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Original Study

Effect of Sit-to-Stand Exercises Combined With Protein-Rich Oral Supplementation in Older Persons: The Older Person's Exercise and Nutrition Study

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A B S T R A C T

Objectives: Nursing home (NH) residents are often undernourished and physically inactive, which contributes to sarcopenia and frailty. The Older Person's Exercise and Nutrition Study aimed to investigate the effects of sit-to-stand exercises (STS) integrated into daily care, combined with a protein-rich oral nutritional supplement (ONS), on physical function, nutritional status, body composition, health-related quality of life, and resource use.
Design: Residents in 8 NHs were randomized by NH units into an intervention group (IG) or a control group (CG) (n = 60/group). The IG was a combination of STS (4 times/day) and ONS (2 bottles/day providing 600 kcal and 36 g protein) for 12 weeks.
Setting and Participants: The participants resided in NH units (dementia and somatic care), were ≥75 years of age, and able to rise from a seated position.
Methods: The 30-second Chair Stand Test was the primary outcome. Secondary outcomes were balance, walking speed, dependence in activities of daily living, nutritional status and body composition, health-related quality of life, and resource use.
Results: Altogether, 102 residents (age 86 ± 5 years, 62% female) completed the study. No improvement in the physical function assessments was observed in the IG, whereas body weight increased significantly (2.05 ± 3.5 kg, $P = .013$) vs the CG. Twenty-one (of 52) participants with high adherence to the intervention (ie, at least 40% compliance to the combined intervention) increased their fat free mass (2.12 kg (0.13, 4.26 interquartile range), $P = .007$ vs CG). Logistic regression analyses indicated that the odds ratio for maintained/improved 30-second Chair Stand Test was 3.5 (confidence interval 1.1, 10.9, $P = .034$) among the participants with high adherence compared with the CG.

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This study has been registered with the number protocol of ClinicalTrials.gov Identifier: NCT02702037.

The study has been approved by the Regional Ethical Review Board in Stockholm, D no. 2013/1659-31/2, 2015/1994-32 and 2016/1223-32. Informed consent from all participants (residents and staff) were obtained prior to study commencement

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Conclusions/Implications: Twelve-week intervention of daily STS combined with ONS in NH residents did not improve physical function, but increased body weight. Subgroup analyses indicated that high adherence to the combined intervention was associated with maintained or improved physical function and a gain of fat free mass.

Loss of muscle strength and mass (ie, sarcopenia) is associated with reduced activities of daily living (ADL) including walking, rising from a chair, balance, and mobility,[1] and combined they constitute major causes for institutionalization. Undernutrition and sarcopenia are main underlying mechanisms for frailty, which is predominately defined by physical vulnerability and reduced mobility. Mobility is identified by older nursing home (NH) residents as a key to their quality of life (QoL) and well-being.[2] Physical exercise is beneficial in frail older adults to improve gait speed, balance, and mobility, and to maintain or improve their ability to perform ADL, as well as their QoL.[3]

Protein deficiency plays an important role in the development of sarcopenia.[4] Recently, the importance of adequate protein intake in older populations has been addressed. For example, the PROT-AGE study group and the Nordic Nutrition Recommendations indicate that older persons need a higher protein intake than younger adults.[5,6] The combination of protein supplementation and physical exercise has been shown to be most effective to maintain[7] and increase muscle mass.[8,9]

High-intensity group exercise programs have been shown to improve balance control, strength, and gait ability in older NH residents.[10] Other studies have shown that it is possible to affect muscle strength with various forms of exercise, even of short duration and with light to moderate intensity.[11,12] Older NH residents might benefit more from shorter exercise sessions several times a day rather than fewer and longer sessions.[13] One functional and essential exercise for older frail persons is standing up from a seated position and sitting down in a controlled manner [ie, the sit-to-stand exercise (STS)].[12,14] The ability to get up from a chair without help from others requires leg muscle strength and is fundamental for independent mobility. It is a simple activity that does not require additional equipment and resources. It is fairly free of unwanted side effects.[15] The exercise can be integrated with daily activities such as dressing, toileting, or transferring.

Cost estimates for providing care to NH residents are most often based on the mean costs and not based on individual characteristics in terms of time for staff to carry out various care activities. There are variations in work load for the staff in NHs, as well as differences in functional and cognitive impairment among NH residents.[16] If it is possible to reduce the impairment of residents, it could have positive effects not only on the resident, but also on the time needed by staff to compensate for their disabilities.

The aim of this study was to investigate the effects of combining STS and daily protein-rich oral nutritional supplementation (ONS) on physical function, nutritional status and body composition, health-related QoL, and resource use in older NH residents.

Methods

Study Design

The study was a 2-arm randomized controlled trial performed in 8 NHs consisting of 62 units (dementia or somatic care units) at 2 municipalities in the Stockholm County. The participants were randomized by NH units into an intervention group (IG) or a control group (CG). The power calculation of the sample size (60 persons per group) was based on observations of an increase of 2 STS completed in 30 seconds in a previous study by Slaughter et al.[17] A more detailed description of the design is published in the Older Person's Exercise and Nutrition Study protocol.[18] This study is reported according to the CONSORT 2010 guidelines.[19] The study has been approved by the Regional Ethical Review Board in Stockholm, Dno. 2013/1659-31/2, 2015/1994-32 and 2016/1223-32. The study is registered under ClinicalTrials.gov; Identifier: NCT02702037.

Participants

NH residents aged ≥75 years and able to rise from a seated position to standing were invited to participate. Verbal informed consent was given before study inclusion. Residents with a body mass index of >30 kg/m^2, already prescribed protein-rich ONS, with severe dysphagia, receiving tube-feeding, bedridden, with severe kidney disease, at a terminal stage of life, unable to give informed consent by participant or legal representative, and/or unable to participate because of psychological or cognitive reasons were excluded.

Demographic data on age, sex, and medical history including diagnoses were registered from the resident's medical records. At baseline, cognitive function was assessed using Mini-Mental State Examination (0–30 points),[20] risk of sarcopenia by the SARC-F questionnaire (0–10 points; ≥4 points = increased risk),[21] and frailty by the FRAIL questionnaire (0–5 points; ≥3 points = frailty; 1–2 points = prefrail).[22]

Intervention and Control Group

The intervention period lasted for 12 weeks. The participants in the IG were encouraged to perform the STS at 4 occasions per day for 7 days per week. The exercises primarily took place in conjunction with daily activities, such as toileting, dressing, or transferring, where the participant was encouraged to get up from a chair to a standing position and then sit down again for as many times at each occasion as the participant could, with or without support. The participants were offered a bottle of ONS (125 mL, 18 g protein, 300 kcal; Fortimel Compact Protein, Nutricia N.V., Zoetermeer, The Netherlands) twice daily for 7 days per week, between main meals. The staff documented the occasions of STS, and the amount of ONS consumed for each participant using specially designed study glasses. Before study start, the staff in the IG units were informed about the purpose of the study, how to support and encourage the participants to perform the intervention, and trained in how to fill in the adherence charts. The CG received standard care.

Data Collection and Outcomes

Data from all participants were collected at baseline and at the 12-week follow-up by 2 clinically experienced physiotherapists. A certified laboratory technician managed the blood samples. Details regarding data collection and outcomes are described in the study protocol.[18]

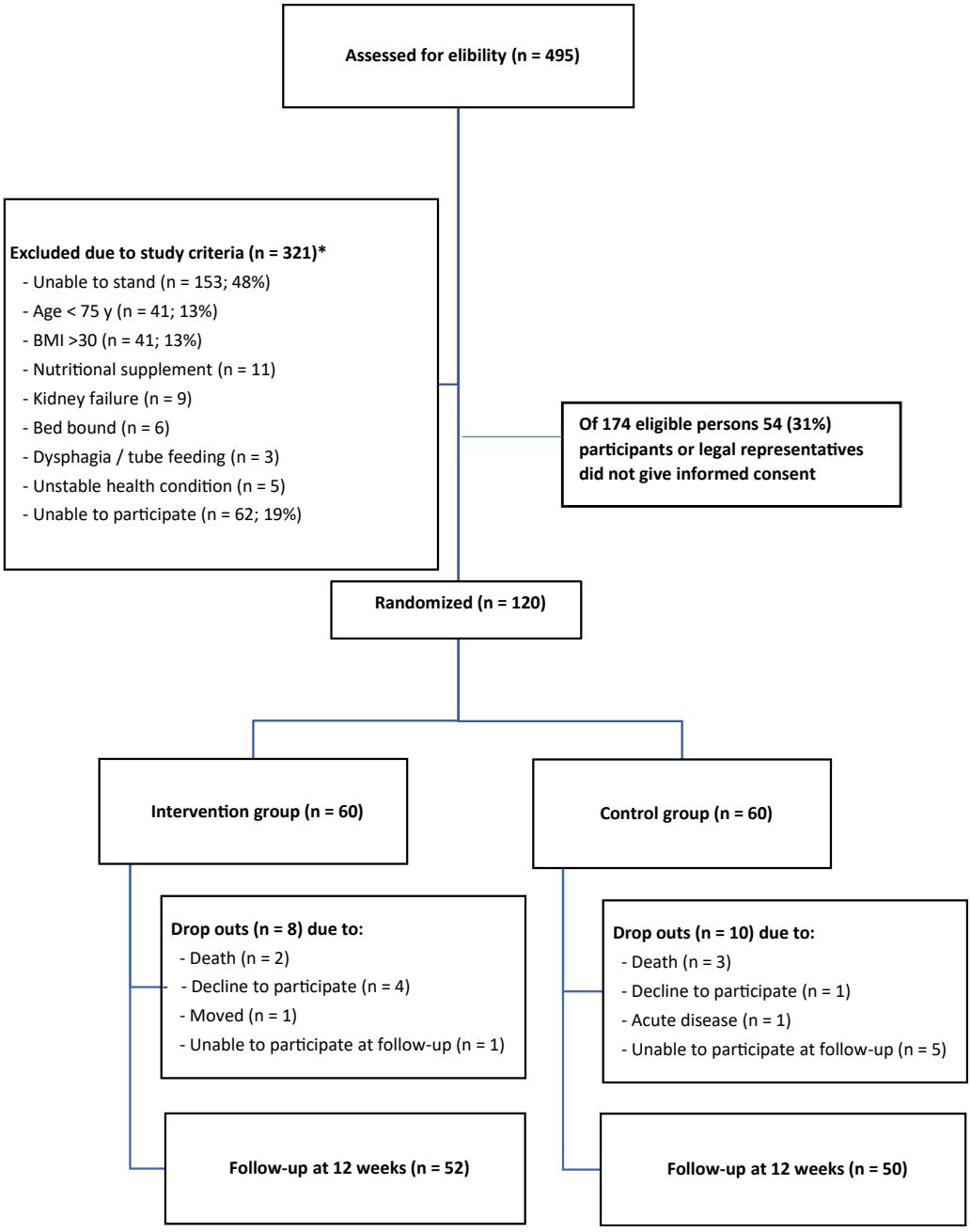

Fig. 1. Flow chart of participants through the trial. *The same resident could be registered for more than one exclusion criterion.

Primary Outcome

The 30-second Chair Stand Test (30sCST) was used as the primary outcome.[23,24] The participants were asked to stand up from a chair and then to sit down again, with arms folded over the chest or with support from the arms of the chair or walking aid, as many times as possible in 30 seconds. The test was performed by each participant in the same way at follow-up as at baseline.

Secondary Outcomes

Physical function

Balance performance was measured by the Berg Balance Scale (BBS) (0–56 points), where higher points indicate better balance.[25,26] Walking speed was measured over a distance of 10 m indoors at self-selected speed (m/s).[27] Dependence in ADL was assessed according to the Functional Independence Measure, which consists of 18 items of physical and cognitive functions. The sum score ranges from 12 to 91 points, where higher scores indicate a higher level of independence.[28]

Nutritional status and body composition

The Mini-Nutritional Assessment-Short Form (MNA-SF; 12–14 points = normal nutritional status; 8–11 points = at risk and ≤7 points = malnourished) was performed.[29] Body composition assessments of fat mass (FM) and fat-free mass (FFM) were made by bioelectrical impedance analysis performed with ImpediMed SFB7 (ImpediMed Ltd, Pinkenba, Australia).[30] FFM index (FFMI) kg/m^{2}was calculated.

Blood chemistry

Plasma concentrations of albumin, transthyretin, C-reactive protein (CRP), and anabolic mediator insulin-like growth factor-1 were analyzed according to routine methods, and reference ranges of the Laboratory of Clinical Chemistry at the Karolinska University Hospital were used. The vitamin D status was assessed by serum-25(OH)VitD concentrations using the electrochemiluminescence method at the Karolinska University Laboratory.

Health-related QoL was assessed using the 5-level EQ-5D version (EQ5D-5L), which comprises of 5 items (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) where each item is scored in 5 levels. EQ5D was administrated as self-ratings. Based on an algorithm, the scoring was expressed in terms of utilities (0–1). A VAS scale (0–100) was also applied in parallel to the scoring.[31]

Healthcare Resource Use data were assessed by The Resource Utilization in Dementia[16] with the aim of analyzing healthcare costs and caregiver time.[32]

Safety and tolerance

Adverse advents (ie, incidence of falls and tolerance of the ONS) were reported by the nurses at the NH units. To evaluate potential effects of the ONS on renal function, the Modification of Diet in Renal Disease formulas were used to estimate the glomerular filtration rate (mL/min/1.73 m^2) at baseline and at follow-up.[33]

Adherence

Previous results from studies in Canadian NHs have shown a mean enactment of nearly 2 STS occasions per day, corresponding to 45% of recommendations in residents similar to those who participated in the current study.[12] Based on these findings, we decided to consider the combination of ≥120 exercise occasions (≥10 times/week; ie, ∼40% of recommended) and ≥60 bottles (≥5 bottles/week; ie, ∼40% of recommended) for 12 weeks as a high adherence to the intervention (HA), whereas participants that did less were considered to have a low adherence (LA).

Statistical Analyses

Data for primary and secondary outcome measures were first analyzed by descriptive and comparative statistical analyses. For comparison within and between groups student *t* test, χ^2 test, Mann-Whitney and Wilcoxon matched pair test were used according to type and distribution of the recorded variables. To further evaluate the effects of the primary outcome, a linear regression model was used. To analyze the effects of the intervention in relation to adherence (as described above), post-hoc analyses were performed. The results of the 30sCST were dichotomized into maintained/improved or decreased for each participant. Subsequently, logistic regression models were used. All statistical tests were performed using SPSS software version 25 for PC (IBM Corporation, Armonk, NY). A *P* value of <.05 was considered to be significant.

Results

Participant Recruitment, Allocation, Characteristics, Drop-Outs, and Adherence

Overall, 495 residents in the 8 NHs were eligible for inclusion in the study. As depicted in the flow chart (Figure 1), 120 participants (60/group) were recruited at baseline and 102 completed the follow-up (50 in the CG and 52 in the IG). Baseline characteristics are shown in Table 1. Mean age was 86 years, and 62% were women. Mean Mini-Mental State Examination was 18 points, indicating an overall moderate cognitive decline. The SARC-F and FRAIL questionnaires indicated that 44 (37%) were at risk of sarcopenia and 47 (51%) were frail or prefrail (Table 1).

A total of 18 participants (13 resided in somatic units) dropped out before the study was completed (Figure 1). Mean age and cognitive function did not differ between the drop-outs and the total group of participants, whereas the drop-outs performed significantly worse at baseline in the 30sCST [mean number was 4 compared with 6 among the total group of participants ($P = .018$)] and had an increased risk of sarcopenia according to SARC-F [mean 5 points compared with 3 points among the total group of participants ($P = .013$)]. In addition, the median score on the FRAIL questionnaire was 2 points in the drop-outs compared with 1 point among the total group of participants ($P = .062$).

In the IG, high adherence to the STS (≥10 occasions/week) was observed in 22 (44%) participants, and to ONS (≥5 bottles/week) in 32 (64%) participants. Twenty-one (42%) IG participants were assessed as being highly adherent (HA) to the combined intervention, whereas the remaining 29 IG participants were considered low adherent (LA).

Table 1
Description of Participants at Baseline in the CG and in the IG Including Participants With HA and LA (n = 102)

Variables (n)	Total Sample, n = 102	CG, n = 50	IG			*P* Value Between Groups		
			Total IG, n = 52	HA, n = 21	LA, n = 29	IG - CG	HA–CG	LA–CG
Age, y (n = 102), mean (SD)	85.9 (5.2)	85.9 (5.4)	85.8 (5.0)	87.5 (5.7)	84.9 (4.3)	.97	.27	.42
Sex (n = 102), n (%)								
Male	39 (38)	21 (42)	18 (35)	9 (43)	8 (28)	.44	.95	.20
Female	63 (62)	29 (58)	34 (65)	12 (57)	21 (72)			
Unit (n = 102), n (%)								
Somatic	41 (40)	22 (44)	19 (36.5)	5 (24)	14 (48)	.44	.11	.71
Dementia	61 (60)	28 (56)	33 (63.5)	16 (76)	15 (52)			
n of medical diagnosis (n = 101), mean (SD)	3.9 (1.9)	4.1 (2.0)	3.8 (1.8)	4.1 (2.0)	3.7 (1.7)	.42	.79	.33
Need of walking aid in persons who could walk (n = 90), n (%)								
Yes, needed aid	58 (64)	29 (64)	29 (64)	14 (67)	14 (64)	1.0	.86	.95
No, did not need aid	32 (36)	16 (36)	16 (36)	7 (33)	8 (36)			
MMSE (n = 71), mean (SD), MMSE (0–30 p)	18.1 (5.9)	18.4 (5.9)	17.9 (6.0)	19.2 (6.0)	16.9 (6.0)	.74	.64	.38
SARC-F (n = 93), mean (SD), (0–10 p)	3.1 (2.8)	2.7 (2.7)	3.5 (2.9)	2.7 (2.6)	4.2 (3.0)	.20	.98	*.040*
FRAIL (n 93), mean (SD), (0–5 p)	0.9 (1.1)	0.9 (1.1)	0.9 (1.2)	0.7 (1.0)	1.2 (1.3)	.99	.43	.36

MMSE, Mini-Mental State Examination; *SD*, standard deviation.
SARC-F questionnaire (0–10 points; ≥4 points = increased risk).
FRAIL questionnaire (0–5 points; ≥3 points = frailty, 1–2 points = prefrail).

Table 2
Comparison of Primary and Secondary Outcomes; i.e. physical function and nutritional status, in nursing home residents allocated to either the CG or the IG. The IG is further divided into participants with HA and LA to the intervention. Data given as mean (SD) if not otherwise depicted.

Variable, n Total (IG-CG)	Total Sample, n = 102	CG, n = 50	IG			*P* Value Between Groups		
			n = 52	HA, n = 21	LA, n = 29	IG-CG	HA-CG	LA-CG
Primary Outcome								
30sCST, n = 102 (52–50)								
Baseline	6.25 (3.14)	6.40 (3.12)	6.13 (3.18)	6.76 (3.66)	5.66 (2.81)	.55	.81	.27
Delta*	0.02 (2.60)	−0.24 (2.83)	0.27 (2.35)	0.86 (2.22)	−0.21 (2.40)	.32	.12	.96
P value within group	.65	.15	.49	.09	.52			
Secondary outcomes - Physical function								
Berg Balance scale (BBS)†, n = 102 (52–50)								
Baseline	28.75 (14.89)	29.98 (13.55)	27.58 (16.13)	31.67 (14.29)	24.17 (16.40)	.42	.57	.08
Delta*	−1.36 (6.83)	−1.40 (6.58)	−1.33 (7.12)	−1.57 (5.85)	−0.72 (8.00)	.96	.92	.69
P value within group	.05	.12	.20	.23	.78			
Walking speed m/s, n = 90 (44–46)								
Baseline	0.735 (0.296)	0.727 (0.298)	0.742 (0.298)	0.814 (0.313)	0.680 (0.266)	.90	.35	.53
Delta*	−0.042 (0.221)	−0.053 (0.239)	−0.031 (0.203)	−0.055 (0.228)	0.021 (0.179)	.45	.92	.31
P value within group	.10	.10	.65	.49	.88			
FIM physical function‡, n = 101 (52–49)								
Baseline	67.75 (19.77)	68.18 (18.31)	67.33 (21.26)	76.43 (13.99)	60.45 (23.32)	.84	.08	.24
Delta*	−0.23 (9.43)	1.53 (11.18)	−1.88 (7.15)	−3.19 (8.76)	−0.76 (5.81)	.12	.09	.24
P value within group	.55	.70	.17	.18	.84			
Secondary outcomes - Nutritional status								
MNA-SF§, n = 97 (49–48) median (IQR)								
Baseline	12 (11–13)	12 (11–13)	12 (10.5–13)	11 (11–13)	12 (10–13)	.58	.22	.85
Delta*, median (IQR)	0 (0–1)	0 (−1 to 1)	0 (0–1)	1 (0–1.5)	0 (−1 to 0)	.36	*.020*	.45
P value within group	.11	.52	.11	*.005*	.63			
Body weight, kg, n = 88 (44–44)								
Baseline	66.59 (11.88)	67.89 (13.0)	65.30 (10.6)	64.11 (10.18)	64.60 (9.69)	.91	.56	.93
Delta*	1.21 (3.19)	0.37 (2.6)	2.05 (3.5)	2.77 (2.60)	1.42 (4.09)	*.013*	*.002*	.20
P value within group	*<.001*	.36	*<.001*	*<.001*	.10			
Body mass index, (kg/m^2), n = 88 (44–44)								
Baseline	25.28 (3.58)	25.25 (3.81)	25.31 (3.39)	24.49 (3.41)	25.59 (3.24)	.64	.47	.34
Delta*	0.48 (1.21)	0.15 (1.01)	0.80 (1.32)	1.06 (0.96)	0.58 (1.56)	*.011*	*.002*	.17
P value within group	*<.001*	.32	*<.001*	*<.001*	.08			
Fat Mass (FM), kg, n = 78 (39–39)								
Baseline	23.71 (7.37)	23.71 (7.92)	23.71 (6.88)	23.15 (5.11)	23.37 (7.71)	.71	.75	.65
Delta*, median (IQR)	0.64 (−1.2 to 2.2)	−0.04 (−1.90 to 1.61)	1.02 (−1.1 to 2.54)	1.02 (−1.21 to 2.15)	0.75 (−1.12 to 2.76)	.16	.45	.31
P value within group	.08	.77	*.040*	.28	.12			
Fat Free Mass (FFM), kg, n = 78 (39–39)								
Baseline	44.00 (9.99)	44.62 (10.9)	43.39 (9.05)	43.19 (9.65)	42.67 (8.62)			
Delta*, median (IQR)	0.28 (−1.03 to 2.18)	−0.44 (−1.14 to 1.67)	1.36 (−0.65 to 2.61)	2.12 (0.13– 4.26)	1.30 (−1.40 to 2.18)	.40	.46	.36
P value within group	*.030*	.89	*.008*	*.007*	.21	.07	*.007*	.37
FFMI‖, kg, n = 78 (39–39)								
Baseline	16.45 (2.38)	16.46 (2.43)	16.45 (2.35)	15.94 (2.52)	16.62 (2.26)	.80	.49	.57
Delta*, median (IQR)	0.11 (−0.41 to 0.89)	−0.15 (−0.41 to 0.65)	0.47 (−0.26 to 0.99)	0.89 (0.05–1.53)	0.46 (−0.49 to 0.89)	.06	*.008*	.33
P value within group	*.024*	.78	*.008*	*.007*	.19			

IQR. Interquartile range.
*Delta, change from baseline to follow-up at 12 weeks.
†Berg Balance scale (0–56 points).
‡Functional Independence Measure (12–91 points).
§Mini Nutritional Assessment-Short Form = (0–14 points).
‖Fat Free Mass Index = FFMI (kg)/height (m^2.)

Effects of the Intervention on Physical Function

Table 2 presents outcome data in the 102 participants who completed the 12-week follow-up. The mean number of the 30sCST was 6 in both groups at baseline as well as at follow-up, with no significant differences within or between groups (Table 2). A linear regression analysis confirmed this result (unstandardized B = 0.509, *P* = .325). There were no significant differences in balance performance (BBS), walking speed, or dependence in ADL between the CG and the IG, or within groups at follow-up. Mean BBS decreased during

the intervention period for the total group, but there were no differences due to group allocation. Corresponding comparisons between the CG and participants with HA to the intervention gave similar nonsignificant results (Table 2). However, when comparing HA with LA participants in the IG, an improvement in 30sCST was observed at the follow-up; 7.62 ± 3.25 vs 5.45 ± 3.09 ($P = .022$).

As displayed in Figure 2, 76% in the HA group maintained or improved their results on the 30sCST as compared with 48% and 55% in the CG and LA groups, respectively ($P = .025$). Logistic regression analyses showed that participants in the HA group maintained or improved their results on the dichotomized 30sCST with an odds ratio of 3.5 (95% confidence interval 1.1, 10.9; $P = .034$) compared with the CG. Corresponding figures were 1.3 (95% confidence interval 0.5, 3.3; $P = .54$) for participants in the LA group compared with the CG.

Post-hoc analyses of the IG to evaluate the effects of the two intervention components separately indicated positive correlations between the change of 30sCST and the total number of ONS intake (rho = .291; $P = .048$), as well as for the total number of STS exercise occasions (rho = .260; $P = .068$), although the latter correlation did not reach statistical significance.

Effects of the Intervention on Nutritional Status, Body Composition, and Biochemistry

Median MNA-SF at baseline was 12 points (out of maximum 14) in both groups (Table 2). The majority (ie, 62% in the IG and 72% in the CG) was assessed as having a normal nutritional status. No significant difference between the IG and the CG was observed in MNA-SF from baseline to follow-up, but there was a significant improvement among the participants in the HA group compared with the CG (Table 2). Body weight increased by approximately 2 kg in the IG, which was significantly different from the CG. FM and FFM increased significantly within the IG at follow-up, and the participants in the HA group significantly improved FFM and FFMI compared to the CG (Table 2).

There were no differences in blood chemistry between or within groups at baseline or at follow-up (Table 3). Around 50% in both groups (27 in IG and 23 in CG) had plasma-CRP concentrations ≥3 mg/L, indicating ongoing minor inflammatory processes. Although average vitamin D concentration was above the reference cut-off value, 13 participants in the IG and 19 in the CG were vitamin D deficient; [ie, serum 25(OH)D concentrations <50 nmol/L]. Plasma-insulin-like growth factor-1 was within the reference range in both groups and did not change at follow-up.

Effects of the Intervention on Health-Related Quality of Life and Resource Use

No statistically significant differences for the self-reported EQ5D-5L between the groups were identified (Table 3). Resource use items such as hospitalizations and clinical visits were very low or zero, and no significant differences were identified between the IG and the CG. Caregiver time decreased significantly only within the IG (15.7 minutes/day; $P = .04$), but the change was not significantly different between any of the groups (Table 3).

Safety and Tolerance

Eleven participants in the IG had 1 or 2 falls, whereas 13 participants in the CG had 1 to 3 falls during the intervention period. Three participants did not tolerate the ONS and ceased the supplement intake. One participant experienced more angina pectoris potentially related to the exercise and dropped out. Mean estimated glomerular filtration rate did not change during the intervention in either group.

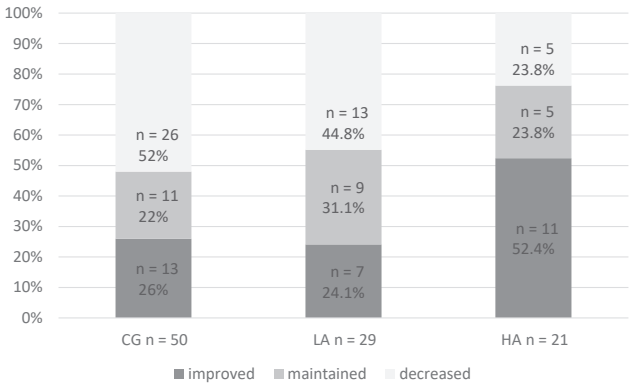

Fig. 2. Percentages of participants in the CG and in the IG with LA, respectively HA who improved, maintained or decreased the number of up-rises in the 30sCST between baseline and follow-up. Differences between the groups were tested with the χ^2 test for linear trend and revealed a significant intervention effect ($P = .025$) on the 30 seconds Chair stand test when the number of up-rises was categorized into improved, maintained and decreased.

Discussion

This study of STS combined with ONS in NH residents did not reveal significant changes in the primary outcome of 30sCST. Secondary outcomes of physical function also did not change significantly, but body weight increased in the IG. Most likely the reason for the weak overall result on 30sCST was the relatively LA to the protocol, with only 21 out of 52 participants demonstrating at least 40% compliance. Accordingly, and potentially encouraging, post hoc analyses indicated that participants with HA to the protocol could improve or maintain their results on the dichotomized 30sCST compared with controls and to participants in the LA group. This subgroup result is in line with earlier findings from Slaughter et al.[17] The crucial role for protocol adherence in intervention studies has been previously reported, for example, in patients with rheumatoid arthritis, where participants with HA demonstrated increased effects of physical activity level in comparison to participants with LA.[34]

Given the methodological challenges of intervention studies in NH contexts, it is perhaps unrealistic to expect positive effects by STS and ONS beyond a fairly fit minority of NH residents. There are several indications that NH populations have changed during the last decades. Because of reasons like ambitions to let older people stay in their home-environment as long as possible, and also economic pressure on the care system, older persons admitted to nursing homes usually are very old, ill, frail, and often in terminal phases of life.[35] This is also evident from the large percentage of screening failures due to inability to stand (48%), and 50% of participants being frail and prefrail.

At baseline, almost two-thirds of the participants had a normal nutritional status according to MNA-SF. However, protein intake may be suboptimal in people with normal nutritional status as well. Therefore, a higher protein intake is now usually recommended to older people because of its importance related to sarcopenia. Interestingly, body weight, FM, FFM, and FFMI increased within the IG, but not in the CG. FFM and FFMI improved and differed significantly between HA group and CG. Such increases in FM, FFM and FFMI may be beneficial, especially for older residents because weight gain, as well as gains in the major body compartments, is associated with improved clinical outcomes. The relatively high proportion of participants having elevated CRP concentrations indicated on-going chronic low-grade inflammatory processes,[36] which may on one hand contribute to muscle catabolism, and on the other hand may counteract anabolic effects of protein supplementation and physical activity. Vitamin D status among the participants was not optimal [ie, one-third (n = 32) displayed serum 25(OH)D concentrations below 50 nmol/L]. Because

Table 3
Comparison of Secondary Outcomes; ie, blood chemistry and health-related QoL and resource use in NH residents allocated to either the CG or the IG. The IG is further divided into participants with HA and LA to the intervention. Data given as mean (SD) if not otherwise depicted.

Variable, n Total (IG + CG)	Total Sample, n = 102	CG, n = 50	IG			*P* Value Between Groups		
			n = 52	HA, n = 21	LA, n = 29	IG-CG	HA-CG	LA-CG
Secondary Outcomes − Blood Chemistry								
P-Albumin, g/L, n = 92 (48 − 44)								
Baseline	34.39 (3.08)	34.34 (3.07)	34.44 (3.12)	35.30 (3.54)	33.85 (2.73)			
Delta	−0.30 (2.35)	−0.20 (2.01)	−0.4 (2.65)	−0.90 (2.27)	−0.07 (2.92)	.53	.17	.72
P value within group	.22	.50	.31	.09	.89	.69	.22	.82
P-Transthyretin, g/L, n = 90 (46–44)								
Baseline	0.21 (0.047)	0.21 (0.04)	0.22 (0.05)	0.22 (0.05)	0.21 (0.05)	.20	.26	.36
Delta median (IQR)	0.00 (−0.02 to 0.01)	0.00 (−0.02 to 0.01)	0.00 (−0.02 to 0.01)	0.00 (−0.01 to 0.01)	0.00 (−0.02 to 0.02)	.30	.26	.47
P value within group	.43	.79	.30	.34	.59			
P-C-reactive protein, mg/L, n = 92 (48–44)								
Baseline	4.15 (5.36)	4.28 (6.40)	4.04 (4.28)	3.70 (4.38)	4.44 (4.27)	.78	.47	.49
Delta, median (IQR)	0.00 (−2.00 to 1.00)	0.00 (−1.50 to 1.00)	0.00 (−2.00 to 1.50)	0.00 (−2.50 to 1.50)	0.00 (−2.00 to 1.00)	.32	.55	.44
P value within group	.35	.58	.45	.52	.82			
S-Insulin-like growth factor-1, μg/L, n = 91 (46–45)								
Baseline	94.05 (36.26)	91.16 (39.64)	96.89 (32.86)	104.45 (37.95)	91.96 (27.81)			
Delta	−0.71 (16.32)	1.51 (15.14)	−2.89 (17.29)	−6.05 (20.12)	−0.12 (14.70)	.46	.25	.78
P value within group	.68	.51	.25	.19	.97	.21	.10	.71
S25 (OH) vitamin D, nmol/L, n = 88 (45–43)								
Baseline	64.6 (27.07)	67.16 (31.2)	62.16 (22.6)	64.35 (22.05)	60.96 (23.62)	.46	.88	.54
Delta	−1.33 (11.15)	−2.44 (10.09)	−0.27 (12.09)	−3.35 ± 11	1.71 ± 12.62	.36	.75	.14
P value within group	.27	.12	.88	.19	.51			
Secondary outcomes − Health-related QoL and Resource Use								
EQ5D-5L, n = 84 (42–42)								
Baseline	0.777 (0.24)	0.791 (0.26)	0.763 (0.23)	0.837 (0.17)	0.693 (0.25)	.60	.48	.16
Delta	0.007 (1.25)	0.031 (0.14)	−0.017 (0.11)	0.011 (0.10)	−0.027 (0.11)			
P value within group	.59	.14	.33	.64	.27	.08	.56	.09
EQ5D-5L VAS, n = 79 (39–40)								
Baseline	67.9 (22.3)	70.5 (22.9)	65.5 (21.6)	68.4 (21.2)	62.6 (22.7)	.32	.74	.21
Delta	−1.18 (24.9)	0.98 (20.0)	−3.17 (28.9)	5.30 (27.9)	−10.00 (29.0)	.46	.51	.09
P value within group	.68	.77	.49	.42	.13			
Caregiver time, min/d, n = 84 (45–39)								
Baseline	92.9 (78.8)	95.1 (86.9)	90.9 (71.9)	59.5 (41.7)	118.3 (82.3)	.81	.09	.30
Delta	−13.2 (55.7)	−10.3 (62.3)	−15.7 (49.8)	−7.1 (39.0)	−23.6 (57.8)	.66	.83	.40
P value within group	*.030*	.31	*.040*	.43	.06			

Delta, change from baseline to follow-up; *SD*, standard deviation.

2622vitamin D deficiency has been associated with reduced muscle mass, strength, and function,[37,38] this finding indicates that vitamin D supplementation could have been beneficial for the participants in this study. Nutritional intervention with an ONS higher in vitamin D and containing specific nutrients with muscle anabolic properties, timed with the STS intervention, may have been able to contribute to a stronger beneficial effect.

Because there were no or very small differences in resource use, it was not regarded as meaningful to calculate and analyze costs. From a health economic view, the focus should be on the outcome, for example, health-related QoL. The self-reported EQ5D-5L is commonly used in health economic studies, but self-reported measures may not be the most appropriate method for older NH residents or for people with dementia.[39] In dementia research, a utility version of the DEM-QOL instrument has been developed that might be more sensitive to detect meaningful changes.[40]

STS is a pragmatic intervention that can be integrated into daily nursing care. However, to change routines in practice is often challenging. Therefore, it is of interest to explore why the participants in the HA group completed the combined intervention to a higher extent compared with the LA group. Reasons could be that the HA participants took larger responsibility and ownership to complete the intervention and/or that they had better physiological preconditions such as less degree of sarcopenia and, therefore, were able to complete the intervention to a higher extent. Maybe the staff members were motivated to integrate the intervention in the daily care and were supported by their managers. A Canadian study exploring NH staff's experiences to support residents to complete STS showed that involvement from management and motivated residents helped the staff to accomplish this task.[41] Forthcoming publications with qualitative interview analyses of residents and staff from the IG will address these stakeholders' perceptions of effects and adherence.

There are several limitations in this study. The current design cannot distinguish which of the 2 modes of intervention (ie, STS or ONS) would be most important for observed effects. We chose to provide the combined intervention because there are indications that

this combination is more effective in older person's than the 2 interventions separately.[7,9] It could also be discussed whether the 30sCST is the best measurement to assess physical function in this population. An alternative could have been to use activity monitors in order to capture smaller changes in daily mobility.[42,43] Another possible weakness is that we did not control for increased voluntary exercise activity besides the STS. A potential confounder could be that we randomized the participants by units and not by NHs, meaning that residents and staff at all units at the NH became aware of the study and its purposes. The sample size was small and hampered subgroup analyses. In addition, because several of the units/clusters consisted of too few participants, we could not conduct multilevel statistics or mixed effect models according to our protocol.[18] As a result, *P* values may be inflated. The adherence documentation was completed by NH staff and because of staff turn-over, information was lacking for 2 residents. The fact that two-thirds of the population had a normal nutritional status may have hampered the anabolic effects of ONS. However, the fact that higher intervention adherence showed improved FFM, and a positive correlation existed between 30sCST and ONS intake, demonstrates that the ONS can be anabolic even under these conditions. Altogether, these weaknesses imply that the findings must be interpreted with caution.

Conclusions and Clinical Relevance

Twelve-week intervention of daily STS combined with ONS in a selected group of NH residents did not improve physical function, but increased body weight. Subgroup analyses indicated that HA to the combined intervention was associated with maintained or improved physical function and a gain of fat-free mass. The nonsignificant result on the primary outcome in this study indicates that the combined intervention is not an optimal intervention for all NH residents, but could be for specific subgroups of residents. We find it important to try to identify subgroups of NH residents that might benefit from this fairly low-intensive intervention. Thus, future analyses from the Older Person's Exercise and Nutrition Study will focus on what characterizes study participants with HA to the intervention, as well as what characterizes those with the greatest improvements on the primary outcome ("responders") during the study period, to understand which subgroups of NH residents would be most suited for this type of intervention in clinical practice.

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