] In healthcare interventions, physical exercise has had
280 an inconclusive effect on HRQoL in pre-frail and frail older adults[20] and HRQoL did not change
281 in previous short-term home-based training studies.[39,40]

282 From the cost-effectiveness point of view, exercise was more effective and more costly within
283 the first 12 months, as the exercise group gained 0.04 QALYs more and the costs were 1.60-
284 fold greater compared with the usual-care group. Our findings are in line with those in the
285 LIFE study, where sedentary older persons who participated in physical activity with a goal of
286 150 minutes per week accrued 0.047 QALYs over 2.6 years compared with the group that
287 received health education.[41] In comparison with our study, not all the participants in the LIFE
288 study[41] were frail at the beginning, as it was not among the inclusion criteria.

289 As a strength of our trial, it had a rigorous randomized design. All 299 participants were
290 followed using register data for 24 months, or until their death. We retrieved data from
291 medical records and were able to identify every contact between a patient and healthcare
292 and homecare professionals, which took place in the services provided by the
293 district. We were also able to retrieve information on visits to private outpatient healthcare
294 services from the social insurance registers, although the number of reimbursed visits was
295 low. As a limitation of our trial, we assessed HRQoL and QALYs only for the first 12 months (as

296 planned). In addition, during our study period (2014–2018), the policies in the district
297 changed: resources were targeted more to services at home such as homecare, and the
298 number of nursing homes was reduced. In 2018, the district had the lowest national
299 percentage of older persons in nursing homes.[42] This development may also have had an
300 impact on the total number of persons assigned to long-term care in our study. A longer
301 follow-up time or including only frail participants might have had more impact on the
302 between-group difference in the days at home. In future trials, finding a way to decrease the
303 costs of the supervised home-based exercise intervention, e.g. with the help of remote
304 technologies, or combining exercise to homecare visits could be beneficial.

305 **CONCLUSIONS AND IMPLICATIONS**

306 Contrary to our hypothesis, the 12 months' physiotherapist-supervised home-based physical
307 exercise in frail and pre-frail persons had no effect on the number of days spent at home. The
308 exercise investment was costly, but the costs were gained back in decreased utilization of
309 healthcare and social services in the exercise frail subgroup over 24 months. Physical exercise
310 had a considerable clinical effect on HRQoL and QALYs when compared with the usual care.

311

312 The authors declare no conflicts of interest.

313

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Figure Legends

Figure 1. Flowchart of the randomized controlled trial; number of participants.

Figure 2. Health-related quality of life (HRQoL) in the physical-exercise group and the usual-care groups, in all participants and in subpopulations of pre-frail and frail over the 12-month intervention period. Means with whiskers representing 95% CI.

437 **Table 1.** Baseline characteristics of participants in the physical-exercise and usual-care groups.

438 Means (SD) or proportions (%).

Characteristics	Physical exercise (n=150)	Usual care (n=149)	p-value
Age, mean (SD)	82.2 (6.3)	82.7 (6.3)	0.44
Women, n (%)	114 (76)	110 (74)	0.67
Body Mass Index (kg/m^2), mean (SD)	28.4 (5.5)	28.6 (6.1)	0.78
MMSE*, mean (SD)	24.2 (3.1)	24.6 (3.2)	0.39
Marital status, n (%)			0.19
Married/in a relationship	56 (37)	62 (42)	
Single/divorced	19 (13)	27 (18)	
Widowed	75 (50)	60 (40)	
Living, n (%)			0.13
Alone	88 (59)	86 (58)	
With spouse	47 (31)	57 (38)	
With another person (other than spouse)	15 (10)	6 (4)	
Home care at least once a week, n (%)	27 (18)	34 (23)	0.30
Education <9 years, n (%)	99 (66)	90 (60)	0.32
Severity of frailty			0.94
Pre-frail, 1-2 of the 5 criteria, n (%)	91 (61)	91 (61)	
Frail, 3-5 of the 5 criteria, n (%)	59 (39)	58 (39)	
Physician-diagnosed diseases or disorders, n (%)			
Cardiovascular diseases†	76 (52)	91 (61)	0.070
Hypertension	110 (73)	110 (74)	0.92
Stroke or TIA‡	37 (25)	33 (22)	0.61
Diabetes	31 (21)	45 (30)	0.059
Musculoskeletal diseases	129 (86)	124 (83)	0.51
COPD§ or asthma	16 (11)	20 (13)	0.46
Dementia	19 (13)	22 (15)	0.60
Number of regular medications, mean (SD)	6.7 (3.2)	7.0 (3.1)	0.43
Health-Related Quality-of-Life, 15D, mean (SD)	0.719 (0.084)	0.705 (0.097)	0.19

439 * Mini-Mental State Examination

440 † includes coronary heart disease, angina pectoris, myocardial infarction, heart failure

441 ‡ Transient Ischemic Attack

442 § Chronic Obstructive Pulmonary Disease

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Table 2. Use of healthcare and social services (outpatient visits to healthcare, inpatient days in hospitals and nursing homes, and home care visits) and their costs (€) per person-year in the physical-exercise and usual-care groups over 0—12 months and 0—24 months.

	Healthcare and social services, visits or days per person-year			Healthcare and social services, costs per person-year		
0—12 months	**Usual care (n=149) Mean (SE)**	**Physical exercise (n=150) Mean (SE)**	**IRR† (95% CI)**	**Usual care (n=149) Mean, € (SE)**	**Physical exercise (n=150) Mean, € (SE)**	**Mean ratio‡ (95% CI)**
Home care, visits	160.5 (24.8)	117.2 (19.3)	0.73 (0.47 to 1.14)	7 187 (1093)	5 269 (866)	0.73 (0.41 to 1.05)
Primary care						
General practitioner, visits	9.57 (0.70)	9.41 (0.74)	0.98 (0.80 to 1.21)	1 234 (114)	1 201 (114)	0.97 (0.72 to 1.23)
Nurse, visits	19.56 (1.60)	17.19 (1.41)	0.88 (0.70 to 1.10)	1 023 (83)	907 (76)	0.89 (0.69 to 1.09)
Rehabilitation*, visits	8.06 (1.09)	91.54 (1.50)	11.35 (8.69 to 14.82)	1 407 (187)	8 153 (145)	5.79 (4.28 to 7.30)
Primary-care ward, days	8.03 (2.74)	6.29 (1.72)	0.78 (0.33 to 1.85)	2 750 (867)	2 468 (708)	0.90 (0.15 to 1.64)
Home healthcare, visits	2.98 (0.50)	2.99 (0.52)	1.00 (0.63 to 1.61)	373 (63)	389 (69)	1.04 (0.54 to 1.54)
Specialized medical care						
Physician, visits	2.50 (0.28)	2.29 (0.28)	0.92 (0.66 to 1.26)	694 (77)	668 (82)	0.96 (0.65 to 1.27)
Nurse, visits	1.30 (0.32)	1.38 (0.34)	1.07 (0.54 to 2.10)	66 (16)	72 (18)	1.11 (0.38 to 1.83)
Emergency department, visits	1.73 (0.23)	1.84 (0.23)	1.06 (0.74 to 1.52)	590 (80)	683 (116)	1.16 (0.66 to 1.65)
Hospital wards, days	3.26 (0.49)	4.57 (0.80)	1.40 (0.89 to 2.21)	3 644 (831)	4 931 (1175)	1.35 (0.48 to 2.22)
Nursing home, days	3.04 (1.15)	5.20 (2.09)	1.71 (0.58 to 5.04)	777 (360)	946 (372)	1.22 (0.24 to 2.67)
Total costs				**21 151 (2 185)**	**33 839 (2 167)**	**1.60 (1.23 to 1.98)**
0—24 months						
Home care, visits	185.2 (27.1)	141.2 (22.6)	0.76 (0.50 to 1.17)	8 268 (1162)	6 475 (1000)	0.78 (0.47 to 1.10)
Primary care						
General practitioner, visits	10.65 (0.68)	9.82 (0.70)	0.92 (0.77 to 1.11)	1 387 (112)	1 289 (113)	0.93 (0.71 to 1.15)
Nurse, visits	20.53 (1.60)	18.32 (1.31)	0.89 (0.72 to 1.10)	1 067 (81)	963 (72)	0.90 (0.71 to 1.09)
Rehabilitation*, visits	7.78 (0.84)	50.34 (1.07)	6.47 (5.21 to 8.04)	1347 (152)	4 847 (155)	3.60 (2.78 to 4.42)
Primary-care ward, days	9.70 (2.60)	6.56 (1.47)	0.68 (0.34 to 1.34)	3 378 (834)	2 880 (712)	0.85 (0.26 to 1.44)
Home healthcare, visits	3.06 (0.41)	3.19 (0.45)	1.04 (0.71 to 1.53)	400 (56)	427 (64)	1.07 (0.64 to 1.49)
Specialized medical care						
Physician, visits	2.40 (0.23)	2.35 (0.25)	0.98 (0.74 to 1.30)	669 (65)	706 (77)	1.06 (0.76 to 1.35)
Nurse, visits	1.37 (0.23)	1.53 (0.32)	1.12 (0.66 to 1.90)	71 (12)	82 (17)	1.16 (0.55 to 1.77)
Emergency department, visits	1.53 (0.18)	1.81 (0.19)	1.18 (0.87 to 1.61)	578 (72)	724 (113)	1.25 (0.76 to 1.75)
Hospital wards, days	3.20 (0.41)	4.22 (0.58)	1.32 (0.91 to 1.91)	3 956 (819)	5 064 (1137)	1.28 (0.53 to 2.03)
Nursing home, days	7.14 (1.99)	6.48 (2.44)	0.91 (0.36 to 2.27)	1 554 (460)	1 240 (431)	0.80 (0.09 to 1.51)
Total costs				**23 961 (2 198)**	**29 428 (2 282)**	**1.23 (0.95 to 1.50)**

*including physiotherapy, occupational therapy, speech therapy and trial intervention (physiotherapist-supervised home-based physical exercise)

†Incidence Rate Ratio, the physical-exercise group over the usual-care group, ‡ mean ratio, the physical-exercise group over the usual-care group

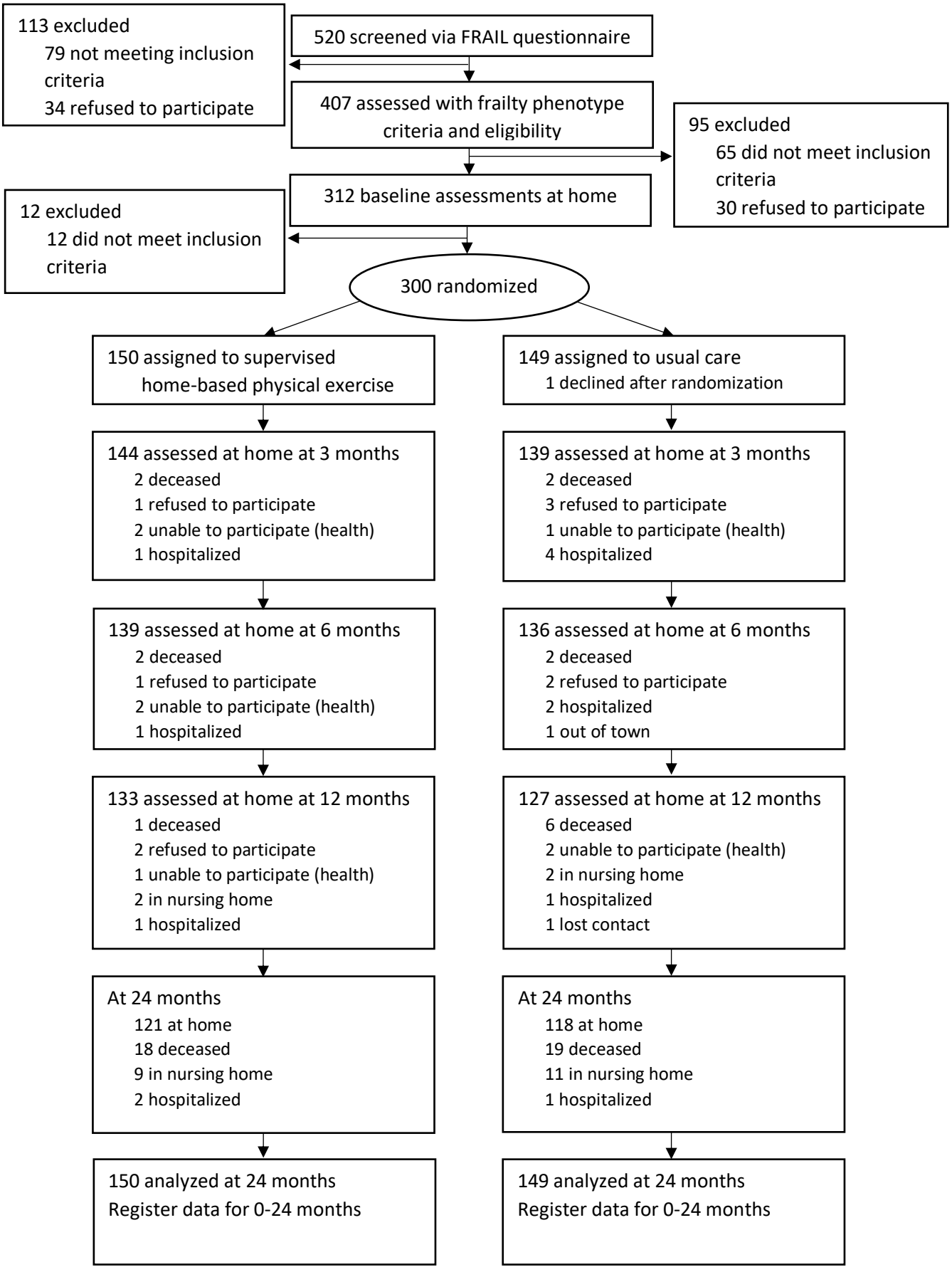

Figure 1. Flowchart of the randomized controlled trial; number of participants.

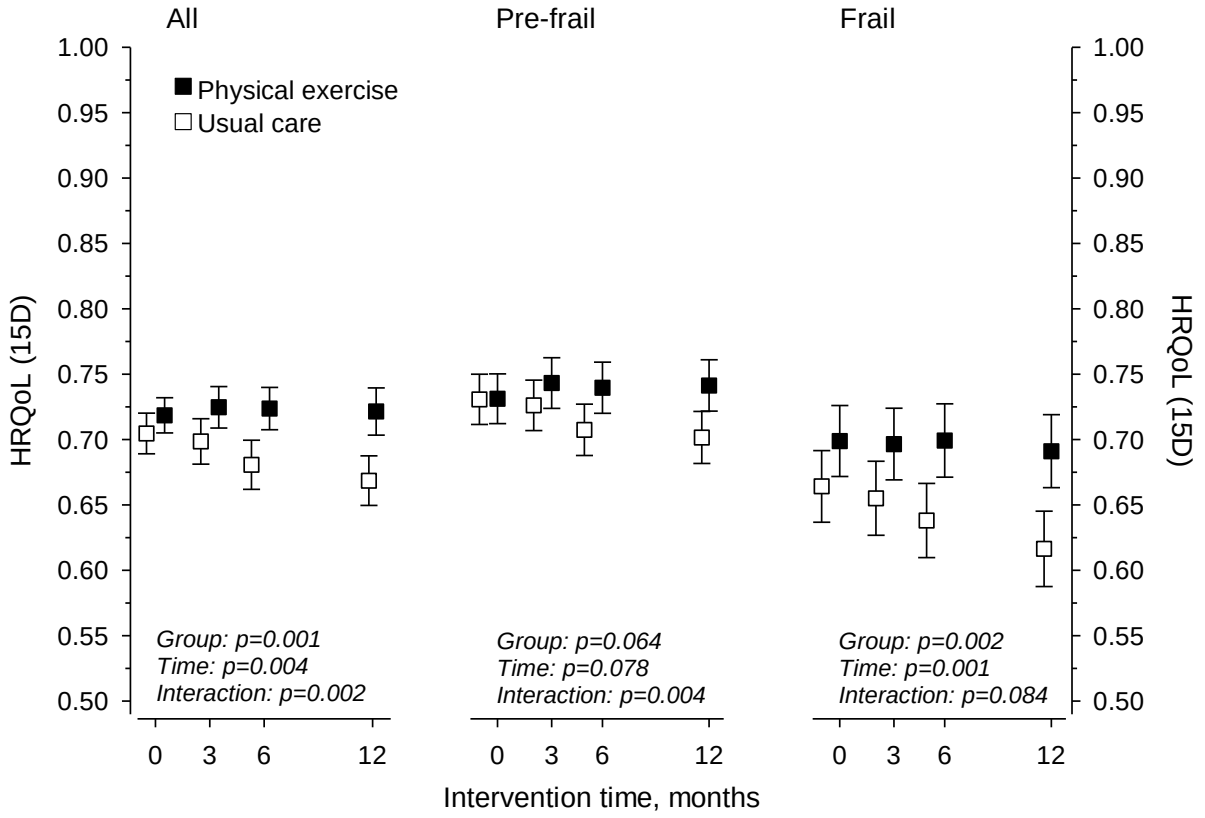

Figure 2. Health-related quality of life (HRQoL) in the physical-exercise group and the usual-care groups, in all participants and in subpopulations of pre-frail and frail over the 12-month intervention period. Means with whiskers representing 95% CI.