# High-intensity functional exercise program and protein-enriched energy supplement for older persons dependent in activities of daily living: A randomised controlled trial

**Erik Rosendahl[1], Nina Lindelöf[1,2], Håkan Littbrand[1], Elinor Yifter-Lindgren[1], Lillemor Lundin-Olsson[1], Lena Håglin[1], Yngve Gustafson[1] and Lars Nyberg[2]**

[1]*Department of Community Medicine and Rehabilitation, Geriatric Medicine and Physiotherapy, Umeå University, Umeå* [2]*Department of Health Sciences, Physiotherapy Unit, Luleå University of Technology, Boden*
*Sweden*

The aims of this randomised controlled trial were to determine if a high-intensity functional exercise program improves balance, gait ability, and lower-limb strength in older persons dependent in activities of daily living and if an intake of protein-enriched energy supplement immediately after the exercises increases the effects of the training. One hundred and ninety-one older persons dependent in activities of daily living, living in residential care facilities, and with a Mini-Mental State Examination (MMSE) score of ≥ 10 participated. They were randomised to a high-intensity functional exercise program or a control activity, which included 29 sessions over 3 months, as well as to protein-enriched energy supplement or placebo. Berg Balance Scale, self-paced and maximum gait speed, and one-repetition maximum in lower-limb strength were followed-up at three and six months and analysed by 2 × 2 factorial ANCOVA, using the intention-to-treat principle. At three months, the exercise group had improved significantly in self-paced gait speed compared with the control group (mean difference 0.04 m/s, $p = 0.02$). At six months, there were significant improvements favouring the exercise group for Berg Balance Scale (1.9 points, $p = 0.05$), self-paced gait speed (0.05 m/s, $p = 0.009$), and lower-limb strength (10.8 kg, $p = 0.03$). No interaction effects were seen between the exercise and nutrition interventions. In conclusion, a high-intensity functional exercise program has positive long-term effects in balance, gait ability, and lower-limb strength for older persons dependent in activities of daily living. An intake of protein-enriched energy supplement immediately after the exercises does not appear to increase the effects of the training. **[Rosendahl E, Lindelöf N, Littbrand H, Yifter-Lindgren E, Lundin-Olsson L, Håglin L, Gustafson Y and Nyberg L (2006): High-intensity functional exercise program and protein-enriched energy supplement for older persons dependent in activities of daily living: A randomised controlled trial. *Australian Journal of Physiotherapy* 52: 105–113]**

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## Introduction

Impairments in balance, mobility, and lower-limb strength are common in the growing population of older individuals and can lead to dramatic consequences such as dependency in activities of daily living, nursing home admission, falls, and fractures (Guralnik et al 1994 and 1995, Myers et al 1996, Tinetti 2003). To improve these physical functions, high-intensity exercise programs, ie training near the individual's maximum capacity, are effective for healthy or moderately impaired older persons (Fiatarone et al 1994, Hauer et al 2001, Latham et al 2004, Lazowski et al 1999, Seynnes et al 2004). To our knowledge, there are only two studies that have used such a program among older persons with severe cognitive and physical impairments (Jensen et al 2004, Morris et al 1999). In one of these studies, exercise was only one aspect of a multi-factorial falls prevention program (Jensen et al 2004). Therefore, knowledge concerning the effect of high-intensity exercise programs is very limited for this group of older persons with multiple diseases.

Functional weight-bearing exercising is a training method which, among healthy or moderately impaired older persons, has wide-ranging effects on physical functions (Bean et al 2002, Lindelöf et al 2002, Rooks et al 1997, Sherrington et al 2003). The training method also seems suitable for frail older persons in residential care facilities, including those with severe cognitive impairment, because the exercises are easy to follow and there is no need for special exercise facilities. In addition, there is the possibility of achieving a high intensity for each individual.

Strength training stimulates muscle protein synthesis, which is required for muscle hypertrophy, and an intake of protein after exercising has a synergistic effect (Dorrens and Rennie 2003, Tipton et al 1999). However, the increase of protein synthesis after strength training decreases with time (Phillips et al 1997). Therefore, an intake of protein immediately after training seems indicated as shown in a study among healthy older men where an immediate intake of 10 g protein after strength training had an effect on muscle hypertrophy and strength (Esmarck et al 2001). Among frail older persons, combinations of strength training and protein-energy supplement have not shown any interaction effects on physical function (Bonnefoy et al 2003, Fiatarone et al 1994). In these studies, however, the supplement was not taken in direct connection to the exercise. Therefore, the effect of an immediate intake of protein after strength training among frail older persons is still unknown.

We hypothesised that a high-intensity functional exercise program would improve balance, gait ability, and lower-limb strength in the short- and long-term in older persons dependent in activities of daily living and living in residential care facilities. We also hypothesised that an intake of protein-enriched energy supplement immediately after the exercises would increase the effect of the training.

# Method

**Setting** The Frail Older People—Activity and Nutrition Study in Umeå (the FOPANU Study) was performed at nine residential care facilities in Umeå, Sweden. All facilities comprised private flats with access to dining facilities, alarms, and on-site nursing and care. Four facilities also comprised units, with private rooms and staff on hand, for persons with dementia.

**Participants** Inclusion criteria were: age 65 or over, dependent on assistance from a person in one or more personal activities of daily living according to the Katz Index (Katz et al 1963), able to stand up from a chair with armrests with help from no more than one person, a Mini-Mental State Examination (MMSE) (Folstein et al 1975) score of 10 or more, and approval from the resident's physician.

All residents (n = 487) were screened by trained physiotherapists. The residents responding to the inclusion criteria, or their relatives when appropriate due to cognitive impairment, gave their informed oral consent. Finally 191 persons, aged 65–100 years, were included in the study (Figure 1). Age ($p = 0.84$), sex ($p = 0.64$), and Katz ADL Index score ($p = 0.66$) did not differ between those included and those who declined participation. The study was approved by the Ethics Committee of the Medical Faculty of Umeå University.

**Study design** This was a stratified cluster-randomised controlled trial comprising both an exercise intervention compared with a control activity and a nutrition intervention compared with placebo in a $2 \times 2$ factorial model. For all outcome measures, assessors were blinded to group allocations. The exercise and control activities were presented to participants and staff at the facilities without indication of the study hypothesis. Regarding the nutrition intervention, participants as well as therapists, who both administered the nutrition intervention and supervised the exercise and control activities, were blinded.

**Randomisation** Randomisation was performed after the inclusion of participants and baseline assessments. To reduce contamination by the exercise intervention, 34 clusters, comprising three to nine participants living on the same floor, wing, or unit, were randomly assigned to exercise or control activity. To minimise the risk of impact by factors associated with the facility, the randomisation was stratified in order to have both groups in each facility. Within each cluster the nutrition intervention was randomised individually. Researchers not involved in the study performed the randomisation using lots in sealed non-transparent envelopes.

**Exercise intervention** The exercise intervention, based on the High-Intensity Functional Exercise Program (the HIFE Program), is described in detail elsewhere (Littbrand et al 2006). The program included functional exercises consisting of everyday tasks challenging leg strength, postural stability, and gait ability. The physiotherapists selected exercises for each participant according to their functional deficits. All exercises were performed in weight-bearing positions, eg squats, turning trunk and head while standing, and walking over obstacles. The participants were encouraged by the physiotherapists to exercise with a high intensity and to increase load and difficulty progressively, considering changes in function and health status. Strength

exercises were intended to be performed at 8–12 repetition maximum (RM) (DeLorme 1945). Balance exercises were intended to challenge the participant's postural stability fully. In co-operation with a staff member, at the end of the exercise period, physical tasks were introduced with the purpose of maintaining physical function. The tasks would be integrated in daily life activities and were recommended individually regarding type (eg walking, squats, and standing without balance support), number (one to four), and frequency (from weekly up to daily). The tasks were followed-up after three months by interviewing staff about compliance during the previous two weeks.

**Control activity** The control activity program was developed for this study by occupational therapists and included activities while sitting, eg watching films, reading, singing, and conversation. The program was based on themes, eg the old country shop, famous persons, and games from the past, and was expected to be interesting and stimulating for older persons including those with severe cognitive impairment.

**Nutrition intervention and placebo** The nutrition intervention consisted of a protein-enriched energy supplement. The supplement was a milk-based 200 ml drink that contained 7.4 g protein, 15.7 g carbohydrate, and 408 kJ per 100 g. The placebo drink (200 ml) contained 0.2 g protein, 10.8 g carbohydrate, and 191 kJ per 100 g. Both drinks were served in the same type of non-transparent package and had similar flavours.

**Procedure** The exercise intervention and the control activity started in March 2002, and was performed in groups of three to nine participants supervised by two physiotherapists (exercise) or one occupational therapist (control). The sessions lasted approximately 45 minutes and were held five times every two weeks for three months (13 weeks), in total on 29 occasions. Both the exercise and the control activity were performed within the facility at a similar distance from the participant's flat or room. When a participant did not attend the group session, individual activity was offered if possible. The nutrition drinks were offered within five minutes after each session and were collected and weighed after 15 minutes. If the participant did not attend the activity, the drink was offered when possible. After each session the supervisors registered adverse events, and for the exercise group the intensity achieved, in a structured report (Littbrand et al 2006).

During the intervention period, five physiotherapists were working full-time and two shared a full-time position. Two occupational therapists were working full-time and one 75% of a full-time position. All physiotherapists and occupational therapists were experienced in working with older persons with impaired physical and cognitive function. Educational meetings were held in order to learn the programs.

**Outcome measures** The outcomes were balance, gait ability and lower-limb strength.

Balance was assessed using the Berg Balance Scale, consisting of 14 balance tasks common in everyday life, with a maximum score of 56 (Berg et al 1992 and 1995).

Gait ability was measured by a 2.4 metre timed test (Guralnik et al 1994), starting in standing position, twice at self-paced gait speed and then twice at maximum speed. The participants used their ordinary walking aid and walked to a visible goal approximately 3 metres away. The timing,

with a digital stopwatch, was stopped when the participant's chest crossed the finish line marked on the wall. The assessor walked along side the participant if necessary for safety reasons, but no physical contact was allowed.

Lower-limb strength was measured by establishing one-repetition maximum (1 RM) (DeLorme 1945) in a leg press machine[a]. The test was performed, normally bilaterally, from a 90 degree knee angle to the participant's complete knee extension. A unilateral 1 RM was established if the participant was not able to use both legs, eg due to paresis. The load was increased by 10 kg per attempt with 45 s rest between. When the participant did not succeed in an attempt, the load was increased by 2 kg from the last successful attempt until 1 RM was obtained. For safety reasons, participants with a hip fracture within the past six months or a hip prosthesis were not assessed.

A modified chair-stand test (Guralnik et al 1994), the ability to stand up once from a chair, was used as an additional outcome measure of lower-limb strength because of expected missing values in 1 RM. The arms were held in front of the body since no support was allowed.

The outcomes were assessed at baseline, three months, and six months by trained physiotherapists blinded to group allocation and previous test results. The participant's use of walking aid, position in the leg press machine, and chair height were repeated on all test occasions. Interrater reliability for Berg Balance Scale and 2.4-metre gait speed, calculated by Intra Class Correlation (ICC 3,1), ranged from 0.99 to 1.00.

The assessors' blinding was evaluated after the follow-ups. At three months, the assessors guessed activity allocation correctly in 60% of the cases (110/182, kappa coefficient 0.21) and nutrition allocation in 50% of the cases (91/182, kappa coefficient 0.004). At six months, corresponding figures were 69% (114/166, 0.37) and 47% (78/166, –0.06). The participant's assessor was replaced at six months if the assessor stated that the blinding was broken at three months. This was the case for 11 (6%) participants. At six months, the blinding was broken for two (1%) participants.

*Baseline descriptive assessments* The resident's registered nurse recorded diagnoses, clinical characteristics, and prescribed drugs. A licensed practical nurse or a nurse's aide were questioned about activities of daily living, using the Barthel Index (Mahoney and Barthel 1965, Wade 1992). Cognitive function was assessed using the MMSE. A score of ≤ 17 indicates severe cognitive impairment (Tombaugh and McIntyre 1992). Depressive symptoms were screened using the Geriatric Depression Scale (GDS–15) (Sheikh and Yesavage 1986). The Philadelphia Geriatric Center Morale Scale (PGCM) was used to assess morale (Lawton 1975). The functional ambulation categories (FAC) scale was used to measure walking ability (0–5) (Collen et al 1990, Wade 1992). A score of 3 (verbal supervision or standby help from one person without physical contact) or less was chosen to indicate severe physical impairment. A dietician assessed nutritional status by using the Mini Nutritional Assessment (MNA), including Body Mass Index (kg/m$^2$). MNA scores below 24 indicate risk or presence of malnutrition (Guigoz et al 1994). A specialist in geriatric medicine evaluated the documentation of diagnoses, drug treatments, assessments, and measurements for completion of the final diagnoses. Dementia and depression were diagnosed using the DSM-IV criteria (American Psychiatric Association 1994).

*Statistics* The study was designed to have 80% power to detect a significant ($p = 0.05$, 2-tailed) difference between groups of ≥ 3 points in Berg Balance Scale, considering an estimated dropout rate of 20%. All analyses were based on the intention-to-treat principle, using all randomised participants. *A priori* outcome analyses were made blinded to the participants' group allocations.

The mean of the two attempts for self-paced gait speed and the best time measured for maximum speed were chosen. If only one time was measured, this was used. Imputations with 0.01 m/s were made in cases where the participant was not able to perform the test because of impaired physical function. No imputations were made for the other variables.

Baseline characteristics were compared between allocation to activity (exercise/control) and nutrition (protein/placebo) group by one-way ANOVA or chi-square test. Within-group effects were analysed by paired sample t-tests, comparing outcome measures at baseline (pre-intervention) with three and six months (post-intervention), respectively.

Outcome measures were evaluated, at three and six months, in between-group analyses by 2 × 2 factorial ANCOVA in which the post-intervention value was the dependent variable. Fixed factors were allocation to activity and nutrition groups. The other independent variables were the pre-intervention value, age, sex, and covariates adjusting for differences ($p ≤ 0.15$) between the groups at baseline (angina pectoris, proton pump inhibitors, Barthel ADL Index, and self-perceived health). The analyses were tested for interactions between allocation to activity and nutrition groups. Effect sizes were calculated as the difference between the marginal means divided by the pooled standard deviations (square root of the mean square error). The chair-stand test was analysed by logistic regression with the same independent variables as in the ANCOVA.

The results of the outcome analyses in the present study are presented without adjustments for the randomisation in clusters. The rationale for this is that the cluster-randomisation was stratified and, further, that there were few participants per cluster (mean 5.6 ± 1.6 participants) and that the intervention was directed to the individuals instead of to the clusters (Kerry and Bland 1998). Nevertheless, the cluster effect was examined in additional analyses by adjusting the outcome regression analyses for clustering (Campbell et al 2004).

Cluster adjustments were performed using Stata software, version 9.1[b]. All statistical tests were 2-tailed; $p < 0.05$ was considered to indicate statistical significance.

## Results

*Flow of participants through the trial* Baseline characteristics of the 191 participants are presented in Table 1. Ninety-two participants (48%) had severe cognitive impairment (MMSE ≤ 17) and 81 (42%) had severe physical impairment (FAC ≤ 3). One hundred and thirty participants (68%) had either severe cognitive or physical impairment. When mobilising in their flat or room, 108 participants (57%) normally used a walker and 27 (14%) used a wheelchair.

At three months, 175 (92%) of the 191 participants were followed up (Figure 1). The corresponding figure at six months was 163 (85%) participants. Twelve drop-outs

**Table 1.** Baseline characteristics of the participants.

| Characteristic | Total n = 191 | Ex + Protein n = 46 | Ex + Placebo n = 45 | Ctrl + Protein n = 50 | Ctrl + Placebo n = 50 | p |
|---|---|---|---|---|---|---|
| Age, mean ± SD | 84.7 ± 6.5 | 85.0 ± 6.7 | 85.5 ± 5.5 | 82.9 ± 6.4 | 85.6 ± 7.0 | 0.13 |
| Female sex, n (%) | 139 (73) | 36 (78) | 31 (69) | 35 (70) | 37 (74) | 0.74 |
| **Diagnoses & medical conditions, n (%)** | | | | | | |
| Depression | 116 (61) | 30 (65) | 25 (56) | 31 (62) | 30 (60) | 0.82 |
| Dementia | 100 (52) | 24 (52) | 23 (51) | 26 (52) | 27 (54) | 0.99 |
| Delirium episodes, the last month | 50 (26) | 9 (20) | 12 (27) | 17 (34) | 12 (24) | 0.43 |
| Previous stroke | 54 (28) | 15 (33) | 11 (24) | 11 (22) | 17 (34) | 0.47 |
| Diabetes mellitus | 37 (19) | 5 (11) | 9 (20) | 10 (20) | 13 (26) | 0.31 |
| Heart failure | 52 (27) | 11 (24) | 14 (31) | 12 (24) | 15 (30) | 0.79 |
| Angina pectoris | 53 (28) | 13 (28) | 14 (31) | 18 (36) | 8 (16) | 0.14 |
| Osteoporosis | 50 (26) | 13 (28) | 10 (22) | 13 (26) | 14 (28) | 0.91 |
| Malignancy, last five years | 24 (13) | 6 (13) | 4 (9) | 9 (18) | 5 (10) | 0.53 |
| **Drugs for regular use, n (%)** | | | | | | |
| Diuretics | 94 (49) | 23 (50) | 22 (49) | 26 (52) | 23 (46) | 0.94 |
| Analgesics | 111 (58) | 32 (70) | 24 (53) | 27 (54) | 28 (56) | 0.34 |
| Bensodiazepines | 76 (40) | 21 (46) | 14 (31) | 21 (42) | 20 (40) | 0.54 |
| Antidepressants | 94 (49) | 26 (56) | 20 (44) | 25 (50) | 23 (46) | 0.66 |
| Neuroleptics | 42 (22) | 8 (17) | 9 (20) | 12 (24) | 13 (26) | 0.74 |
| Oestrogene | 56 (29) | 11 (24) | 12 (27) | 14 (28) | 19 (38) | 0.45 |
| Laxatives | 102 (53) | 23 (50) | 23 (51) | 30 (60) | 26 (52) | 0.75 |
| Proton pump inhibitors | 40 (21) | 7 (15) | 10 (22) | 18 (36) | 5 (10) | 0.01 |
| Number of drugs, mean ± SD | 9.1 ± 4.4 | 8.7 ± 3.8 | 9.8 ± 5.9 | 9.4 ± 4.2 | 8.6 ± 3.7 | 0.56 |
| **Assessments** | | | | | | |
| Barthel ADL Index (0–20), mean ± SD | 13.1 ± 4.2 | 13.7 ± 4.2 | 11.9 ± 4.6 | 13.8 ± 3.7 | 13.0 ± 4.0 | 0.09 |
| Independent gait indoors (with or without walking aid)*, n (%) | 121 (63) | 31 (67) | 25 (56) | 32 (64) | 33 (66) | 0.65 |
| Mini-Mental State Examination (0–30), mean ± SD | 17.8 ± 5.1 | 17.2 ± 5.1 | 17.9 ± 4.9 | 18.5 ± 5.4 | 17.4 ± 5.2 | 0.56 |
| Geriatric Depression Scale (0–15), mean ± SD (n = 180) | 4.4 ± 3.2 | 4.4 ± 3.6 | 4.7 ± 3.3 | 4.1 ± 2.8 | 4.4 ± 3.0 | 0.79 |
| Philadelphia Geriatric Center Morale Scale (0–17), mean ± SD (n = 188) | 11.0 ± 3.5 | 11.1 ± 4.0 | 11.1 ± 3.3 | 11.0 ± 3.1 | 10.9 ± 3.5 | 0.99 |
| Body Mass Index, mean ± SD (n = 189) | 24.8 ± 4.5 | 24.9 ± 4.6 | 24.8 ± 4.4 | 24.9 ± 4.4 | 24.5 ± 4.9 | 0.96 |
| Mini Nutritional Assessment (0–30), mean ± SD (n = 188) | 20.5 ± 3.7 | 20.9 ± 3.3 | 19.9 ± 4.3 | 20.9 ± 3.2 | 20.4 ± 3.9 | 0.54 |
| Health, self-perceived as better than age peers†, n (%) (n = 189) | 77 (41) | 9 (20) | 21 (47) | 26 (54) | 21 (42) | 0.005 |
| **Outcome variables, mean ± SD** | | | | | | |
| Berg Balance Scale (0–56), points (n = 190) | 26.6 ± 14.8 | 28.1 ± 15.1 | 25.2 ± 15.5 | 28.8 ± 13.6 | 24.5 ± 14.9 | 0.39 |
| Gait speed, self paced m/s (n = 188) | 0.36 ± 0.20 | 0.35 ± 0.17 | 0.34 ± 0.22 | 0.38 ± 0.20 | 0.36 ± 0.21 | 0.88 |
| Gait speed, maximum m/s (n = 187) | 0.55 ± 0.31 | 0.58 ± 0.30 | 0.51 ± 0.33 | 0.57 ± 0.30 | 0.53 ± 0.32 | 0.67 |
| 1 RM in lower-limb strength, kg (n = 128) | 89.5 ± 38.7 | 91.7 ± 35.5 | 82.9 ± 41.9 | 93.6 ± 38.7 | 89.8 ± 39.9 | 0.71 |

Ex + Protein = exercise and protein; Ex + Placebo = exercise and placebo; Ctrl + Protein = control activity and protein; Ctrl + Placebo = control activity and placebo; SD = standard deviation; RM = repetition maximum. The range of each assessment is indicated in parenthesis. For all assessments, except Geriatric Depression Scale, higher scores indicate better status. Numbers after a characteristic indicates that there are missing assessments. *According to the Barthel ADL Index. †According to the Mini Nutritional Assessment.
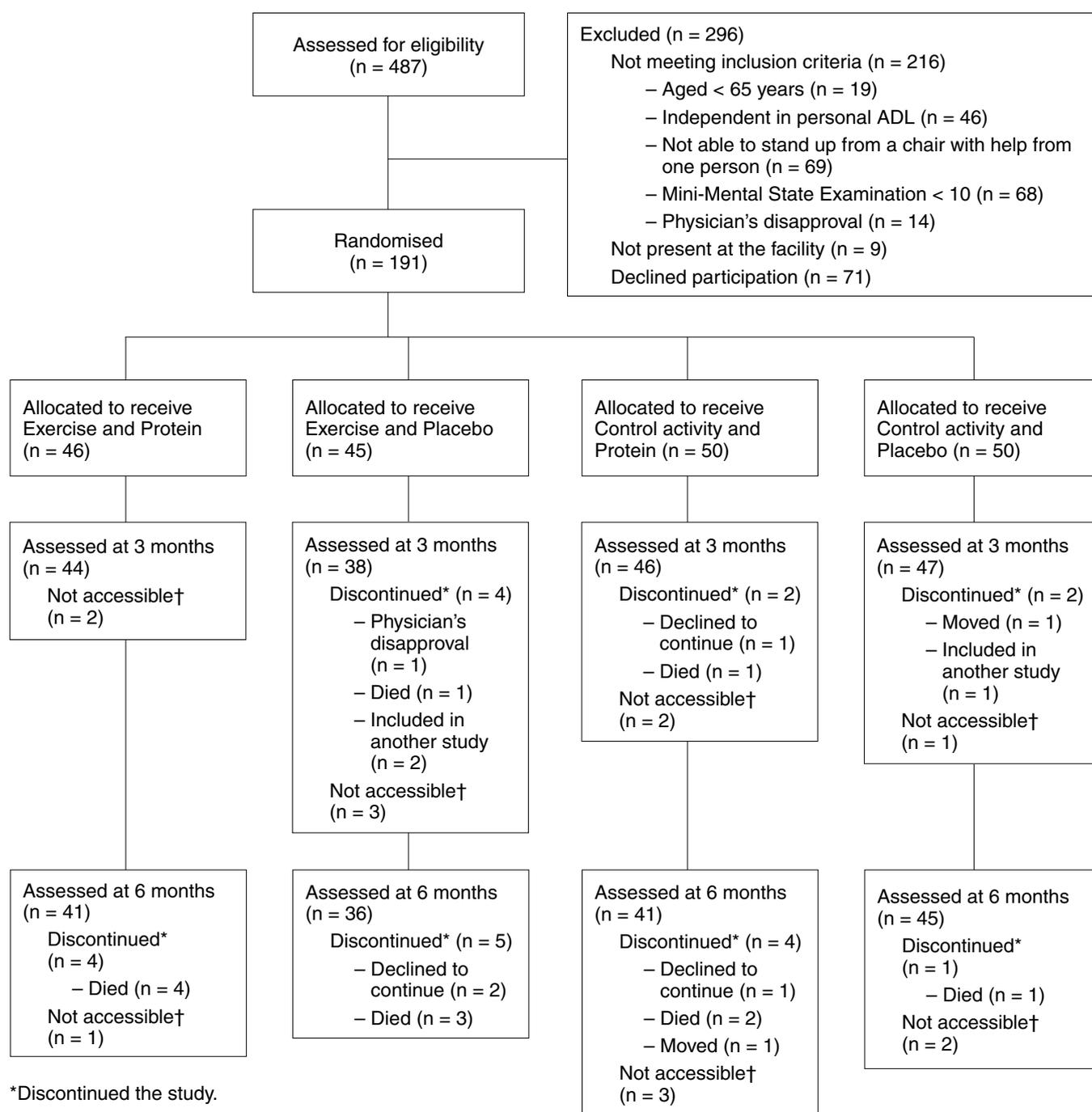
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Assessed for eligibility
(n = 487)
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Excluded (n = 296)
    Not meeting inclusion criteria (n = 216)
        – Aged < 65 years (n = 19)
        – Independent in personal ADL (n = 46)
        – Not able to stand up from a chair with help from
          one person (n = 69)
        – Mini-Mental State Examination < 10 (n = 68)
        – Physician's disapproval (n = 14)
    Not present at the facility (n = 9)
    Declined participation (n = 71)
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Randomised
(n = 191)
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Allocated to receive
Exercise and Protein
(n = 46)
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Allocated to receive
Exercise and Placebo
(n = 45)
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Allocated to receive
Control activity and
Protein (n = 50)
```

```
Allocated to receive
Control activity and
Placebo (n = 50)
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Assessed at 3 months
(n = 44)
    Not accessible†
    (n = 2)
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```
Assessed at 3 months
(n = 38)
    Discontinued* (n = 4)
        – Physician's
          disapproval
          (n = 1)
        – Died (n = 1)
        – Included in
          another study
          (n = 2)
    Not accessible†
    (n = 3)
```

```
Assessed at 3 months
(n = 46)
    Discontinued* (n = 2)
        – Declined to
          continue (n = 1)
        – Died (n = 1)
    Not accessible†
    (n = 2)
```

```
Assessed at 3 months
(n = 47)
    Discontinued* (n = 2)
        – Moved (n = 1)
        – Included in
          another study
          (n = 1)
    Not accessible†
    (n = 1)
```

```
Assessed at 6 months
(n = 41)
    Discontinued*
    (n = 4)
        – Died (n = 4)
    Not accessible†
    (n = 1)
```

```
Assessed at 6 months
(n = 36)
    Discontinued* (n = 5)
        – Declined to
          continue (n = 2)
        – Died (n = 3)
```

```
Assessed at 6 months
(n = 41)
    Discontinued* (n = 4)
        – Declined to
          continue (n = 1)
        – Died (n = 2)
        – Moved (n = 1)
    Not accessible†
    (n = 3)
```

```
Assessed at 6 months
(n = 45)
    Discontinued*
    (n = 1)
        – Died (n = 1)
    Not accessible†
    (n = 2)
```

*Discontinued the study.

†Not accessible at the follow-up, still continuing the study

**Figure 1.** Flow of participants through the trial.

during the study were due to death and two occurred during the intervention period (Figure 1). The relations between cause of death and the study (interventions and test procedures) were evaluated by a specialist in geriatric medicine. In one case, an association to the study could not be definitely excluded. This participant died suddenly of an acute ruptured aortic-abdominal aneurysm one week after the three month follow-up tests were performed.

***Compliance with intervention*** Attendance was 72% for the exercise group and 70% for the control group. No adverse event during the sessions led to a manifest injury or disease. Participants performed strength training of high-intensity in a median of 53% of the attended exercise sessions and

balance exercises in a median of 73% (Littbrand et al 2006). Eighty-one participants in the exercise group were given a mean of 2.0 (0.8 SD) physical tasks. At follow-up, 29 of the remaining 74 participants (39%) had performed one task or more as frequently as recommended, and 29 (39%) had not done any.

The protein-enriched energy supplement was taken on 82% of the occasions and the placebo drink on 78%. The package was completely emptied on 80% of these occasions.

***Effect of intervention*** At three months, the exercise group had improved significantly in self-paced gait speed compared with the control group (Table 2). At six months,

**Table 2.** Outcome analyses, between-group differences based on the intention-to-treat principle.*

| Outcome measure | Follow-up | n | Exercise mean (SE) | Control mean (SE) | Difference mean (95% CI) | p |
|---|---|---|---|---|---|---|
| Berg Balance Scale, points | 3 mo | 172 | 29.5 (0.7) | 28.0 (0.7) | 1.5 (–0.4 to 3.4) | 0.13 |
| | 6 mo | 161 | 31.0 (0.7) | 29.1 (0.6) | 1.9 (0.004 to 3.8) | **0.05** |
| Gait speed, self-paced, m/s | 3 mo | 166 | 0.40 (0.01) | 0.36 (0.01) | 0.04 (0.01 to 0.08) | **0.02** |
| | 6 mo | 156 | 0.41 (0.01) | 0.37 (0.01) | 0.05 (0.01 to 0.08) | **0.009** |
| Gait speed, maximum, m/s | 3 mo | 165 | 0.57 (0.02) | 0.54 (0.02) | 0.03 (–0.02 to 0.08) | 0.30 |
| | 6 mo | 154 | 0.62 (0.02) | 0.59 (0.02) | 0.03 (–0.03 to 0.09) | 0.30 |
| 1 RM in lower-limb strength, kg | 3 mo | 103 | 102.9 (3.0) | 97.9 (3.2) | 5.1 (–3.9 to 14.0) | 0.26 |
| | 6 mo | 97 | 105.4 (3.3) | 94.5 (3.3) | 10.8 (1.3 to 20.4) | **0.03** |

*Between-group effects analysed by $2 \times 2$ factorial ANCOVA in which the post-intervention value was the dependent variable. Independent covariates adjusting for differences ($p \leq 0.15$) between the groups at baseline (angina pectoris, proton pump inhibitors, Barthel ADL Index and (square root of the mean square error). †p value for test of interaction effect between the exercise and nutrition interventions. Bold font

**Table 3.** Within-group differences between post-and pre-intervention values, based on the intention-to-treat principle.

| Outcome measure | Follow-up | n | Ex + Protein mean (SD) | p | n | Ex + Placebo mean (SD) |
|---|---|---|---|---|---|---|
| Berg Balance Scale, points | 3 mo | 44 | 1.3 (7.5) | 0.26 | 38 | 3.3 (6.0) |
| | 6 mo | 41 | 2.4 (6.2) | **0.02** | 36 | 3.5 (5.7) |
| Gait speed, self-paced, m/s | 3 mo | 42 | 0.02 (0.12) | 0.36 | 36 | 0.02 (0.13) |
| | 6 mo | 39 | 0.00 (0.11) | 0.80 | 36 | 0.05 (0.12) |
| Gait speed, maximum, m/s | 3 mo | 42 | –0.03 (0.15) | 0.18 | 36 | 0.03 (0.17) |
| | 6 mo | 39 | –0.02 (0.22) | 0.63 | 36 | 0.07 (0.20) |
| 1 RM in lower-limb strength, kg | 3 mo | 31 | 11.3 (21.2) | **0.006** | 24 | 10.9 (18.0) |
| | 6 mo | 28 | 11.6 (28.8) | **0.04** | 22 | 10.1 (20.6) |

Ex + Protein = exercise and protein; Ex + Placebo = exercise and placebo; Ctrl + Protein = control activity and protein; Ctrl + Placebo = $p < 0.05$.

significant improvements in favour of the exercise group were obtained in Berg Balance Scale, self-paced gait speed, and 1 RM in lower-limb strength. Regarding the nutrition intervention, there was a significant difference in self-paced gait speed in favour of the placebo group at six months. No interaction effects were seen between the exercise and nutrition interventions for any of the outcome measures at any of the follow-ups.

At six months, the exercise group had improved significantly in the chair-stand test compared with the control group ($p = 0.01$). In the exercise group, 57% of participants were able to stand up once compared with 44% of participants in the control group. Corresponding figures at baseline were 48% versus 46%. At three months there was no significant difference between groups (data not shown).

All groups showed within-group improvements in Berg Balance Scale and in 1 RM in lower-limb strength at both follow-ups (Table 3). These improvements were in most cases statistically significant for the exercise groups, but not for the control groups.

Outcome analyses adjusted for cluster-randomisation produced essentially the same results, compared with unadjusted analyses (data not shown).

## Discussion

This study demonstrated positive long-term effects in physical function of a high-intensity exercise program for older persons dependent in activities of daily living, of whom most had severe cognitive or physical impairments. No increased effect of the training was seen by an intake of a protein-enriched energy supplement immediately after the exercises.

The positive effects in physical function are in accordance with high-intensity exercise studies targeting frail older persons with higher physical abilities than in the present study (Fiatarone et al 1994, Hauer et al 2001, Lazowski et al 1999, Seynnes et al 2004), one of which included persons with severe cognitive impairments (Lazowski et al 1999). Contradictory results were presented in a study among older persons with severe cognitive and physical impairments where no improvements in physical function were seen (Morris et al 1999). However, a reduction in the decline of activities of daily living was found.

The study design must be considered when interpreting the results. Only two of the studies mentioned above provide information that intention-to-treat analyses were used (Fiatarone et al 1994, Hauer et al 2001), two that assessors were blinded for all outcome measures (Hauer et al 2001,

| ES | Protein mean (SE) | Placebo mean (SE) | Difference mean (95% CI) | *p* | ES | Interaction *p*† |
|---|---|---|---|---|---|---|
| 0.24 | 28.2 (0.7) | 29.3 (0.7) | −1.1 (−3.1 to 0.8) | 0.26 | −0.18 | 0.68 |
| 0.33 | 29.8 (0.7) | 30.3 (0.7) | −0.6 (−2.5 to 1.4) | 0.56 | −0.10 | 0.87 |
| 0.36 | 0.38 (0.01) | 0.38 (0.01) | 0.00 (−0.04 to 0.04) | 0.96 | −0.01 | 0.39 |
| 0.44 | 0.37 (0.01) | 0.41 (0.01) | −0.04 (−0.07 to-0.00) | **0.03** | −0.37 | 0.21 |
| 0.17 | 0.54 (0.02) | 0.57 (0.02) | −0.04 (−0.09 to 0.01) | 0.16 | −0.23 | 0.74 |
| 0.17 | 0.58 (0.02) | 0.62 (0.02) | −0.04 (−0.10 to 0.02) | 0.16 | −0.24 | 0.33 |
| 0.23 | 99.7 (3.0) | 101.1 (3.2) | −1.4 (−10.3 to 7.5) | 0.76 | −0.06 | 0.47 |
| 0.49 | 100.0 (3.2) | 99.9 (3.4) | 0.2 (−9.4 to 9.7) | 0.97 | 0.01 | 0.40 |

variables were the allocation to activity (exercise/control) and nutrition (protein/placebo) groups, pre-intervention value, age, sex and self-perceived health). Effect sizes were calculated as the difference between the marginal means divided by the pooled standard deviations highlights results with statistical significance $p < 0.05$. ES = effect size; SE = standard error; CI = confidence interval; RM = repetition maximum.

| *p* | Ctrl + Protein | | | Ctrl + Placebo | | |
|---|---|---|---|---|---|---|
| | n | mean (SD) | *p* | n | mean (SD) | *p* |
| **0.001** | 45 | 0.3 (6.0) | 0.71 | 46 | 2.0 (5.7) | **0.02** |
| **0.001** | 40 | 0.8 (5.8) | 0.38 | 45 | 1.8 (6.1) | 0.06 |
| 0.32 | 44 | 0.00 (0.12) | 0.91 | 45 | −0.02 (0.12) | 0.18 |
| **0.02** | 40 | 0.00 (0.11) | 0.81 | 42 | −0.01 (0.11) | 0.47 |
| 0.33 | 44 | −0.03 (0.19) | 0.26 | 44 | −0.01 (0.14) | 0.69 |
| **0.03** | 40 | 0.01 (0.17) | 0.68 | 40 | 0.00 (0.13) | 0.87 |
| **0.007** | 25 | 7.1 (22.9) | 0.13 | 23 | 8.2 (24.7) | 0.13 |
| **0.03** | 23 | 1.5 (20.9) | 0.74 | 24 | 2.8 (17.4) | 0.43 |

control activity and placebo; SD = standard deviation; RM = repetition maximum. Bold font highlights results with statistical significance

Lazowski et al 1999), and none that randomisation was concealed. According to a systematic review of strength training studies among older persons, studies using intention-to-treat analysis, blinded assessors, or concealed randomisation (all used in the present study) have lower effect sizes than studies with lower methodological quality (Latham et al 2004). The effect sizes in the present study seem rather high compared with these studies. A direct comparison is, however, not applicable since the effects sizes in the review by Latham et al (2004) are calculated on the effect and standard deviation at the follow-up, instead of using the change from baseline to follow-up as in the present study. Thus, the calculation of effect size used in the present study takes into account any differences between groups in baseline values of the outcome measure and is less dependent on variation in ability between participants.

The long-term effects in the present study are in accordance with another study of a functional exercise program (de Vreede et al 2005). Perhaps the effects on physical function of this training method influence performance in daily life which consequently preserves the exercise effects. The physical tasks used in our study might also have had a preserving effect. However, compliance with these tasks was low.

The lack of increased effect of the training by an intake of protein immediately after the exercises is in contrast to a study among healthy older men (Esmarck et al 2001). A possible explanation for this difference in effect may be that the participants in our study had a poor nutritional status, which indicates a negative energy balance. Thus, the protein might have been absorbed as energy to compensate for this. In addition, the majority of the participants were women with many diseases and drug treatments which might have affected the absorption and metabolism of the protein. Further research is needed regarding combined interventions of exercise and nutrition in this frail group of older persons. Perhaps the nutrition intervention, similar to the exercise intervention, should be individualised in order to be successful.

It was interesting that no decline in function in the control group was seen during the study, in contrast to an expected decline (Jensen et al 2004, Morris et al 1999). One possible reason is that the control activity program had some effect on physical function in performance of this sedentary group, eg through the impact of social stimulation, performance of a meaningful activity, or transferring to another location in the facility. The use of this elaborate control activity strengthens the interpretation that the differences between groups in physical outcomes were mainly due to training itself.

A higher level of achieved exercise intensity might have improved the results, but the participants' high prevalence of different diseases probably influenced the intensity. Despite these characteristics, no adverse events led to a manifest injury or disease. The approvals from the participants' physicians prior to the study were probably important to safety, as well as the supervision of the sessions by persons who were experienced in working with frail older persons.

Even though the exercise intervention was randomised in clusters there were few differences between groups at baseline that had to be adjusted for in the outcome analyses. A contributing factor might be that the randomisation was performed after the inclusion of participants which eliminated the risk of selection bias. In addition, the randomisation was performed using a relatively high number of clusters.

The exclusion of persons with a MMSE score of less than 10 or needing more than one helper to stand up from a chair limits the external validity of the study. In addition, almost half of the available participants were not assessed for lower limb strength using 1 RM. However, the positive long-term effect in lower-limb strength was confirmed by analysis of the chair-stand test. Another study limitation might be that the blinding of the assessors was not complete. However in our view blinding was adequate as there were few cases of broken blindness and not more than slight agreements between the assessors' guesses and the group allocations (Byrt 1996).

The main finding of this study is that older persons with severe cognitive or physical impairments can benefit from a high-intensity functional exercise program. A recent meta-analysis presented positive effects of exercise, regardless of intensity, in older persons with cognitive impairments and dementia (Heyn et al 2004). However, most studies reviewed had an important deficiency in methodological quality, eg regarding the blinding procedure. In addition, the impact of different training methods used was not considered and exercise intensity was examined insufficiently, ie in total minutes per exercise session instead of using an intensity estimation related to the individual's maximum capacity.

The improvements obtained in physical function may be of great importance in daily life, by achieving higher activity level or more independence. The exercise effects may seem small in absolute values but, in our view, when related to the low baseline values they are of clinical importance. The use of an elaborate control activity and high methodological quality prevented an overestimation of the effect. Further, the use of intention-to-treat analyses in combination with fairly wide inclusion criteria suggests that this effect might be applicable to many older persons. The issue of transfer improvements in physical function to activities in daily life is of interest for future research, as well as whether a high-intensity functional exercise program is as effective for persons with different diagnoses and conditions such as dementia, depression, or malnutrition.

***Correspondence*** Erik Rosendahl, Department of Community Medicine and Rehabilitation, Geriatric Medicine, Umeå University, Sweden.
Email: erik.rosendahl@germed.umu.se

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