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## EXERCISE TRAINING AND NUTRITIONAL SUPPLEMENTATION FOR PHYSICAL FRAILTY IN VERY ELDERLY PEOPLE

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**Abstract Background.** Although disuse of skeletal muscle and undernutrition are often cited as potentially reversible causes of frailty in elderly people, the efficacy of interventions targeted specifically at these deficits has not been carefully studied.

**Methods.** We conducted a randomized, placebo-controlled trial comparing progressive resistance exercise training, multivitamin supplementation, both interventions, and neither in 100 frail nursing home residents over a 10-week period.

**Results.** The mean ( $\pm$ SE) age of the 63 women and 37 men enrolled in the study was  $87.1 \pm 0.6$  years (range, 72 to 98); 94 percent of the subjects completed the study. Muscle strength increased by  $113 \pm 8$  percent in the subjects who underwent exercise training, as compared with  $3 \pm 9$  percent in the nonexercising subjects ( $P < 0.001$ ). Gait velocity increased by  $11.8 \pm 3.8$  percent in the exer-

cisers but declined by  $1.0 \pm 3.8$  percent in the nonexercisers ( $P = 0.02$ ). Stair-climbing power also improved in the exercisers as compared with the nonexercisers (by  $28.4 \pm 6.6$  percent vs.  $3.6 \pm 6.7$  percent,  $P = 0.01$ ), as did the level of spontaneous physical activity. Cross-sectional thigh-muscle area increased by  $2.7 \pm 1.8$  percent in the exercisers but declined by  $1.8 \pm 2.0$  percent in the nonexercisers ( $P = 0.11$ ). The nutritional supplement had no effect on any primary outcome measure. Total energy intake was significantly increased only in the exercising subjects who also received nutritional supplementation.

**Conclusions.** High-intensity resistance exercise training is a feasible and effective means of counteracting muscle weakness and physical frailty in very elderly people. In contrast, multivitamin supplementation without concomitant exercise does not reduce muscle weakness or physical frailty. (N Engl J Med 1994;330:1769-75.)

THE decline in muscle strength and mass during aging<sup>1,2</sup> has been linked to physical frailty, falls, functional decline, and impaired mobility in very elderly people.<sup>3-5</sup> Although many factors, including chronic illness, a sedentary lifestyle, nutritional deficiencies, and aging itself, may contribute to muscle weakness and loss of skeletal-muscle mass in people of

advanced age,<sup>6-10</sup> currently only skeletal-muscle disuse<sup>11,12</sup> and undernutrition<sup>13-15</sup> are potentially preventable or reversible with targeted interventions.

Muscle dysfunction associated with malnutrition may improve with nutritional supplementation in younger patients.<sup>16,17</sup> Even in healthy elderly men, a multivitamin supplement augmented muscle hypertrophy, although not muscle strength, during a resistance training regimen similar to the one described here.<sup>18</sup>

We hypothesized that physical frailty is partially mediated by skeletal-muscle disuse and marginal nutritional intake, and should therefore be reduced by interventions designed to reverse these deficits.

## METHODS

### Study Design

Detailed descriptions of the rationale and design of the Boston FICSIT (Frailty and Injuries: Cooperative Studies of Intervention Techniques) study<sup>19</sup> and the entire FICSIT trial<sup>20</sup> have been published elsewhere. Briefly, the Boston FICSIT study was a randomized, placebo-controlled, 10-week clinical trial in which the subjects were assigned to receive lower-extremity resistance training, a multivitamin supplement, both treatments, or a placebo activity and

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supplement. The study was approved by the human investigations review committees at New England Medical Center and the Hebrew Rehabilitation Center for Aged, and written informed consent was obtained from each subject.

### Study Population

Volunteers were recruited from the residents of a 725-bed facility providing long-term care of the elderly. The criteria for inclusion were residential status, an age over 70 years, and the ability to walk 6 m. Subjects were excluded if they had severe cognitive impairment, rapidly progressive or terminal illness, acute illness or unstable chronic illness, myocardial infarction, fracture of a lower extremity within the six months before the study, or insulin-dependent diabetes mellitus; if they were on a weight-loss diet or undergoing resistance training at the time of enrollment; or if tests of muscle strength revealed a musculoskeletal or cardiovascular abnormality.

### Interventions

#### Resistance Training

Subjects assigned to exercise training underwent a regimen of high-intensity progressive resistance training<sup>21</sup> of the hip and knee extensors 3 days per week for 10 weeks. These muscle groups were chosen because of their importance in functional activities.<sup>22</sup> For each muscle group, the resistance was set at 80 percent of the one-repetition maximum (the maximal load that could be lifted fully one time only).<sup>23</sup> To maintain the intensity of the stimulus, the load was increased at each training session, as tolerated by the subject. Strength testing was repeated every two weeks to establish a new base-line value.

Training sessions lasted 45 minutes and were separated by one day of rest. Each repetition lasted six to nine seconds, with a one- to two-second rest between repetitions and a two-minute rest between the three sets of eight lifts. All exercise sessions were supervised individually by a single exercise trainer, who was a certified therapeutic recreation specialist.

The knee extensors were trained with the use of the UNEX II chair (J.A. Preston, Clifton, N.J.). The hip extensors were trained in the first 53 subjects with the use of a wall-mounted cable-pulley system (G.E. Miller, New York). In the other 47 subjects, a double leg press (Keiser Sports Health Equipment, Fresno, Calif.) was used in place of the cable-pulley system, since it allowed for better positioning of the subject. There were no differences at base line or in treatment outcomes between subjects trained on these two machines.

#### Placebo Activities

All subjects not randomly assigned to resistance training engaged in three activities of their choice offered by the recreational-therapy service of the facility. No resistance training was allowed, but aerobic or flexibility exercises were permitted. Typical activities were walking, calisthenics while the subject was seated, board games, crafts, concerts, and group discussions.

#### Nutritional Supplement

The nutritional supplement (Exceed; Ross Laboratories, Columbus, Ohio) was given once each day in the evening for 10 weeks to minimize the effect of exercise training on habitual food intake. The supplement, a 240-ml liquid supplying 360 kcal in the form of carbohydrate (60 percent), fat (23 percent), and soy-based protein (17 percent), was designed to augment caloric intake by about 20 percent<sup>24</sup> and provide one third of the recommended daily allowances of vitamins and minerals.<sup>25</sup>

#### Placebo Supplement

All subjects not receiving the experimental supplement were given an equal volume of a minimally nutritive (4 kcal), artificially sweetened, flavored liquid (Crystal Light; Kraft General Foods, White Plains, N.Y.).

The supplements and placebos were administered in unmarked

containers by the nursing staff, who were unaware of the contents of the containers and the group assignments.

### Clinical Characteristics

Medical records were abstracted to obtain clinical information and ratings of functional status by the clinical nursing staff; scores on the Katz Activities of Daily Living Index were derived from these data. The Mini-Mental State Examination<sup>26</sup> and the Geriatric Depression Scale<sup>27</sup> were administered by the research staff.

### Muscle Function

The maximal weight that could be lifted correctly for one repetition only was used as the measure of dynamic concentric muscle strength in the hip and knee extensors. To minimize improvement related to repeated testing, the better of two measurements obtained one week apart was used as the base-line value. Strength measurements in this population are highly reliable ( $r = 0.85$ ,  $P < 0.001$ ). The final test of muscle strength was performed during the week after the intervention. All measurements were made by a single observer (who was aware of group assignments but not involved in training). During the first session only, continuous electrocardiographic monitoring was used.

### Physical Function

Gait velocity over a 6.1-m course was measured to the nearest 0.01 second and calculated as the average velocity in two trials, with a test-retest correlation coefficient of 0.99 ( $P < 0.001$ ). Stair-climbing power was calculated<sup>28</sup> as the better value in two trials on a four-riser staircase with banisters. Repeated measures were reliable ( $r = 0.98$ ,  $P < 0.001$ ).

### Nutritional Intake

Habitual dietary intake, calculated to the nearest 0.1 g, was measured by weighing food over a three-day period during the week before and the 10th week of the intervention.<sup>29</sup> Food records were analyzed by the Human Nutrition Research Center, Division of Scientific Computing, with the Grand nutrient software system (Grand, release 9127190; Department of Agriculture Grand Forks Human Nutrition Research Center, Grand Forks, N.D.). The coefficient of variation for daily energy intake was 13.9 percent. The variables used in the analyses of energy intake included dietary energy intake (energy intake from diet and any clinically prescribed supplements) and total energy intake (dietary energy intake plus the energy content of the research supplement or placebo drink).

### Body Composition

#### Anthropometric Measurements

Each subject's weight (without clothing), calculated to the nearest 0.001 kg, was measured on a computerized force-transducer scale (Sartorius, Model F330S; Berlin, Germany) after a 12- to 14-hour fast. Standing height, calculated to the nearest 0.25 cm, was measured with a wall-mounted stadiometer. The body-mass index was calculated as the weight in kilograms divided by the square of the height in meters. Midthigh circumference, calculated to the nearest 0.1 cm, was measured with a fiberglass tape (Lafayette Instrument, Indianapolis) at the midpoint between the inguinal crease and the proximal pole of the patella.

#### Whole-Body Potassium

Whole-body potassium was measured as an index of body cell mass, which includes skeletal muscle.<sup>29</sup> The coefficient of variation for weekly anthropomorphic phantom measurements was 5 percent.

#### Computed Tomographic Scans of the Midthigh

The muscle groups involved in the resistance training and mobility tests were scanned at the nondominant midthigh site.<sup>30</sup> The scanner used for the first 85 subjects was a Siemens DR3 (Somatom-Siemens; Erlangen, Germany). For the other 15 subjects, the scanner was a Sytec 4000 (General Electric, Milwaukee). All computed

tomographic (CT) images were analyzed according to optical density on a computer (Macintosh IIci, Apple; Sunnyview, Calif.) by a single investigator in a blinded fashion, with Image software (Version 1.49, National Institutes of Health) modified for quantification of cross-sectional areas of muscle, bone, and fat to the nearest 0.01 cm<sup>2</sup>. The coefficient of variation for repeated measurements of a single scan was less than 0.5 percent. CT data were complete for 61 of the subjects; incomplete data for the other 39 were due to technical difficulties with data extraction or artifacts on scans. There were no differences between the subgroups of subjects who had scans at either time and the entire sample.

### Physical Activity

The level of physical activity was estimated with large-scale, integrated activity monitors (GMM; Verona, Pa.) worn around both ankles during the 72-hour period when food intake was being recorded.<sup>31</sup> Habitual physical activity included all control and experimental activities, as well as all spontaneous leg movements. The average count per 24 hours (summing the values for both legs) was used in subsequent analyses. The manufacturer ceased production of the monitors in the middle of the study, after the activity level had been measured in 45 subjects. There were no differences between this subgroup and the entire study group. The coefficient of variation for sequential daily recordings was 24.7 percent.

### Statistical Analysis

All data were analyzed with Systat statistical software (Systat; Evanston, Ill.) or Statview (Abacus; Berkeley, Calif.).<sup>32</sup> Intention-to-treat analyses were used for the primary outcome variables. Lin-

ear regression was used to determine the appropriateness of the subsequent analyses of variance and covariance. Non-normally distributed data were subjected to log transformation before being analyzed for variance and covariance. A three-factor, repeated-measures analysis of variance was used to determine the effects of exercise and nutritional supplementation on the primary outcome variables, as well as to determine any interaction between exercise and nutritional supplementation. Analyses of covariance were used to adjust for clinically pertinent base-line characteristics (age, sex, muscle strength, and functional status) and any differences in other clinical characteristics. When F ratios were significant, post hoc comparisons of means were analyzed with Tukey's multiple-comparison test. Relations among variables of interest were analyzed pairwise with Pearson's correlation coefficients or Spearman's rank correlation coefficients, as appropriate, with the Bonferroni correction for multiple comparisons. Forward stepwise multiple-regression models were used to determine multivariate relations among variables that were significant in the univariate analyses. A two-sided P value less than or equal to 0.05 was considered to indicate statistical significance.

## RESULTS

### Recruitment

Of the 1306 residents of the Hebrew Rehabilitation Center for Aged who were available during the enrollment period, 349 were considered potentially eligible to participate in the study, none of whom were excluded during initial tests of muscle strength. One

Table 1. Base-Line Characteristics of the Subjects.\*

CHARACTERISTIC	STUDY GROUP			
	EXERCISE (N = 25)	EXERCISE PLUS SUPPLEMENT (N = 25)	SUPPLEMENT (N = 24)	CONTROL (N = 26)
Demographic and clinical characteristics				
Age (yr)	86.2±1.0 (72-95)	87.2±1.2 (76-98)	85.7±1.2 (75-97)	89.2±0.8 (78-98)
Female sex (% of subjects)	64	64	71	54
Level of dependence (% of subjects)				
Independent	32.0	36.0	41.7	38.5
Semidependent	64.0	56.0	54.2	53.9
Dependent	4.0	8.0	4.2	7.7
Functional status score	2.0±0.3	1.9±0.2	2.0±0.3	1.7±0.2
Length of stay (mo)	9.0 (2-83)	10.0 (1-115)	9.0 (1-98)	7.5 (1-85)
Regular medications (no.)	4.5±0.5	5.3±0.5	6.4±0.6	5.1±0.5
Diagnoses (no.)	5.6±0.4	4.9±0.5	5.0±0.4	4.7±0.3
Mini-Mental State score	20.9±1.2	23.1±1.0	22.7±1.3	22.2±1.0
Depression score	8.2±5.3	9.9±7.2	9.5±6.1	12.7±8.7
Muscle strength and mobility				
Leg strength (kg)	34.3±2.9	24.8±1.8†	29.6±2.6	30.8±2.3
Ambulatory assistance (% of subjects)				
None	26	8	17	15
Cane	44	25	35	42
Walker	22	54	39	35
Wheelchair	9	13	9	8
Falls in past year				
% of subjects	72	68	57	65
No. of falls	1 (0-21)	1 (0-93)	1 (0-14)	1 (0-6)
Activity level (counts/day)	16,416±2759	15,440±3487	12,614±1859	17,728±3713
Gait velocity (m/sec)	0.51±0.04	0.44±0.04	0.45±0.05	0.47±0.04
Stair-climbing power (W)	39.1±3.4	36.7±3.6	34.3±4.2	38.9±3.3
Nutritional status and body composition				
Body-mass index	24.9±0.7	24.5±0.8	25.4±0.7	25.8±0.5
Energy intake (kcal/day)	1,439±63	1,425±66	1,558±53	1,485±58
Whole-body potassium (g)	85.1±4.6	79.6±3.9	78.6±3.8	84.7±4.3
Thigh-muscle area (cm <sup>2</sup> )	62.70±3.48	61.05±3.92	56.90±3.70	60.17±3.86
Muscle cross-sectional area (% of total leg cross-sectional area)	48±2	46±3	44±2	44±3

\*Normally distributed data are presented as means ±SE; skewed data are presented as medians. Values in parentheses are ranges. Level of dependence was determined according to the level of care received. Functional status was determined according to the Katz Activities of Daily Living Index; a score of 0 signifies independent functioning, and a score of 6 dependent functioning. The Mini-Mental State Examination has a scale of 0 to 30; a score under 24 denotes cognitive impairment. On the Geriatric Depression Scale (0 to 30), a score over 10 denotes depressive symptoms. Leg strength was determined by summing the values of the one-repetition maximum for the right and left hip and knee extensors. The activity level was determined in 45 subjects by summing the values on the right- and left-ankle activity monitors; the mean three-day value was used. The muscle cross-sectional area was determined by CT in 85 subjects.

†P = 0.05 for the comparison with the exercise group.

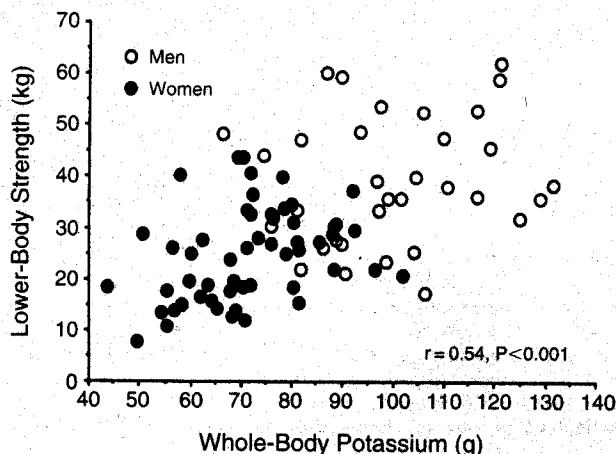


Figure 1. Relation between Body Composition and Muscle Function in 89 Elderly Subjects.

Base-line lower-extremity muscle strength (calculated as the sum of the one-repetition maximum for hip and knee extensors) was directly related to whole-body potassium, an index of active cell mass, including muscle mass (partial  $r$ , adjusted for sex, = 0.25;  $P < 0.05$ ).

hundred residents consented to participate in the study. The reasons given for not consenting to participate included the perceived time commitment and the inconvenience of the study.

#### Characteristics of the Subjects

The base-line characteristics of the subjects are summarized in Table 1. Their mean ( $\pm$ SE) age was  $87.1 \pm 0.6$  years, and 38 percent were 90 years old or older. Eighty-three percent of the subjects required a cane, walker, or wheelchair, and 66 percent had fallen during the previous year; their physical activity counts were about 25 percent of the levels we have recorded in sedentary young adults. The most prevalent chronic conditions included arthritis (in 50 percent of the subjects), pulmonary disease (in 44 percent), osteoporotic fracture (in 44 percent), hypertension (in 35 percent), and cancer (in 24 percent). The control group had a higher prevalence of hypertension than the treatment groups (63 percent vs. 20 to 28 percent,  $P < 0.01$ ), and this factor was accounted for in the analyses of covariance. Fifty-one percent of the subjects met the screening criteria for cognitive impairment, and 38 percent met the criteria for depression. The base-line nutritional intake was  $25.8 \pm 0.5$  kcal per kilogram of body weight per day, less than the level shown to be adequate for short-term weight maintenance (30 to 33 kcal per kilogram per day).<sup>33,34</sup>

The muscle-strength values (the one-repetition maximum) for the four muscle groups (right and left hip and knee extensors) were summed in order to derive a unitary variable representing lower-body strength. For the entire study sample, lower-body strength was  $29.9 \pm 1.2$  kg (range, 7.7 to 61.8). There was a difference in strength at base line ( $F = 2.71$ ,

$P = 0.05$ ), with the subjects assigned to exercise training and nutritional supplementation weaker than those assigned to exercise training alone ( $24.8 \pm 1.8$  vs.  $34.3 \pm 2.9$  kg, respectively). Base-line strength was included as a covariate in all analyses.

#### Base-Line Relation between Muscle Strength and Body Composition

Whole-body potassium (Fig. 1) was significantly related to muscle strength ( $r = 0.54$ ,  $P < 0.001$ ), as was regional muscle area determined by CT scanning ( $r = 0.57$ ,  $P < 0.001$ ). However, age, medical diagnoses or medications, functional status, length of stay in the facility, cognition, or depressive symptoms did not explain the base-line variance in strength or body composition.

#### Compliance with the Protocol and Adverse Events

Ninety-four percent of the randomized subjects completed the trial. There were two unrelated deaths (one in the supplement group and one in the control group) the first week of the study, and two subjects (one in the exercise group and one in the supplement group) dropped out before the start of the study because of lack of interest. Two subjects in the exercise group dropped out during training: one after the first training session because of generalized musculoskeletal pain, and the other in the seventh week of the study because of pneumonia.

The values for median compliance with exercise sessions (97 percent), control activities (100 percent), and use of the nutritional (99 percent) or placebo (100 percent) supplement were high. The mean training load was  $84.5 \pm 0.0$  percent of the most recent one-repetition maximum.

Diarrhea occurred in two subjects receiving the nutritional supplement. Two subjects in the exercise group reported joint pain (one in a prosthetic hip joint and the other in an osteoarthritic knee), necessitating an alteration of the training regimen. No cardiovascular complications occurred during any testing or training sessions.

#### Primary Outcomes

##### Muscle Strength and Size

Exercise significantly improved the results of all muscle-strength tests and increased the muscle cross-sectional area (Table 2 and Fig. 2). The changes in muscle strength after exercise were unrelated to age, sex, medical diagnosis, or functional level. A forward multiple-regression model of the variables that showed significant univariate associations with the relative change in strength after exercise training included assignment to the exercise group, base-line strength, and whole-body potassium (all  $P < 0.001$ ); this model explained 66.3 percent of the variance in increased strength. The subjects in the exercise group who had initially weaker muscles but larger reserves of whole-body potassium (an index of mus-

Table 2. Primary Outcome Variables.\*

OUTCOME VARIABLE	NO. OF SUBJECTS†	STUDY GROUP				P VALUE		
		EXERCISE	EXERCISE PLUS SUPPLEMENT	SUPPLEMENT	CONTROL	EFFECT OF EXERCISE	EFFECT OF SUPPLEMENT	INTERACTION
<i>change (percent change)</i>								
Muscle strength and mobility								
Right knee (kg)	89	4.9±0.6 (156.1±29.3)	5.0±0.5 (215.7±28.3)	-0.8±0.6 (-24.6±32.1)	0.1±0.6 (18.3±29.1)	<0.001 (<0.001)	0.45 (0.79)	0.41 (0.10)
Left knee (kg)	87	5.2±0.6 (178.8±29.1)	5.0±0.6 (204.2±28.5)	-1.1±0.6 (-24.4±32.7)	-0.3±0.6 (13.8±28.8)	<0.001 (<0.001)	0.41 (0.84)	0.69 (0.31)
Right hip (kg)	48	8.8±1.2 (81.4±16.4)	6.3±1.0 (90.3±14.5)	0.7±1.0 (4.3±14.3)	1.3±1.0 (19.6±14.0)	<0.001 (<0.001)	0.84 (0.51)	0.63 (0.20)
Left hip (kg)	48	8.1±1.0 (75.3±16.2)	6.8±0.9 (100.2±14.3)	0.6±0.9 (4.9±14.7)	0.7±0.8 (14.0±13.7)	<0.001 (<0.001)	0.72 (0.41)	0.70 (0.22)
Right leg press (kg)	38	8.3±2.9 (26.1±14.4)	14.9±3.0 (82.1±15.0)	0.6±3.7 (6.3±18.5)	1.8±3.3 (6.1±16.7)	0.007 (0.012)	0.40 (0.09)	0.23 (0.09)
Left leg press (kg)	39	9.3±2.1 (33.3±9.2)	12.9±2.4 (67.6±10.3)	1.4±2.9 (7.2±12.3)	-1.1±2.6 (-3.5±11.2)	<0.001 (<0.001)	0.24 (0.05)	0.82 (0.28)
Gait (m/sec)	90	0.04±0.02 (8.6±5.5)	0.06±0.02 (14.9±5.7)	0.00±0.02 (5.2±5.6)	-0.02±0.02 (-7.2±5.4)	0.009 (0.02)	0.31 (0.11)	0.97 (0.60)
Stair-climbing power (W)	83	11.1±2.5 (33.8±9.3)	7.9±2.7 (23.0±10.0)	4.2±2.7 (12.5±10.0)	-2.5±2.7 (-5.2±9.8)	0.001 (0.01)	0.53 (0.74)	0.08 (0.17)
Physical activity (counts/day)	45	3412±1700 (51.0±18.4)	553±1751 (17.6±18.9)	142±1600 (-6.7±17.3)	-1230±1670 (-2.6±18.1)	0.12 (0.03)	0.68 (0.34)	0.24 (0.46)
Body composition								
Weight (kg)	88	0.2±0.4 (0.4±0.6)	1.0±0.4 (1.8±0.6)	0.8±0.4 (1.5±0.7)	-0.5±0.4 (-0.8±0.6)	0.19 (0.21)	0.01 (0.01)	0.48 (0.48)
Whole-body potassium (g)	75	0.4±1.5 (0.4±1.9)	1.5±1.4 (2.2±1.9)	1.0±1.6 (1.1±2.0)	0.2±1.4 (0.9±1.9)	0.79 (0.86)	0.53 (0.62)	0.91 (0.71)
Thigh-muscle area (cm <sup>2</sup> )	61	0.9±1.7 (2.0±2.5)	1.7±1.7 (3.4±2.6)	-2.7±2.1 (-2.8±3.1)	-0.4±1.9 (-0.9±2.9)	0.14 (0.11)	0.69 (0.93)	0.43 (0.56)

\*Data are means ±SE. All means and analyses have been adjusted for base-line age, sex, functional status, lower-body strength, and hypertension.

†A total of 94 subjects completed the trial. Smaller numbers of subjects are shown here because of technical problems (see text) or illness at the time of testing.

cle mass) than the other subjects had the largest relative gain in muscle strength.

#### Body Composition

The supplement significantly increased body weight, although much less than had been anticipated with a total of 25,200 kcal added to the diet over a period of 10 weeks (360 kcal per day for 70 days). The supplement did not have a significant effect on whole-body fat-free mass.

#### Mobility

Use of a cane, walker, or wheelchair at base line was associated with lower values of strength, gait velocity, and stair-climbing power. Four subjects in the exercise group who had previously used a walker required only a cane after the study, whereas one non-exercising subject who had used a cane required a walker after the study. The exercise intervention significantly improved habitual gait velocity, stair-climbing ability, and the overall level of physical activity (Table 2 and Fig. 3). The nutritional supplement had no effect on mobility.

#### Dietary Intake

The median energy intake from the supplement was 353 kcal per day in the subjects receiving only the supplement and 358 kcal per day in those receiving both the supplement and exercise training (98 and 99 percent of the planned intake, respectively). Exercise

significantly blunted the decrease in ad libitum energy intake during the trial ( $P = 0.04$ ), the decrease was largest in the group of patients receiving only nutritional supplementation (Fig. 4). Total energy intake was significantly increased only in the group re-

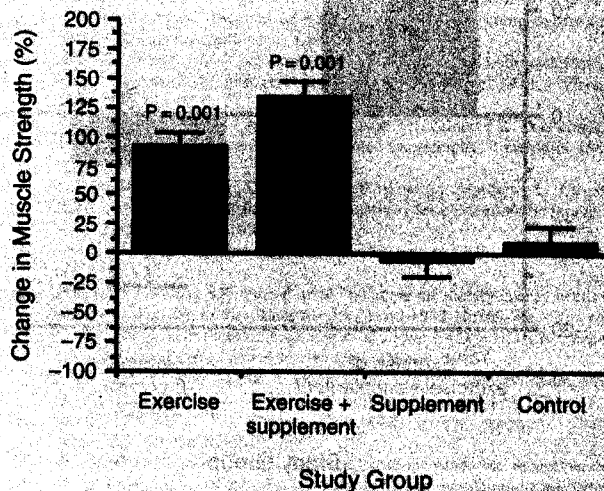


Figure 2. Mean (±SE) Changes in Muscle Strength after Exercise, Nutritional Supplementation, Neither, or Both.

Bars indicate the average relative change from the base-line maximal loads with one repetition for all muscle groups trained. There was a significant effect of exercise after adjustment for age, sex, functional status, base-line muscle strength, and hypertension. The nutritional supplement had no primary or interactive effect on muscle strength.

ceiving both exercise training and nutritional supplementation, because of the primary effect of exercise ( $P < 0.01$ ), with a trend toward an interaction between the two treatments ( $P = 0.08$ ).

### DISCUSSION

This trial demonstrates that a high-intensity, progressive regimen of resistance exercise training improves muscle strength and size in frail elderly people. These changes are accompanied by improvement in mobility and an increased level of spontaneous physical activity. Multinutrient supplementation has neither an independent nor an additive effect on these outcomes, despite a marginal nutritional intake at base line. The subjects who were initially the weakest but did not have severe muscle atrophy had the largest benefit from weight-lifting exercise. This pattern, as well as the large gain in strength as compared with the

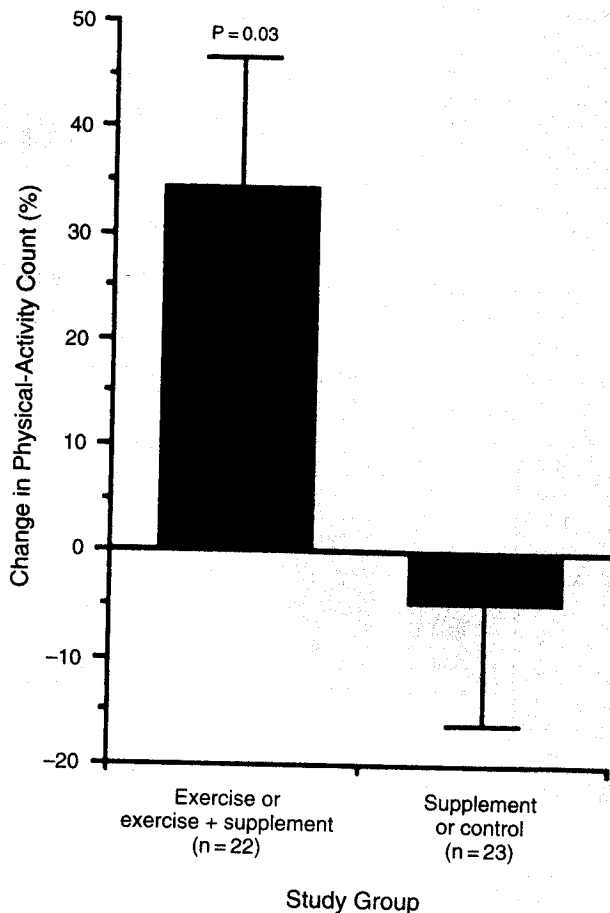


Figure 3. Mean ( $\pm$ SE) Changes in the Level of Spontaneous Physical Activity, According to the Presence or Absence of Exercise.

Bars indicate the percentage of change in the physical-activity count after adjustment for age, sex, functional status, base-line muscle strength, and hypertension. Nutritional supplementation had no effect on the mean daily physical-activity level, which was calculated from measurements over a 72-hour period. Exercise training was associated with a significant increase in the mean daily level of physical activity.

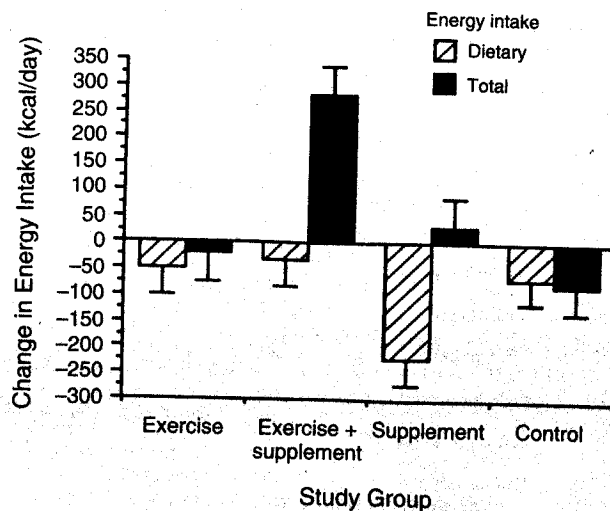


Figure 4. Mean ( $\pm$ SE) Changes in Energy Intake in the Four Study Groups.

Dietary energy intake included the energy content of meals, snacks, and nutritional supplements other than the supplement or placebo drink used in the study. Total energy intake included dietary energy intake plus the energy content of the nutritional supplement or placebo drink used in the study. Values are adjusted for age, sex, functional status, base-line muscle strength, and hypertension. Exercise significantly blunted the decline in dietary energy intake after the trial ( $P = 0.04$ ), a decline that was most pronounced in the supplement-only group (trend for interaction between exercise and supplement,  $P = 0.09$ ). There was a significant augmentation of total energy intake that was attributable to exercise ( $P < 0.01$ ), particularly in the subjects receiving both exercise training and nutritional supplementation (trend for interaction between exercise and supplement,  $P = 0.08$ ).

modest change in muscle area, suggests that improved neural recruitment of existing but underused skeletal muscle may have accounted for most of the functional improvement.

Only two other studies (both uncontrolled) have specifically addressed adaptation to resistance training in institutionalized elderly people. The first<sup>24</sup> also demonstrated a large gain in strength (174 percent), as well as improvements in muscle area and tandem gait speed after eight weeks of training. In the only other study of isolated resistance training in nursing home residents,<sup>35</sup> a combination of isometric training and low-intensity weight lifting for six weeks resulted in a small but significant gain in strength (15 percent). Several studies have shown the superiority of high-intensity, dynamic resistance training for the acquisition of maximal strength, even in patients of advanced age and those with chronic disease.<sup>23,36,37</sup> Our randomized controlled trial demonstrates the additional clinical benefits of improved mobility and function associated with the physiologic changes observed. The applicability of this mode of training is noteworthy; we excluded only subjects with acutely decompensated or terminal illness, and our study sample was even older than the average U.S. nursing home population.

In contrast to resistance training, endurance train-

ing has generally resulted in relatively small physiologic and functional benefits in nursing home residents.<sup>38,39</sup> Since a self-selected walking pace accounts for approximately 30 to 50 percent of maximal aerobic capacity,<sup>40</sup> a low endurance capacity may not be the primary factor limiting mobility in the frail elderly. Therefore, attempting to correct mobility through endurance training may not have the anticipated clinical benefit. Fear of falling, weight-bearing pain due to arthritis, and difficulty transferring from a seated to an upright position due to muscle weakness are likely to lead to self-imposed restrictions in mobility among the very old.

There are several reasons why our nutritional intervention may have been ineffective. First, there was a significant reduction in dietary energy intake after the trial, particularly in the subjects receiving only the supplement. This suggests that without exercise, there was no drive to increase energy intake, and the subjects who received the supplement alone reduced their ad libitum intake accordingly. In the subjects who received both exercise training and the nutritional supplement, the change in total energy intake (282 kcal per day, or 22 percent above the base-line value) may not have been of sufficient magnitude or duration to augment muscle function. In addition, the base-line nutritional status may not have been sufficiently compromised to benefit from this intervention.

In conclusion, low muscle mass and muscle weakness are strongly related to impaired mobility in the frail elderly, and this relation is independent of the effects of chronic disease, dementia, depression, and other characteristics of advanced age. The aging musculoskeletal system retains its responsiveness to progressive resistance training, and most important, the correction of disuse is accompanied by significant improvement in the levels of functional mobility and overall activity.

This article is dedicated to the memory of Dr. Abraham Daitch (1892 to 1993), whose intellectual curiosity and indomitable spirit led him to join our research study at the age of 98 years and whose vision of healthful aging continues to inspire our efforts. We are indebted to Ross Laboratories for the nutritional supplement, and to Keiser Sports Health Equipment for the resistance training equipment.

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