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Title: Effect of 12-month supervised, home-based physical exercise on functioning among persons with signs of frailty : Randomized Controlled Trial

Year: 2021

Version: Accepted version (Final draft)

Please cite the original version:

Suikkanen, S., Soukkio, P., Aartolahti, E., Kääriä, S., Kautiainen, H., Hupli, M. T., Pitkälä, K., Sipilä, S., & Kukkonen-Harjula, K. (2021). Effect of 12-month supervised, home-based physical exercise on functioning among persons with signs of frailty : Randomized Controlled Trial. Archives of Physical Medicine and Rehabilitation, 102(12), 2283-2290. https://doi.org/10.1016/j.apmr.2021.06.017

Running head: Physical exercise, functioning & frailty

Title: Effect of 12-month supervised, home-based physical exercise on functioning among persons with signs of frailty – Randomized Controlled Trial

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Acknowledgments

Meeting presentation: Presented as a poster at the International Association of Geriatrics and Gerontology-European Region Congress in Gothenburg, Sweden on May 25, 2019, and in the European Geriatric Medicine Society in Krakow, Poland on September 27, 2019.

Funding: This work was supported by the South Karelia Social and Health Care District (Eksote; register number 1236/00.01.05.01/2013); The Social Insurance Institution of Finland (SII; register number 94/331/2013); and the Finland State Research Funding for Academic Health Research (Ministry of Social Affairs and Health). The funders played no role in the design, collection, analysis, or interpretation of the data, nor in writing the manuscript.

Conflicts of interest disclosure: Authors declare no conflicts of interest

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No preprints available

Trial Registration: ClinicalTrials.gov, NCT02305433

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Additional contributions: We would like to thank Ms. Kaija Paajanen, and Ms. Virpi Äärimaa for their valuable contribution to study recruitment and data collection. We would also like to thank the South Karelia Social and Health Care District´s (Eksote) personnel for their contribution in recruiting participants.

ABSTRACT

Objectives: To investigate the effects of a 12-month home-based exercise program on functioning and falls among persons with signs of frailty.

Design: A randomized controlled trial with a 1:1 allocation

Setting: Home-based

Participants: Home-dwelling persons aged ≥65 years meeting at least one frailty phenotype criteria (n=300).

Intervention: 12-month, individually tailored, progressive and physiotherapist-supervised, physical exercise twice a week (n=150) vs. usual care (n=149).

Main outcome Measures: Functional Independence Measure (FIM), Short Physical Performance Battery (SPPB), handgrip strength, instrumental activities of daily living (IADL), and self-reported falls and physical activity (other than intervention). Assessed four times at home over 12 months.

Results: The mean age of the participants was 82.2 (SD 6.3), 75% were women, 61% met 1–2 frailty criteria and 39% ≥3 criteria. FIM deteriorated in both groups over 12 months, -4.1 points (95% CI: -5.6 to -2.5) in the exercise group and -6.9 (-8.4 to -2.3) in the usual care group (group p=0.014, time p<0.001, interaction p=0.56). The mean improvement in SPPB was significantly greater in the exercise group [1.6 (1.3 to 2.0)] than in the usual care group [0.01 (-0.3 to 0.3)] (group p<0.001, time p=0.11, interaction p=0.027). The exercise group reported significantly fewer falls per person-year compared to the usual care group (incidence rate ratio, IRR 0.47 [95% CI 0.40 to 0.55]; p<0.001). There was no significant difference between the groups over 12 months in terms of handgrip strength, IADL function or self-reported physical activity.

Conclusions: One year of physical exercise improved physical performance and decreased the number of falls among people with signs of frailty. FIM differed between the groups at 12 months, but exercise did not prevent deterioration of FIM, IADL or handgrip strength.

Keywords: physical therapy, physical functional performance, functional status, falls, aging

List of abbreviations: CI Confidence Interval, FDR False Discovery Rate, FIM Functional Independence Measure, FRAIL Fatigue, Resistance, Ambulation, Illnesses, Loss of weight, IADL

92 Instrumental Activities of Daily Living, IQR Inter-Quartile Range, IRR Incidence Rate Ratio, MMSE
93 Mini-mental State Examination, NYHA New York Heart Association, RCT Randomized Controlled
94 Trial, SPPB Short Physical Performance Battery

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Frailty is a syndrome which occurs especially in older adults[1] and is often associated with sarcopenia[2]. People with frailty often suffer from impaired functioning, and diminished muscle strength and endurance[3,4] and frailty increase the risk of disability and falls.[5] Physical frailty can be defined via five phenotypic criteria: weight loss, weakness, slowness, low physical activity, and exhaustion.[6]

Physical exercise is a promising treatment option for frailty.[3,7,8] Group-based exercise training for frail older adults has shown positive effects on physical performance[9,10] and physical activity can postpone harmful consequences[8] such as disabilities, falls and mortality.[3,4,6] The strongest evidence comes from multicomponent training programs with resistance training as the central component, accompanied by aerobic, balance and flexibility exercises.[8,11]

Even though physical exercise is a treatment option for frailty, persons with signs of frailty may think that they lack the capacity to be physically active.[12] The barrier to participate in physical activities may be lowered by providing opportunities to instructed exercise near their own homes.[12] Supervised home-based training might be a valuable option for frail older adults but evidence on its effectiveness is still scarce. Previous home-based exercise trials targeting frail older adults have consisted of interventions of a maximum of six months with limited supervision from professionals and inconclusive results.[13]

The aim of this randomized trial was to investigate the effects of a 12-month physiotherapist-supervised, home-based exercise program on functioning and falls among people with signs of frailty, in comparison with usual care.

METHODS

Study design

This article reports secondary outcomes of our trial which was registered to ClinicalTrials.gov (NCT02305433) prior to recruitment. The study protocol has been published,[14] and the primary outcome, days lived at home, has been reported earlier.[15] In short, we performed a parallel, randomized clinical trial, with a 1:1 allocation ratio. After the baseline assessments, the research personnel randomized participants into two groups, using a computer-generated random sequence allocation program with randomly varying block sizes from 2 to 10, without stratification. A statistician, who had no role in the trial, created the randomization program. One person in the research group used the randomization program and informed the participants of their allocation by phone. The allocation groups were a physiotherapist-supervised physical exercise group (n=150) and a usual care-group (n=150).

Participants

Home-dwelling individuals aged ≥65 years were recruited between December 2014 and August 2016, via advertisements in newspapers and with the help of the home healthcare personnel of

the social and health care district. To be eligible, the individuals needed to pass through a two-phase recruitment process and had to fulfill at least one phenotype criterium of frailty. First, they were evaluated using the FRAIL questionnaire.[16,17] FRAIL has five domains with one point each: Fatigue (feeling tired all the time or most of the time), Resistance (unable to climb 1 flight of stairs), Ambulation (unable to walk 1 block), Illnesses (more than 5), Loss of weight (>5% during the previous years). If a person scored at least one point in FRAIL they advanced to the second phase, where the research nurse checked their eligibility criteria and verified their frailty status using Fried et al.´s phenotype criteria[6] with slight modifications. The criteria used were: weight loss ≥5% during the preceding year[6], physical activity under 30 minutes/week[18], a feeling of "not getting going" or "everything is an effort" for most or all of the time[6], handgrip strength under cut-off values based on BMI and gender[6], and walking speed under 0.46 m/s (walking length either 4 or 2.44 m)[19].

Other eligibility criteria were residing at home, ability to walk indoors with or without mobility aids, scoring ≥17 in Mini-Mental State Examination (MMSE) test,[20] and the ability to communicate in Finnish. Individuals were excluded if they were living in an institutional care facility or nursing home, or had alcohol or drug abuse problems, severe problems with hearing or eyesight, terminal illnesses (e.g., cancers), or other severe illnesses (e.g., a cardiovascular disease with New York Heart Association Functional Classification class III or IV, severe pulmonary disease or a stroke) that was contraindication to physical exercise. The study received ethics approval on November 12, 2014 from the Coordinating Ethics Committee and was conducted in accordance with the standards of the Helsinki declaration. All the participants were volunteers and signed a written informed consent document prior to the baseline assessments.

Outcomes

Here we report the secondary outcomes of our trial. A research physiotherapist/nurse, not blinded to the allocation, performed assessments at the participant's home using interviews, questionnaires, and measurements at baseline, and at three, six, and twelve months. If necessary, details of demographic characteristics and illnesses were complemented with electronic medical records of the social and health care district. The assessors did not participate in the implementation of the intervention.

Functioning was assessed using several measurements. The Functional Independence Measure (FIM)[21] evaluates the participant's ability to perform 13 motor and five cognition tasks and was performed via an interview. Each task was graded on a scale of seven (fully independent) to one (needs assistance from two people). Maximum points were 126; 91 for motor and 35 for cognition. Instrumental activities of daily living (IADL) were assessed via Lawton´s eight-item questionnaire,[22] using polytomous item scoring (1–3, 1–4 or 1–5) with higher scores indicating better functioning and an item sum ranging from 8–31.[23] Physical performance was assessed using the Short Physical Performance Battery (SPPB),[19] which has three parts (balance, walking and the chair rise test) and a maximum summary score of 12 points. Handgrip strength was measured in seated position, three times from both hands using a handheld dynamometer[a], the elbow unsupported in a 90-degree angle, placed next to the body, and the wrist in a neutral position.[24] The mean of the best values of both hands was used in the analyses to eliminate possible joint conditions in one hand that would hinder the maximal performance. Frequency of physical activity (intervention physical exercise not included) was assessed by two structured questions[25] during

the interviews: 1) How often did you have a walk outdoors at least 30 minutes at a time in the previous month, and 2) how often did you perform physical activities other than walking at least 30 minutes at a time in the previous month. Physical activity was reported as weekly sessions, which was calculated by summing up the number of sessions from both questions.

Falls were queried during the assessment visits as participants reported the number of all falls during the previous three or six months.

Physical exercise intervention

The 12-month exercise program comprised physiotherapist-supervised, one-hour sessions twice a week at the participant's home. The research group trained the physiotherapists to conduct a structured, periodical, progressive, and multicomponent physical exercise program, which included strength, balance, mobility, and functional exercises (Table 1).[14] The physiotherapists modified the sessions to suit the participants' current health status. The physiotherapists were instructed to periodically perform multiple-repetition maximum-tests for lower extremities with ankle weights (0.5 to 10 kg) to ensure progression and define suitable training resistance. At the end of each session, its intensity was evaluated with Borg's Ratings of Perceived Exertion (RPE) scale[26], with the targeted range from moderate (12) to vigorous (17), and the intensity of the following session was modified accordingly. The physiotherapist also gave brief counseling on nutrition and encouraged the participant to be physically active outside the supervised exercise sessions as well. The physiotherapists reported contents of all the exercise sessions and adverse

effects monthly. In addition, the participants could receive any social and health care (including rehabilitation) services they needed during the trial.

Usual care

In the usual care group, the participants continued to live their lives “as usual”. They received any health care or social services they needed during the study period, including home care and rehabilitation delivered according to the social and health care district’s normal policies.

Statistical analysis

The sample sizes were calculated in proportion to the primary outcome, which was number of days living at home over 24 months. In brief, to detect a difference (α (significance level) 0.05, β (power) 80%) of the hypothesized 180 (SD 431) days between the physical exercise and usual care groups, a sample size of 91 persons in each group would have been needed (simulation-based effect size was 0.40). To allow for discontinuation (estimated as 15%) and death (20%) of participants, our targeted sample size was 300 participants. More detailed description of power calculations is reported elsewhere.[14,15]

All analyses were performed based on the intention-to-treat principle. The characteristics of the participants are reported as means with standard deviations (SD), as medians with inter-quartile

ranges (IQR) or as counts with percentages. Repeated measurements taken at different assessment points, were analyzed using mixed-effects models with an unstructured covariance structure (Kenward-Roger method to calculate the degrees of freedom). The fixed effects were group, time, and group-time interaction. Mixed models allowed analyses of unbalanced datasets without imputation; therefore, all available data were analyzed with the full analysis set. The Benjamin-Hochberg step-up FDR[27] (false discovery rate) was applied to correct the levels of significance for multiple testing in the single FIM items. Poisson regression was used to calculate the incidence rate ratio (IRR) for falls. The Poisson regression model was tested using the goodness-of-fit test of the model, and the assumptions of over dispersion in the Poisson model were tested using the Lagrange multiplier test, and over dispersion was not detected. Normal distributions were evaluated graphically and using the Shapiro–Wilk W test. Stata 16.1[b] was used for the analyses.

RESULTS

At baseline, the mean age was 82.2 (SD 6.3) years in the exercise group and 82.7 (SD 6.3) in the usual care group. Most of the participants were female (75%), and 61% met 1–2 frailty criteria and 39% three or more, 80% of the participants used walking aid (Table 2). Soon after randomization, one participant withdrew and refused use of their data, decreasing the number of participants in the usual care group to 149. One hundred thirty-three participants in the exercise and 127 in the usual care group participated in the assessments at 12 months (Figure 1).

In the exercise group, attendance of the home-based exercise sessions ranged from three to 104 with a median of 96 (IQR 87 to 99). Participation rate over 75% was achieved by 128 participants (85%). The median of other rehabilitation sessions (e.g., physiotherapy, occupational therapy) received from the social and health care district during the intervention year was 0 (IQR 0 to 2) in the exercise group and 1 (0 to 8) in the usual care group.

In both groups, the mean FIM score deteriorated over the 12 months (group p=0.014, time p<0.001, interaction p=0.56; Figure 2). Overall, in the exercise group, the mean FIM score changed by -4.1 points (95% CI: -5.6 to -2.5) and in the usual care group by -6.9 points (-8.4 to -2.3). When compared with the 12-month change in single FIM motor items (Figure 3), the exercise group performed better in transferring to the bath/shower (p=0.037) and walking on stairs (p=0.036) than the usual care group, after correcting the levels of significance for multiple testing.

In IADL the baseline mean scores were 23 (SD 5) in the exercise and 23 (6) in the usual care group. Over 12 months IADL functions deteriorated in both groups, the mean change was -1.4 points (95% CI: -1.9 to -0.9) in the exercise and -2.1 (-2.6 to -1.6) in the usual care group (group p=0.095, time p<0.001, interaction p=0.92).

In the SPPB, the mean improvement over 12 months was 1.6 (95% CI: 1.3 to 2.0) points in the exercise group, and 0.01 (-0.3 to 0.3) points, in the usual care group (p<0.001) (Figure 2). The mean change in handgrip strength was -0.5 kg (-1.0 to 0.1) in the exercise group and -1.2 kg (-1.7 to -0.6) in the usual care (group p=0.26, time p<0.001, interaction p=0.29).

At baseline, the participants in the exercise group reported on average 2.2 (95% CI: 1.8 to 2.7) and in the usual care group 2.2 (1.8 to 2.6) weekly physical activity sessions lasting for at least 30 minutes at a time. At six months, the exercise group had increased the number of weekly sessions to 3.3 (2.7 to 4.0) and the usual care group to 2.7 (2.2 to 3.2). At 12 months, the number of weekly sessions declined close to baseline level, to 2.5 (1.9 to 3.0) and 2.1 (1.7 to 2.5), respectively (group $p=0.26$, time $p<0.001$, interaction $p=0.32$) (Figure 2).

During the intervention year, the participants in the exercise group had 1.4 (95% CI: 1.2 to 1.6) and in the usual care group 3.1 (2.8 to 3.4) falls per person-year. The difference between the groups was significant (IRR 0.47 (95% CI: 0.40 to 0.55; $p<0.001$).

DISCUSSION

Persons with signs of frailty who participated in a yearlong home-based physical exercise program improved their SPPB more, and they experienced fewer falls than those who received usual care. In both groups, FIM declined over 12 months. However, at 12 months, the physical exercise group had a significantly better FIM score than the usual care group, whereas there was no difference between the groups in handgrip strength or IADL functions. The frequency of self-reported physical activity sessions during leisure time increased in both groups until six months but reverted to baseline level at 12 months, with no significant difference between the groups.

Over 12 months, all motor and cognitive components of FIM deteriorated in both of our groups. The FIM evaluates a person's need for care in everyday tasks and has mainly been used in inpatient rehabilitation.[21] We assessed FIM by an interview at the person´s home. Only a few other studies have used FIM in outpatient settings among older adults. In two Finnish studies, FIM was used to measure the change over 12 months among older people at risk of institutionalization, (AGE study),[28] and people with Alzheimer´s disease, (FINALEX study).[29] In both studies, FIM deteriorated in the intervention and usual care groups, like in our study, and among the people in the intervention groups, deterioration was slower. The AGE[28] and FINALEX[29] participants were on average a few years younger than those in our sample, and the FINALEX study used a home-based intervention[29] similar to ours. Some of our participants might have been unable to improve their FIM scores because of the aids they used at home (e.g., dentures, walking aids, shower handles, raised beds, use of a banister) and which they were unwilling or unable to discard.

Because SPPB predicts nursing home admissions[19] and all-cause mortality,[30] and is a fast and easy way to measure physical performance, it is widely used in clinical practices. In our trial, SPPB improved in the exercise group by 1.6 points over 12 months, which can be considered clinically important. In previous studies a substantially clinical meaningful change in SPPB has been estimated to range from 0.4 to 1.5 points,[31] and from 0.5 to 1.3 points.[32] In community-living older adults with frailty, group-based supervised exercise training of 24 weeks improved their SPPB score by 0.9 points, whereas that of the usual care group deteriorated by 1.5 points.[10] In all these studies[10,31-33] the participants had better baseline SPPB scores than ours. Among frail nursing home residents[34] with a similar SPPB baseline level to ours, a six-month progressive

multicomponent group-based exercise intervention improved the mean SPPB score by 1.8 points, whereas the mean score in the control group declined by 0.9 points.

Another important gain was the smaller number of falls in our exercise group than in the usual care group. We based our intervention on the exercises from the OTAGO exercise program, which effectively reduced the number of falls among community-dwelling older adults.[35] An Italian cross-sectional study on older outpatients in a geriatric clinic[36] found an association between lower SPPB scores and history of falls. In our trial, no severe complications occurred; only one injurious fall during exercise session needed medical care.

Our physical exercise intervention included brief counselling on physical activity as physiotherapists encouraged the participants to be active outside the supervised sessions. Even though the usual care group received no counseling, both groups increased their number of physical activity sessions per week in the first half of the trial. However, both groups decreased back to baseline level in the later half.

Training with the physiotherapists at home enabled people also in rural areas to participate in our study. Adherence to home-based programs has been better than in center-based programs,[37] as older adults prefer activities close to home.[12] Furthermore, the effects of supervised home-based training on strength and functional ability have been greater,[38,39] and the intensity of the sessions can be higher[40] than in training without supervision. In our trial, supervision meant higher intervention expenses, but in the subgroup of frail participants, there was a decrease in total costs of social and health care services over 24 months compared to the frail participants in the usual care.[15]

As a strength, our study was a rigorously performed RCT with good compliance. Furthermore, our sample was identified as frail or pre-frail at baseline[41] based on two validated frailty assessments.[6,16] We also used validated measurements to assess functioning and physical performance, and the proportion of missing measurements during the intervention year was very low (13% at 12 months).

Study limitations

Falls and physical activity were self-reported, which is more unreliable than diaries[42] and objective measurements.[43] Our validated questions[24] included only frequencies of physical activities lasting over 30 minutes but neither intensity nor exact duration. Therefore, our findings regarding falls and physical activity are only indicative and need to be interpreted with caution. In addition, the assessors were not blinded to the allocation status of the participants.

CONCLUSION

In conclusion, among people with signs of frailty, 12-month supervised, home-based exercise improved SPPB and decreased the number of falls. At 12 months, the physical exercise group had a better FIM than the usual care group, but there was no difference in IADL or handgrip strength between the groups. Supervised exercise did not enhance physical activity during leisure time.

SUPPLIERS

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510 **Figures and tables**

511

512

513 **Figure 1**. Flowchart of participants in randomized clinical trial. Numbers of participants.

514

515 **Figure 2.** Mean changes in Functional Independence Measure (FIM) (A), and in Short Physical
516 Performance Battery (SPPB) (B), and mean weekly frequency of physical activity sessions (C) in
517 physical exercise and usual care groups over 12 months. Whiskers denote 95% confidence
518 intervals.

519

520 **Figure 3.** Mean changes in FIM items in the physical exercise and usual care groups from 0 to 12
521 months. Whiskers denote 95% confidence intervals. Benjamin-Hochberg step-up false discovery
522 rate was applied to correct levels of significance for multiple testing in single FIM items.

523

524 **Table 1.** Contents of one 60-minute physical exercise session, supervised by physiotherapist.

525

526 **Table 2.** Baseline characteristics of participants in physical exercise and usual care groups. Means
527 (SD) and frequencies (%).

Table 1. Contents of one 60-minute physical exercise session, supervised by a physiotherapist.

	Warm-up exercises	Resistance training	Balance training	Flexibility training	Functional exercises	Counseling
Duration	5–10 minutes	30–40 minutes	5–10 minutes	5–10 minutes	5–10 minutes	Individual
Main exercises	Walking, chair exercises, stationary cycling	Focus on lower limbs, main exercises based on Otago program.[44] Exercises included e.g., knee extension, knee flexion, hip abduction, calf raises, toe raises. Upper limbs: no specific movements assigned.	Static, dynamic, and dual task exercises based on Otago program[44], e.g., tandem stand, squats, walking in various directions.	Stretching, reaching	Tasks of IADL* such as climbing stairs, washing dishes, handling laundry, piling firewood, walking outside, grocery shopping	Nutrition: energy intake, protein intake, meal pattern, fluid intake Physical activity counseling and encouragement
Intensity	Low to moderate	Moderate to vigorous	Moderate	Low	Moderate to vigorous	Individual
RPE † [26]	10–12	12–17	12–14	10–11	12–17	
Progression	Longer distance or more challenging terrain, or e.g., higher resistance in the stationary cycle	Increasing the number of sets, repetitions, and resistance with ankle weights to match the targeted RPE and the phase of the training cycle: 1st mo.‡ getting used to exercises; 2nd to 3rd mo. strength (sets 2–5, reps§. 8–12, 60-80% of maximum muscle strength according to multiple RM-test[45]); 4th to 6th mo. power (sets 3–5, reps 4–10, 20-60%); 7th to 9th mo. endurance (sets 2-3, reps. 12-30, 20-60%); 10th to 12th mo. strength/power.	More challenging surfaces and tasks to challenge the participant's balance. Starting from static exercises, progressing to dynamic and dual-task exercises	Larger range of motion	Advancing to more challenging tasks and combined with strength and balance training	From broad and general to the more specific
Accessories	Walking aid (if needed), fitness equipment e.g., stationary bike	Resistance with ankle weights from 0.5 kg to 10 kg, dumbbells, kettlebells, rubber bands	Balance pads, different types of floor surfaces, outdoor environment	Stick	Natural home environment	Pamphlets and booklets
Goal	To warm-up and prepare the body before other exercises	To increase the strength of lower limbs and to enhance physical performance	To challenge individual balance abilities, to prevent falls	To enlarge the range of motion in large joints to maintain ADL‖	To support individual abilities to live independently at home	To provide knowledge and motivate to follow nutrition and exercise guidelines

*IADL, Activities of Daily Living; † RPE, Ratings of Perceived Exertion[26]; ‡ mo., month(s); § reps., repetitions; ‖ ADL, Activities of Daily Living

530 **Table 2.** Baseline characteristics of participants in physical exercise and usual care groups. Means
531 (SD) and frequencies (%).

Characteristic	Physical exercise (n=150)		Usual care (n=149)	
Age (years), mean (SD)	82.2	(6.3)	82.7	(6.3)
Women, n (%)	114	(76)	110	(74)
Number of frailty criteria [a], n (%)				
1	44	(29)	48	(32)
2	48	(32)	44	(30)
3	40	(27)	42	(28)
4	13	(9)	13	(9)
5	5	(3)	2	(1)
Mini-Mental State Examination (MMSE)[b], mean (SD)	24.2	(3.1)	24.6	(3.2)
Functional Independence Measure (FIM)[c], mean (SD)	109	(10)	109	(11)
Instrumental Activities of Daily Living (IADL)[d], mean (SD)	23	(5)	23	(6)
Short Physical Performance Battery (SPPB)[e], mean (SD)	6.1	(2.7)	6.3	(2.5)
Handgrip strength[f] (kg), mean (SD)	18.9	(7.8)	19.7	(7.8)
Living alone, n (%)	88	(59)	86	(58)
Walking aids, n (%)	122	(81)	117	(79)
Number of regular medications, mean (SD)	6.7	(3.2)	7.0	(3.1)

532 Note. [a] According to modified Fried et al.'s[4] phenotype criteria; [b] Points range from 0 to 30, a higher value indicating
533 better cognition; [c] Points range from 18 to 126, a higher score indicating better functional independence; [d] Reported
534 as an item sum, (points range from 8 to 31); a higher score indicates better functioning; [e] Scores range from 0 to 12, a
535 higher score indicates better performance; [f] Mean of best values of both hands.

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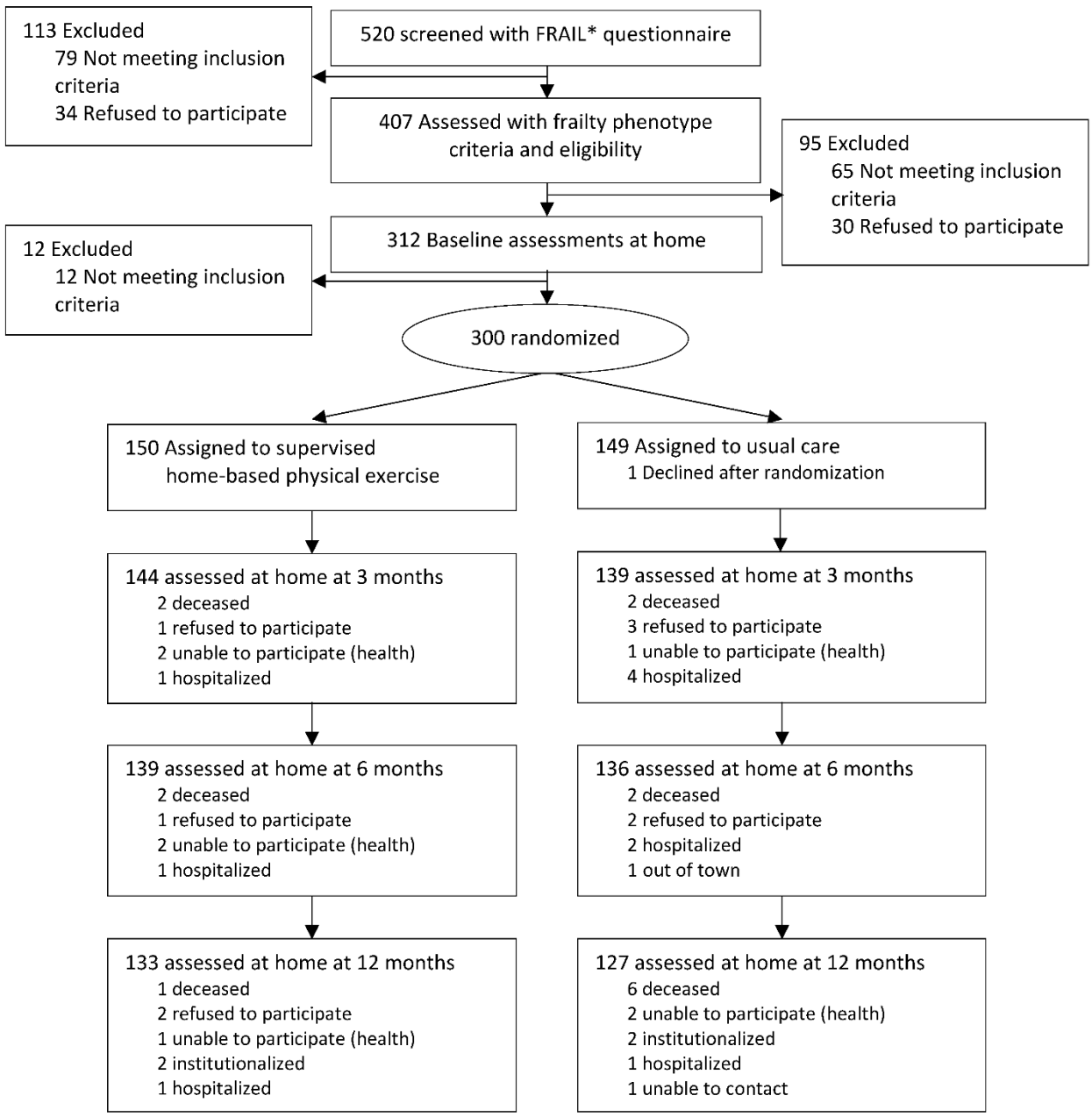
537

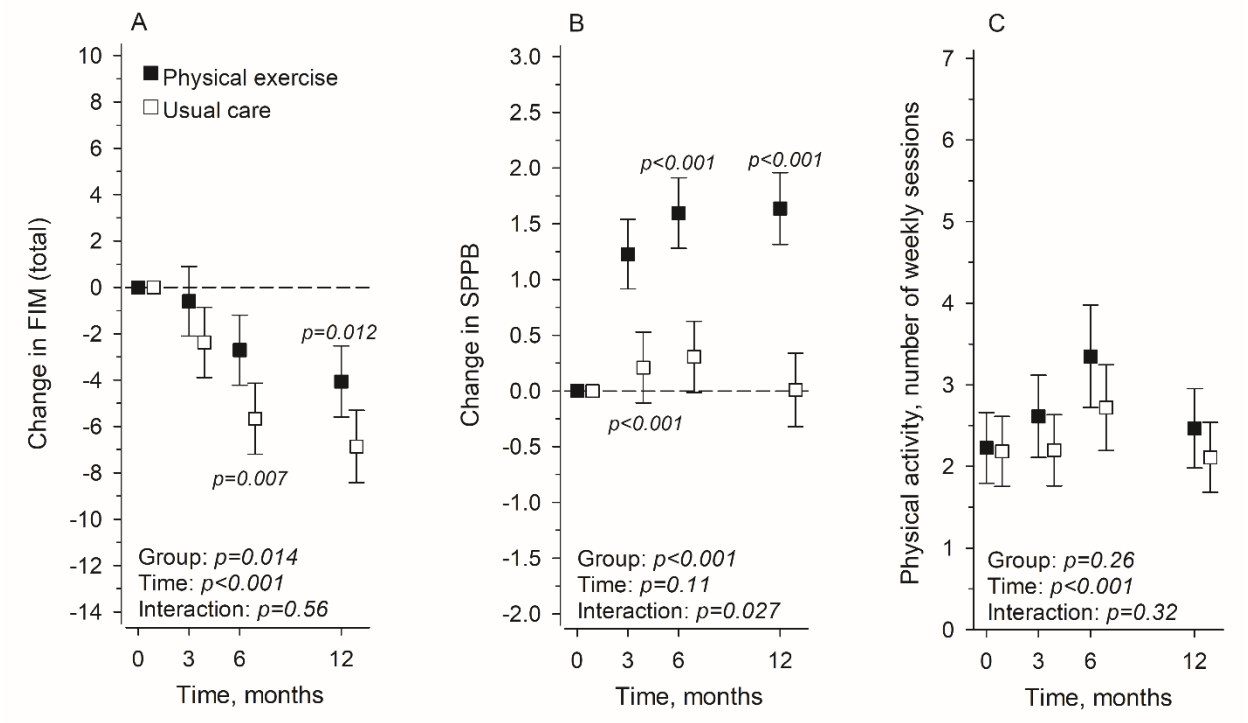
538 **Figure 1**. Flowchart of participants in randomized clinical trial. Numbers of participants.



* FRAIL Fatigue, Resistance, Ambulation, Illnesses, Loss of weight

539

Figure 2. Mean changes in Functional Independence Measure (FIM) (A), and in Short Physical Performance Battery (SPPB) (B), and mean weekly frequency of physical activity sessions (C) in physical exercise and usual care groups over 12 months. Whiskers denote 95% confidence intervals.



546 **Figure 3.** Mean changes in FIM items in the physical exercise and usual care groups from 0 to 12
547 months. Whiskers denote 95% confidence intervals. Benjamin-Hochberg step-up false discovery
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