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

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

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

41

42 ABSTRACT

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

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

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

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

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

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

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

68

69

70 INTRODUCTION

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

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

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

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

100 **METHODS**

101 **Design and settings**

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

107 **Participants**

108 To be eligible, a person needed to score at least one point in the FRAIL questionnaire²² and
109 fulfill at least one of the frailty phenotype criteria.⁸ Two of the phenotype criteria were slightly
110 modified.²³ To define “low physical activity” we used 30 minutes per week as a cut-off value.
111 For the slowness criterion, we used a common gait speed cutoff-value of 0.46 m/s for both
112 genders, which was based on the lowest quartile in the Short Physical Performance
113 Battery.^{24,25} Participants were classified as pre-frail if they met 1–2 phenotype criteria and
114 frail if they met 3–5. Other eligibility criteria were: age ≥ 65 years, home-dwelling (with or

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

121 **Outcomes**

122 The primary outcome was the number of days spent at home during the 24-month period
123 (730 days), beginning at the date of randomization. The outcome was considered relevant as
124 the national policy in our country is focused on supporting the older people's abilities to live
125 at home, and postponing a possible nursing home placement. Overnight stays in hospital
126 wards, long-term wards, nursing homes, and days after death up to the end of the two-year
127 period were summed up, and defined as days not lived at home. Information was gathered
128 from the medical records of the social and healthcare district, which is responsible for primary
129 and secondary healthcare and social services.

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

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

146 HRQoL was assessed via the 15D questionnaire²⁸ at baseline and after three, six and 12
147 months. 15D has fifteen items, each having five answer options. The questionnaire was sent
148 to the participants prior to the assessor's home visits. Each person completed the
149 questionnaire by themselves or with the help of their relatives. If needed, the research
150 physiotherapist or nurse helped the participant to complete the form. A weighted HRQoL
151 index ranging from one (full health) to zero (death) was calculated.

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

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

158

159 **Intervention**

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

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

177 **Statistical analysis**

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

182 the fracture. To detect a difference ($\alpha=0.05$, power=80%) from the hypothesized difference
183 of 180 days between the physical-exercise and usual-care groups, a sample size of 91 persons
184 in each group would be needed. To allow for discontinuation (estimated as 15%) and death
185 (20%) of participants during 24 months, our targeted sample size was 300 participants.

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

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

205 RESULTS

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

211 Primary outcome

212 At 24 months, the primary outcome was analyzed in 299 participants. Over the 24 months
213 (730 days) the mean number of days spent at home was 659 (95% CI 635 to 683) in the
214 exercise group and 638 (95% CI 611 to 665) in the usual-care group (IRR 1.03 [95% CI 0.98 to
215 1.09], $p=0.26$). In addition, there was no difference in the days at home between the exercise
216 and usual care groups by the frailty subgroups, for frail IRR 1.04 (0.96 to 1.12) and pre-frail
217 IRR 1.03 (0.96 to 1.11). Eleven persons (7%) in the exercise group and 13 persons (9%) in usual
218 care were permanently placed in nursing homes ($p=0.66$). In the exercise group 18 persons
219 and in usual care 19 persons died within the 24-month study period; of these five and 10
220 persons died during the first 12 months, respectively (Figure 1). Sixty-one persons (41%) in
221 the exercise group and 57 persons (38%) in usual care lived at home for the full 730 days
222 without temporary inpatient care.

223 Secondary outcomes

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

227 the exercise group (33,839 €) when compared with those in usual care (21,115 €). Over the
228 24-month period, mean costs per person-year were 1.23-fold (95% CI 0.95 to 1.50) in the
229 exercise group (29,428 €) compared with those in usual care (23,961 €). Over the 24 months,
230 in the exercise frail subgroup the mean costs were 1.02 times (95% CI 0.75 to 1.38) higher
231 [32,507€ (SE 3,625) vs. 31,979€ (SE 3,597)] and in the exercise pre-frail subgroup 1.46 times
232 (95% CI 1.03 to 2.06) higher [27,431 € (SE 3,348) vs. 18,851€ (SE 2,301)] when compared with
233 the corresponding subgroups in the usual care.

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

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

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

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

253 **DISCUSSION**

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

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

265 Our secondary aim was to study if costs of healthcare and social services can be reduced by
266 way of the physical-exercise regimen. Frailty is associated with higher rates of
267 hospitalization,³⁵ longer hospital stays¹³ and higher healthcare costs³⁶ and clinical guidelines
268 recommend physical exercise as a treatment option for frailty.³ Over intervention year the
269 costs per person-year in the exercise group were found to be increased vs. usual care, but the
270 difference decreased over the next 12 months., The total costs over 24 months in the frail
271 subgroup were the same between the exercise and usual-care, but the pre-frail exercise
272 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 frail³⁷.

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 adults²⁰ 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 study⁴¹ 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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429 **Figure Legends**

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

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

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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		
	Usual care (n=149)	Physical exercise (n=150)	IRR [†] (95% CI)	Usual care (n=149)	Physical exercise (n=150)	Mean ratio [‡] (95% CI)
0–12 months	Mean (SE)	Mean (SE)		Mean, € (SE)	Mean, € (SE)	
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

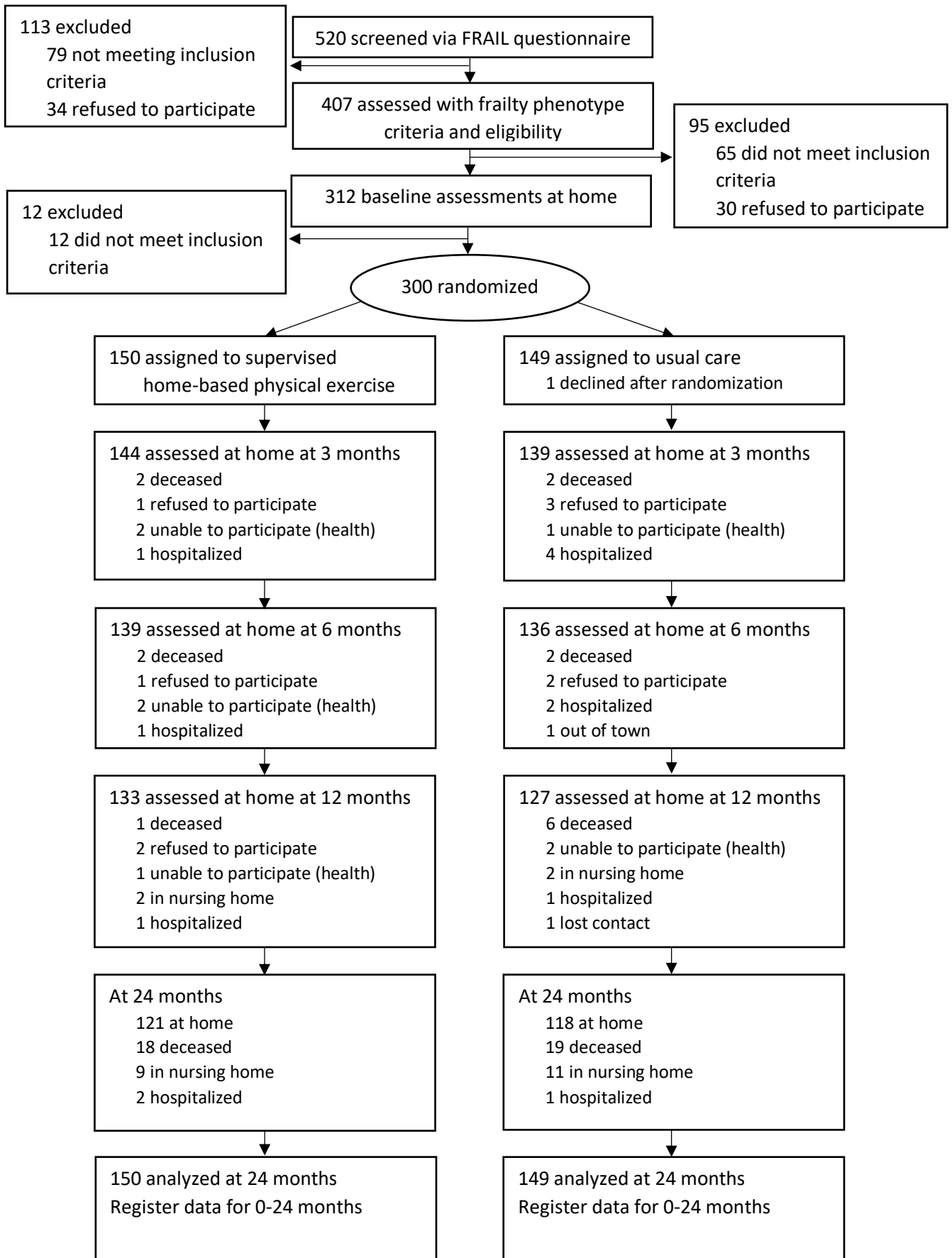


Figure 1. Flowchart of the randomized controlled trial; number of participants.

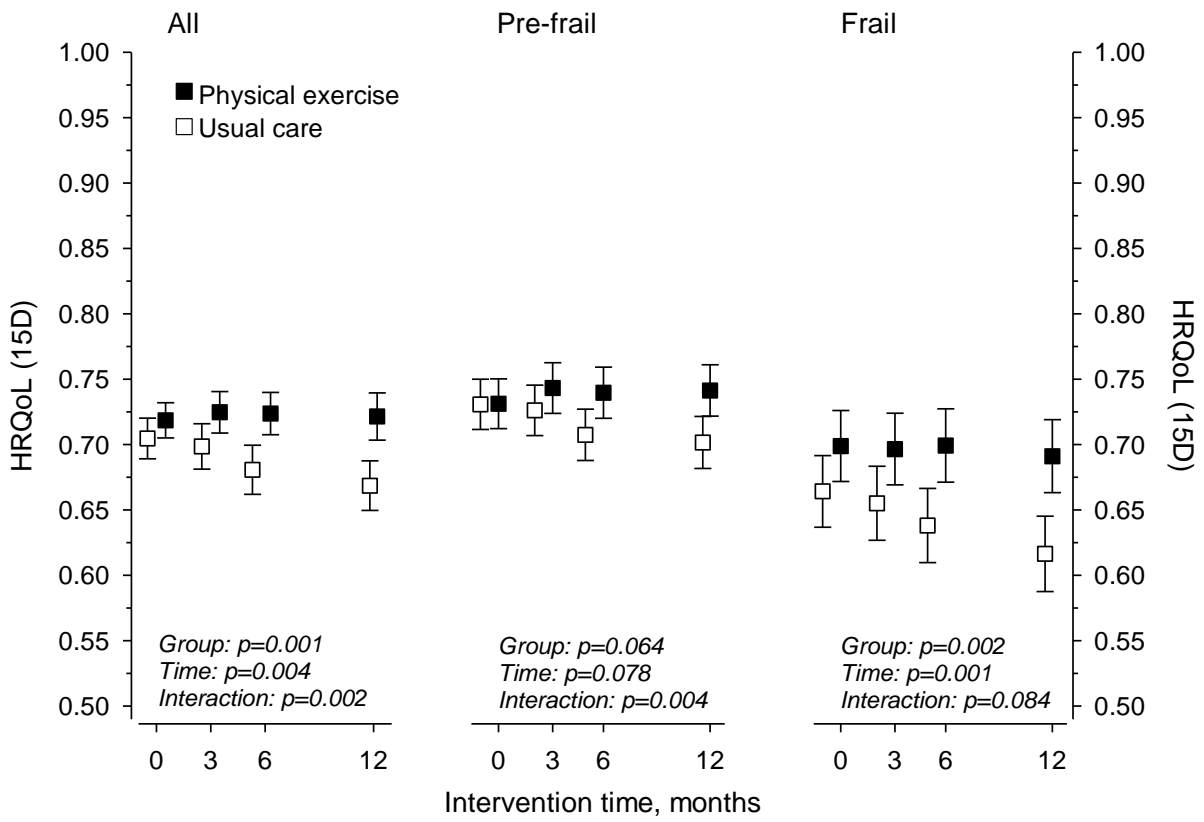


Figure 2. Health-related quality of life (HRQoL) in the physical-exercise group and the usual-care groups, in all participants and in subpopulations of pre-frail and frail over the 12-month intervention period. Means with whiskers representing 95% CI.