The Journal of Nutrition, Health & Aging©
Volume 16, Number 2, 2012

EFFECTS OF NUTRITIONAL INTERVENTION AND PHYSICAL TRAINING ON ENERGY INTAKE, RESTING METABOLIC RATE AND BODY COMPOSITION IN FRAIL ELDERLY. A RANDOMISED, CONTROLLED PILOT STUDY

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Abstract: *Objectives:* To analyse the effect of nutritional intervention and physical training on energy intake, resting metabolic rate (RMR) and body composition in the frail elderly. *Design:* Open, randomised, controlled pilot treatment study. *Setting:* Community-based research centre. *Participants:* Ninety-six community-dwelling frail elderly people aged 75 and older, 40% men. *Intervention:* Four treatment arms: i) individual nutritional advice and group sessions on nutrition for the elderly, ii) physical training 2 x 45 minutes per week for 3 months, iii) combined nutritional and physical intervention and iv) control group. *Measurements:* The outcomes were energy intake (4-day food diary); resting metabolic rate (indirect calorimetry) and body composition (anthropometry) performed at baseline, after 3 months' intervention (completed by 79 individuals), and as a follow-up at 9 months (completed by 64 individuals). *Results:* The training group showed a significantly increased RMR at 3 months. Otherwise, there were no observed differences within or between the four groups. There was no correlation over time between energy intake, RMR and fat free mass. The participants with a low energy intake who managed to increase their energy intake during the study ('responders') had a statistically significantly lower BMI (21 vs. 24) and a lower fat percentage (23 vs. 30) at baseline than the 'non-responders.' The 'non-responders' showed a small but statistically significant decrease in body fat percentage at F1, and in body weight, BMI and FFM at 9 months (F3). *Conclusion:* Individual nutrition counselling and physical exercise had no effect on energy intake, RMR or fat free mass in community-dwelling frail elderly people aged 75 and older. Interventions in frail elderly people should be targeted according to the needs of the individual patients. The issues of randomisation, targeting and responders in are problematised and discussed.

Key words: Energy intake, frail elderly, resting metabolic rate, body composition, physical training.

Introduction

Nutritional problems in multimorbid elderly people are often accompanied by poor physical function and disablement. The combination of poor nutritional state and impaired physical function constitutes frailty (1) and increases the risk for dependency in daily living and further deterioration of health status. It would be desirable to prevent the frail elderly from reaching the stage where they can no longer live independently.

There are a few published randomised controlled trials (RCT) focusing on both nutrition and physical function in the frail elderly (2-6). A positive energy balance seems to have a positive effect on body weight and possibly on body composition (2-4). Physical training can affect both muscle strength and integrated physical functions such as gait velocity, balance, stairclimbing power, and the overall level of physical activity (2; 4-6). There seems to be little combined effect of nutrition and physical training.

Considering the low number of studies using both nutritional and physical intervention, we decided to conduct a controlled intervention trial in frail elderly people analysing the effects of individualised nutritional intervention and supporting group sessions as well as physical training focusing on endurance, muscle strength and balance. The study was a pilot study working with methods of individualised nutritional intervention, as most other studies have used standardised doses of supplements.

The aim of this pilot RCT was to analyse:

- the effect of individualised nutritional intervention and physical training on energy intake, resting metabolic rate and body composition in frail, community-dwelling elderly, aged 75 and older
- the correlation between energy intake, resting metabolic rate and fat-free mass in the frail elderly

Material and methods

The study was performed on an outpatient basis in an elderly research centre in Solna, a suburb of Stockholm, Sweden, between 2003 and 2005. The study was approved by the research ethics committee at Karolinska Institutet. All participants gave written, informed consent.

Subjects

Subjects were recruited through questionnaires and advertisements in local newspapers, as well as through referrals from primary care and the home service administration organised by the local municipal authorities. Subjects (n=437) who were interested in having their nutritional state analysed and who met the inclusion criteria were contacted by telephone for screening. A final sample of 96 subjects was included in the

Received July 1, 2010
Accepted for publication January 6, 2011

The Journal of Nutrition, Health & Aging©
Volume 16, Number 2, 2012

study.

Inclusion criteria

Included were elderly people, aged 75 and older, defined as frail using the definition by Chin A Paw, comprising both a nutritional and a physical focus (1):

- unintentional weight loss of ≥ 5% during the last year and/or body mass index (BMI) <20 kg/m^2
- low physical activity level (≤ grade 3 in the Mattiasson-Nilo classification of physical activity (7-8).

Exclusion criteria were age under 75, BMI > 30 kg/m^2, non-walkers, recent cardiac problems requiring hospital care, hip fracture or surgery during the last six months, current cancer treatment, stroke within the last two years and less than 7 points of a total 9-point score on the short form of the Mini Mental State Examination (9), and institutionalised residents.

Randomisation

The subjects were randomised consecutively into four different groups. The randomisation procedure was conducted in an open manner by the study personnel with the instructions of a statistician. For each new group, randomisation started with the oldest individual to avoid age differences between groups.

Randomisation was done to the following four intervention groups:

1. Nutrition (N) (n=25): Individual dietary counselling and group session education; general physical training advice
2. Training (T) (n=23): Specific physical training; general dietary advice
3. Nutrition and training (NT) (n=25): Individualised dietary counselling and group session education; specific physical training
4. Control (C) (n=23): General advice regarding diet and physical training

Assessment

The subjects were assessed at baseline (0 months), after three months of treatment (F1) and a 9-month follow-up (F2). The study was completed without blinding.

The subjects were initially examined by the geriatrician for medical history, continuous medication, physical status, living arrangements and type of walking aid.

Nutritional intake

Food intake was analysed using a four-day food record, where the participants reported intake of all foods and beverages. At the home visit, a nutritionist/dietician went through the record verifying details of foods and amounts consumed. Questions were asked regarding appetite, cooking, buying groceries and meal patterns. The food intake data was computerised, and energy content was calculated using StorMATS (version 4.06, 2002, RUDANS LÄTTDATA, Västerås, Sweden) and the Swedish national nutrient database, PC-kost (version 02_1, National Food Administration, 2002). Missing values in the database were queried on the producers' websites, and entered into the program when available; otherwise similar products were chosen.

Mini nutritional assessment

The Mini Nutritional Assessment (MNA) (10) was completed.

Resting metabolic rate

Resting metabolic rate (RMR) was measured by indirect calorimetry, using an MBM-200 Delta Trac II metabolic monitor (DATEX, Engström, Finland). Each morning a calibration was done using a test gas of known composition. The study subjects arrived at the centre fasting and rested for 30 minutes before RMR was measured for another 30 minutes. The results were extrapolated to MJ per 24 hours. The physical activity level (PAL) was estimated as energy intake/RMR.

Body composition

The patients were weighed, in underwear, to the nearest 0.1 kg on a digital chair scale (UMEDICO SV-600, Rosersberg, Sweden). Height was measured to the nearest centimetre using a stadiometer. Four skinfolds were measured using a Harpenden calliper (British indicators Ltd, Bedfordshire, UK) (11) and the mean of three measurements to the nearest 0.1 mm was recorded. Body density and fat mass were calculated from the sum of these four skinfolds using prediction equations (12-13). Fat-free mass (FFM) was calculated as body weight minus fat mass. Body composition was also measured using whole-body dual energy x-ray absorptiometry (DXA). Due to the expense of the scan, DXA was only used at baseline and at the nine-month follow-up. Conventional anthropometric results were used for the longitudinal analyses.

Physical performance

Personal activities of daily living (pADL) were estimated with the Functional Independence Measure (FIM) (14-15). This is a 13-item (motor items), 7-graded ordinal scale with a maximal score of 91. Grade 6 and 7 indicate independence with or without devices, respectively. Instrumental activities of daily living (iADL) were estimated using Instrumental Activity Measures (IAM), a supplementary scale to FIM (16). This is a 8-item (e.g. cleaning, washing, cooking, shopping, public transportation, etc.), 7-graded ordinal scale with a maximal score of 56. Grade 6 and 7 indicate independence with or without devices, respectively.

After baseline examinations and randomisation, participants were invited to a meeting, where each group received information on their treatment and written summaries of their individual baseline results.

Intervention

Nutritional intervention

The nutritional intervention consisted of individual dietary counselling based on the baseline food record data focusing on food choices and meal patterns. Energy needs of each individual were estimated as 1.4 x RMR for the N group, and

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1.5 x RMR for the NT group.

When analysing the results a sufficient energy intake was considered 1.4 x RMR for the C-group and 1.5 x RMR for the T-group, in analogy with the N and NT groups, respectively.

At each session, a nutritionally well-balanced snack was served. The T and C groups received general advice regarding nutrition for the elderly. Protein and micronutrients were considered during counselling, however, not analysed in this study. Suggestions that would cover the needs of each individual were presented and discussed at an individual session lasting about one hour. The nutritional intervention included five group sessions that covered such topics as nutritional needs for the elderly, meal frequency and cooking methods.

Physical training

The exercise program has been described elsewhere (17). In short, the physical training consisted of 60-minute organised sessions twice a week for twelve weeks, with emphasis on endurance, muscle strength and balance. The program consisted of three corresponding sections: i) warm-up including aerobic training, ii) individually prescribed muscle strength training, and iii) Qigong including cool-down. The warm-up/aerobic training section consisted of standing exercises, such as walking/jogging on the spot, walking forwards/backwards and sideways, and arm movements. The muscle-strength training section consisted of two separate stations: high intensity strength training on stationary equipment and functional strength training with weight belts. The balance training section consisted of different Qigong exercises performed on different degrees of supporting area combined with arm and trunk movements. These exercises were progressed with increasing difficulty. The training program was planned by the physiotherapist and led by a trained instructor with the assistance of a physiotherapy assistant.

Statistical analysis

Longitudinal changes within study groups, based on an intention-to-treat analysis, were tested by pairwise t-tests, as were comparisons between "responders" and "non-responders" regarding adherence to the recommendation to increase energy intake. For treatment effects at F1 compared to baseline within study groups, confidence intervals were used in addition to t-tests.

Comparisons between treatment groups were made by analysing variance (ANOVA) using the differences between baseline and follow-up. The level of significance was $p<0.05$ for all analyses.

The correlations between energy intake, RMR and FFM were tested at baseline and the two follow-ups. A correlation matrix was also calculated and mean correlations and confidence intervals were created for each pair of correlations to test the longitudinal relationship between these parameters.

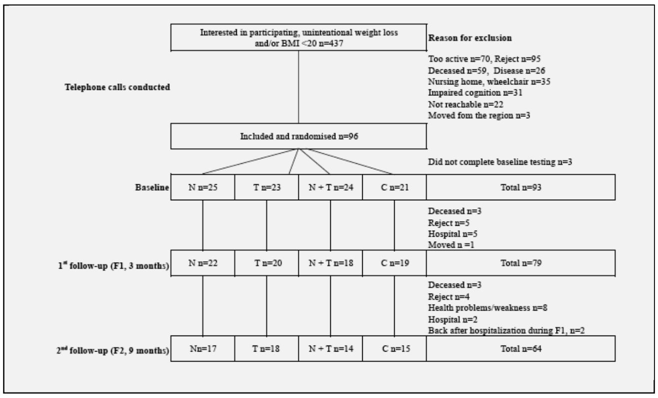
The matter of power calculation is addressed in Discussion. The statistical analysis was conducted in JMP 5.0 (SAS Institute, USA) and in Microsoft Excel 2000. Continuous data is presented by mean (m) and standard deviation (sd), and ordinal data with median (md) and first and third quartiles (q1-q3).

Results

Figure 1 shows detailed information on inclusion criteria and drop-out rates. All data collection was complete by December 2005. Three individuals dropped out during baseline testing and were excluded from analysis. This left 93 individuals in the study (40% men). Table 1 shows the baseline characteristics of the study population for each treatment group. The four groups were comparable at baseline, except that there were significantly more men in the training group compared with the control group. The median MNA score was just at or above the "risk for malnutrition" cut-off point of 23.5, and three individuals were classified as "malnourished" by the MNA (10). The majority of participants were practically independent in pADL, but there was a large variation between individuals in iADL.

Figure 1

Flow of study participants: Recruitment, inclusion/exclusion and dropout from baseline to 2nd follow-up



N = nutrition, T = training, C = control, F1 = 1st follow-up, F2 = 2nd follow-up

The baseline anthropometric data of the body fat percentage were statistically different from the DXA results, but as this difference was only 1.3 percentage units, and the correlation coefficient between the two methods was 0.85, we did not consider this difference relevant for the further analysis.

Table 2 shows the outcome variables at baseline and first follow-up (F1). The mean energy intake at baseline was 6.6 MJ/d (1,574 kcal/d) for the total study population, with no significant differences between treatment groups. The mean RMR was approximately 4.7 MJ/d (1,120 kcal/d) in all groups, resulting in a mean physical activity level (PAL) of 1.4. The mean percentage of body fat varied between 24 and 27% in the groups. The data for F2 did not differ significantly from the data on F1 (not shown).

Results of intervention

When analysing the results, a sufficient energy intake was considered 1.4 x RMR for the C-group and 1.5 x RMR for the

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Table 1
Baseline characteristics of study participants

	Treatment group									
Variable	**N[a]**	**SD[b]/ q1;q3[c]**	**T[g]**	**SD/ q1;q3**	**N + T**	**SD/q1;q3**	**C[h]**	**SD/q1;q3**	**All**	**SD/q1;q3**
Number of participants	25		23		24		21		93	
Men, %	40		52*		36		30		40	
Age, mean (SD)	82.5	4.4	83.0		82.6	4.0	82.4	3.9	82.6	4.0
BMI[i], mean (SD)	21.8	3.4	21.9		21.9	3.4	21.6	3.6	21.8	3.5
MNA[d], median (q1;q3)	24.5	21.5;25.5	23.5	22;25	24	21;26	24.5	23;26.5	24.5	22;25.5
pADL[e] median (q1;q3)	88	87;89	88	83;89	85	81;88	88	83;90	88	83;89
iADL[f] median (q1;q3)	45	39;49	38	33;43	42	30;48	43	37;48	42	35;48
Living alone, n	14		8		16		16		54	
Sheltered living for elderly, n	1		1		2		1		5	
Use of walking aids indoors, n	4		6		9		5		24	
Prescribed medications, median (q1;q3)	7	5;8	6	4.5;8.5	6	4;7	6.5	4;8	6	4;8

a. N, nutrition; b. SD, standard deviation; c. 1;q3, 1st and 3rd quartiles; d. MNA, Mini Nutritional Assessment, scale maximum 30; e. pADL, personal activities of daily living, using Functional Independence Measure (FIM), scale maximum 91; f. iADL, instrumental activities of daily living, using Instrumental Activity Measures (IAM), scale maximum 56; g. T, training; h. C, control; i. BMI, body mass index (kg/m^2); * Significantly different from control group ($p<0.05$)

Table 2
Baseline results and changes within groups at first follow-up at 3 months for the four treatment groups

	Treatment group									
Variable	**N[a]**	**SD[b]**	**T[c]**	**SD**	**N + T**	**SD**	**C[d]**	**SD**	**All**	**SD**
Number of participants at baseline/follow-up 1	25/22		23/20		24/18		21/18		93/79	
Energy intake (MJ/d)[e]										
Baseline, mean	6.8	2.0	6.0	1.5	6.8	2.0	6.7	1.7	6.6	1.8
Change at follow-up 1	0.27		0.31		0.14		0.27		0.25	
95% CI[f] for change	-0.41,0.95		-0.21,0.83		-0.68,0.97		-0.50,1.04		-0.09,0.60	
RMR[g] (MJ/d)										
Baseline, mean	4.7	0.6	4.8	0.7	4.7	1.0	4.7	0.8	4.7	0.8
Change at follow-up 1	0.08		0.12*		0.14		0		0.14	
95% CI for change	-0.07,0.23		0.03,0.21		-0.10,0.39		-0.20,0.20		0.00,0.28	
Body weight (kg)										
Baseline, mean	60.1	10.3	58.3	11.1	59.0	11.8	57.1	9.9	58.6	10.7
Change at follow-up 1	0.8		-0.1		-0.3		0.6		0.3	
95% CI for change	-0.1,1.7		-0.8,0.6		-1.1,0.6		-0.5,1.7		-0.2,0.7	
Fat-free mass (kg)										
Baseline, mean,	43.5	8.0	43.9	8.1	43.1	8.9	42.4	8.2	43.3	8.2
Change at follow-up 1	0.7		-0.4		0.2		0.3		0.2	
95% CI for change	0, 1.5		-1.1,0.2		-0.3,0.7		-0.5,1.1		-0.1,0.6	
Body fat (%)										
Baseline, mean	24.2	7.5	27.4	7.9	27.3	7.1	26.5	6.4	26.4	7.3
Change at follow-up 1	0.6		-0.3		-0.6		0.1		-0.04	
95% CI for change	-0.2,1.4		-0.8,0.3		-1.8,0.6		-0.6,0.8		-0.5,0.4	
Waist circumference (cm)										
Baseline, mean	83	11.6	83.6	11.1	84.2	10.3	82.7	9.5	83.4	10.5
Change at follow-up 1	0.05		-0.6		-0.2		2.3*		0.4	
95% CI for change	-1.7,1.8		-1.9,0.7		-1.7,1.3		0.6, 3.9		-0.4,1.2	

a. N, nutrition; b. SD, standard deviation; c. T, training; d. C, control e. MJ/d, megajoule per day; f. CI, confidence interval; g.RMR, resting metabolic rate; * Significantly different from baseline ($p<0.05$).

T-group, in analogy with the N and NT groups, respectively. Analysis within treatment groups showed that the changes from baseline to follow-up 1 (F1) at three months and follow-up 2 (F2) at nine months were very small. At F1, there was a significant increase in RMR in the T group at F1. The C group showed a significant increase in waist circumference. Otherwise, we observed no effects of the intervention in energy intake, RMR, or body composition.

Analysis between treatment groups by ANOVA showed no significant differences. An analysis of the combined nutrition groups (N+NT) compared with the combined training and control groups (T+C) provided no further information.

Table 3 shows the number of individuals in each treatment group who would have needed to increase their energy intake by 20% or more to reach 1.4/1.5 x RMR. Of the 49 subjects receiving nutritional treatment (N+NT), 16 needed to increase their energy intake by 20% or more to reach 1.4/1.5 x RMR, but only 6 reached the desired level ("responders"). Similarly, of the 44 individuals in the training and control groups, 16 would have needed to increase their energy intake by 20% or more to reach 1.5/1.4 x RMR. Without nutrition intervention, 7 individuals reached this level. The 13 energy intake responders of all four groups combined had a lower BMI (21 vs. 24) and a lower fat percentage (23 vs. 30) at baseline than the non-responders. The responders did not show any change in any outcome variable, but the non-responders showed a small, statistically significant decrease in body fat percentage at F1, and in body weight, BMI and FFM at F2.

Table 3
Energy intake: need and outcome

Variable	Treatment group				
	N[a]	T[b]	N + T	C[c]	ALL
Number of participants	25	23	24	21	93
Number of individuals who would have needed to increase energy intake by ≥ 20%[d]	7	11	9	5	32
Number who received individual recommendations to increase energy intake	7	0	9	0	16
Number of those in need of increased energy intake who succeeded, "responders"	3	5	3	2	13
Number of those in need of increased energy intake who failed, "non-responders"	4	6	6	3	19
Total number who increased energy intake	7	6	4	7	24
Number of drop-outs who needed to increase energy intake (of total number of drop-outs)	0 (3)	2 (3)	1 (6)	2 (2)	5 (14)

a. N, nutrition; b. T, training; c. C, control; d. Increase in energy intake refers to an increase of ≥20% throughout the table

Analysing the correlation between energy intake, RMR, and FFM showed a correlation of about 0.75 between FFM and RMR for all groups combined at each of the three assessments. Correlations with energy intake for both FFM and RMR varied between 0.27 and 0.49, with the lowest correlation at F2. Analysis of correlation at an individual level for all three assessments did not provide any further information. The results regarding physical function and effect of physical training has been published separately (17).

Discussion

To our knowledge, this is the first RCT in community-dwelling frail, elderly people aged 75 and over that has applied individualised dietary counselling and tried to work with food choices and eating patterns instead of standardised supplements. This approach resembles clinical routine practice and also serves an educational and participatory purpose.

Except for a small, but statistically significant, increase in RMR in the T group, we observed no evident mean treatment effects on energy intake, RMR or body composition. Those participants assessed as needing increased energy intake and also managed to actually increase their energy intake regardless of treatment (responders), seemed to be protected against further negative effects on body composition. We believe that the small differences and lack of significant effects of nutrition intervention in this and similar studies (2-5, 18) may be due to the heterogeneity of the study population, and the non-targeted treatment due to randomisation (see below).

Levels of energy intake

The levels of energy intake were estimated in relation to the measured RMR, which showed that the majority of the study participants had a sufficient energy intake. In healthy elderly individuals, a level of 1.5 x RMR has been recommended when estimating energy needs (19). Using the doubly labelled water technique, this seems to be correct in those aged 80 and older, but in younger populations it is probably too low (20-21). The frail elderly in this study were included partly based on their low physical activity, and were estimated to have a low ratio between energy intake and RMR; i.e., energy available for physical activity.

The optimal energy intake in the frail elderly is not known. Of those subjects who were recommended to increase energy intake, only 6 of 16 actually managed to increase their intake, while 7 of 16 with a low energy intake in the training and control groups also increased energy intake without specific dietary advice. We do not know the reason for this. One may speculate that the lower BMI and fat mass of the "responders" might have made them more aware of their need for nutritional improvement. We chose a cut-off level of 20% for increase in energy intake because we considered this to exceed day-to-day variation, and therefore to be of clinical relevance.

Correlation between energy intake, FFM, and RMR

There were no correlations over time between energy intake, RMR and FFM. We became aware of this issue in a previous study, when we analysed the relationship between energy intake and body weight over time and found no such relationship (22). This indicates that one may not expect a direct effect of an increased energy intake on body composition in this patient group.

Nutritional intervention and its effects

Since all food diaries were evaluated in detail by a nutritionist or dietitian together with each elderly person, we believe that the recorded dietary intake represented the actual intake. We were not as successful as we had hoped in changing the eating patterns and food choices of these elderly individuals. This is, however, a general problem in studies intending to change food habits, well known in, for example, the obesity literature. Most studies in the existing literature have used standardised oral nutrition supplements in the nutritional intervention, which have the advantages of precision and the ability to use a placebo. There are also disadvantages:

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Standardised doses of oral supplements do not consider differing individual needs. Moreover, compliance can be poor and supplements may decrease food intake, giving no net effect on energy intake (2). Some previous supplement studies have shown an increase in body weight, but no effect on muscle mass (4, 23).

Limitations of the study

The large clinical heterogeneity for the included frail population regarding mixture of diseases and/or injuries and unknown degree of potential effect(s) of interventions with physical exercise and/or nutrition made it impossible to perform a standard power calculation. We therefore decided to conduct the intervention study as a pilot RCT to provide both methodological and clinical information. Available resources made it reasonable to include around 100 subjects.

There is no consensus regarding the definition of frailty and many different definitions are presented in the literature (1, 24-25). The definition of frailty used in the present study was chosen on the basis of the published literature at that time, but also for logistic and economical reasons. A more narrow definition would probably have resulted in a more homogeneous group. On the other hand, it has been suggested that a broad definition increases generalization (26).

Study design development

The lack of observed effect of nutritional intervention on body composition in the frail elderly in this and previous studies demonstrates the need to develop the methods for nutritional intervention, including educational support to the participants and choice of outcome measures.

It is generally accepted and taught that the randomised controlled design constitute a scientific standard for treatment studies. During this study, we questioned if it is ethically acceptable to provide only physical training to individuals who are in obvious need of nutritional support, and vice versa. In the training group, 11 of 23 individuals would have needed an increased energy intake of 20% or more to reach 1.5 x RMR, but did not receive any specific nutritional support. Our experiences during this study highlighted the importance of targeting the treatment according to the needs of the patient. We realise that scientific quality will be questioned without randomisation, but we hope our results will stimulate a discussion regarding this issue in the field of treatment studies in the frail elderly.

Acknowledgements: The authors give special thanks to dietician Stina Engelheart for her excellent participation in the practical work during the study. Thanks to statistician Anna Törner for statistical advice. Thanks to the responsible municipal authorities of the city of Solna for supporting the start-up of the project and for putting premises at our disposal. The study was financed by Äldreforskning NordVäst, a local research centre for the elderly, where the authors were employed full time when performing the study. There were no conflicts of interest. Eva Lammes planned the nutritional analyses and intervention of the study and performed them in collaboration with the dietician. She analysed data and wrote the core of the manuscript. Elisabeth Rydwik planned the physical part of the study and performed the physical tests, and took part in the writing of the manuscript. Gunnar Akner was responsible for the overall planning of the study, performed the medical assessments, and took part in the writing of the manuscript.

References

1. Chin A Paw MJ, Dekker JM, Feskens EJ, Schouten EG, Kromhout D, How to select a frail elderly population? A comparison of three working definitions. J Clin Epidemiol 1999; 52: 1015-21
2. Fiatarone MA, O'Neill EF, Ryan ND, Clements KM, Solares GR, Nelson ME, Roberts SB, Kehayias JJ, Lipsitz LA, Evans WJ. Exercise training and nutritional supplementation for physical frailty in very elderly people. N Engl J Med 1994; 330: 1769-75
3. Singh MA. Combined exercise and dietary intervention to optimize body composition in aging. Ann N Y Acad Sci 1998; 854: 378-93
4. Bonnefoy M, Cornu C, Normand S, Boutitie F, Bugnard F, Rahmani A, Lacour JR, Laville M. The effects of exercise and protein-energy supplements on body composition and muscle function in frail elderly individuals: a long-term controlled randomised study. Br J Nutr 2003; 89: 731-9
5. Chin A Paw MJ, de Jong N, Schouten EG, Hiddink GJ, Kok FJ. Physical exercise and/or enriched foods for functional improvement in frail, independently living elderly: a randomized controlled trial. Arch Phys Med Rehabil 2001; 82: 811-7
6. Rosendahl E, Lindelof N, Littbrand H, Yifter-Lindgren E, Lundin-Olsson L, Haglin L, Gustafson Y, Nyberg L. High-intensity functional exercise program and protein-enriched energy supplement for older persons dependent in activities of daily living: a randomised controlled trial. Aust J Physiother 2006; 52: 105-13
7. Mattiasson-Nilo I, Sonn U, Johannesson K, Gosman-Hedstrom G, Persson GB, Grimby G. Domestic activities and walking in the elderly: evaluation from a 30-hour heart rate recording. Aging (Milano) 1990; 2: 191-8.
8. Frändin K, Grimby G. Assessment of physical activity, fitness and performance in 76-yearolds. Scand J Med Sci Sports 1994; 4: 41-6
9. Callahan CM, Unverzagt FW, Hui SL, Perkins AJ, Hendrie HC. Six-item screener to identify cognitive impairment among potential subjects for clinical research. Med Care 2002; 40: 771-81
10. Vellas B, Guigoz Y, Garry PJ, Nourhashemi F, Bennahum D, Lauque S, Albarede J. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. Nutrition 1999; 15: 116-22
11. Edwards DA, Hammond WH, Healy MJ, Tanner JM, Whitehouse RH. Design and accuracy of calipers for measuring subcutaneous tissue thickness. Br J Nutr 1955; 9: 133-43
12. Siri W. Techniques for measuring body composition. 1961. Washington D.C.: National Academy of Sciences, National Research Council.
13. Durnin JV, Womersley J. Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. Br J Nutr 1974; 32: 77-97
14. Kidd D, Stewart G, Baldry J, Johnson J, Rossiter D, Petruckevitch A, Thompson AJ. The Functional Independence Measure: a comparative validity and reliability study. Disabil Rehabil 1995; 17: 10-14
15. Daving Y, Andren E, Nordholm L, Grimby G. Reliability of an interview approach to the Functional Independence Measure. Clin Rehabil 2001; 15: 301-10
16. Grimby G, Andren E, Daving Y, Wright B. Dependence and perceived difficulty in daily activities in community-living stroke survivors 2 years after stroke: a study of instrumental structures. Stroke 1998; 29: 1843-9
17. Rydwik E, Lammes E, Frändin K, Akner G. Effects of a physical and nutritional intervention program for frail elderly people over age 75. A randomized controlled pilot treatment trial. Aging Clin Exp Res 2008; 20: 159-70
18. de Jong N, Chin APMJ, de Groot LC, Hiddink GJ, van Staveren WA. Dietary supplements and physical exercise affecting bone and body composition in frail elderly persons. Am J Public Health 2000; 90: 947-54
19. FAO-WHO-UNU. Energy and protein requirements. 1985. WHO technical report series. Geneva: World Health Organization
20. Starling RD, Poehlman ET. Assessment of energy requirements in elderly populations. Eur J Clin Nutr 2000; 54: Suppl 3, S104-11
21. Roberts SB, Dallal GE. Energy requirements and aging. Public Health Nutr 2005; 8: 1028-36
22. Lammes E, Akner G. Repeated assessment of energy and nutrient intake in 52 nursing home residents. J Nutr Health Aging 2006; 10: 222-230
23. Payette H, Boutier V, Coulombe C, Gray-Donald K. Benefits of nutritional supplementation in free-living, frail, undernourished elderly people: a prospective randomized community trial. J Am Diet Assoc 2002; 102: 1088-95
24. Fried LP, Tangen CM, Walston J et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001; 56: M146-56.
25. Studenski S, Hayes RP, Leibowitz RO et al. Clinical global impression of change in physical frailty: Development of a measure based on clinical judgement. J Am Geriatr Soc 2004; 52: 1560-6.
26. Ferrucci L, Guralnik JM, Studenski S, Fried LP, Cutler GB, Walston JD. Designing randomized, controlled trials aimed at preventing or delaying functional decline and disability in frail older persons: a consensus report. J Am Geriatr Soc 2004; 52: 625-34.