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Original Study

Effect of Physical Activity Intervention on Gait Speed by Frailty Condition: A Randomized Clinical Trial

Carlo Custodero MD[a], Pasquale Agosti MD[b], Stephen D. Anton PhD[c], Todd M. Manini PhD[c], Madia Lozupone MD, PhD[d], Francesco Panza MD, PhD[d,*], Marco Pahor MD[c], Carlo Sabbà MD, PhD[a], Vincenzo Solfrizzi MD, PhD[a,*]

[a] *Dipartimento Interdisciplinare di Medicina, Clinica Medica e Geriatria "Cesare Frugoni", University of Bari Aldo Moro, Bari, Italy*
[b] *Department of Pathophysiology and Transplantation, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, and Fondazione Luigi Villa, Università degli Studi di Milano, Milan, Italy*
[c] *Department of Aging and Geriatric Research, University of Florida, Gainesville, FL, USA*
[d] *Population Health Unit—"Salus In Apulia Study", National Institute of Gastroenterology "Saverio de Bellis", Research Hospital, Castellana Grotte, Bari, Italy*

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A B S T R A C T

Objectives: There is uncertainty about effects of physical activity on physical performance, such as gait speed, among community-dwelling older adults according to their physical frailty status. We determined whether a long-term, moderate-intensity physical activity program was associated with different responses on gait speed over 4 m and 400 m based on physical frailty status.
Design: Post hoc analysis from the Lifestyle Interventions and Independence for Elders (LIFE) (NCT01072500), a single-blind randomized clinical trial testing the effect of physical activity intervention compared with health education program.
Setting and Participants: We analyzed data on 1623 community-dwelling older adults (78.9 ± 5.2 years) at risk for mobility disability.
Methods: Physical frailty was assessed at baseline using the Study of Osteoporotic Fractures frailty index. Gait speed over 4 m and 400 m was measured at baseline, and 6, 12, and 24 months.
Results: We estimated significantly better 400-m gait speed at 6, 12, and 24 months for nonfrail older adults in the physical activity group, but not for frail participants. Among frail participants, physical activity showed a potentially clinically meaningful benefit on 400-m gait speed at 6 months (0.055; 95% CI 0.016–0.094; $P = .005$), compared with the healthy educational intervention, only in those who, at baseline, were able to rise from a chair 5 times without using their arms.
Conclusions and Implications: A well-structured physical activity program produced a faster 400-m gait speed potentially able to prevent mobility disability among physically frail individuals with preserved muscle strength in lower limbs.

Frailty is a potentially reversible geriatric condition characterized by reduced homeostatic reserves and higher vulnerability to stressor events that affects 12% to 24% of older adults.[1] Frailty may predispose to negative health-related outcomes including hospitalization, institutionalization, and mortality.[2] Therefore, the clinical identification of frailty has an important role in the development of preventive strategies to improve quality of life and assist frail older adults in coping with age-related conditions according to the practical framework used to identify frailty.[3,4]

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* Address correspondence to Vincenzo Solfrizzi, MD, PhD, Dipartimento Interdisciplinare di Medicina–Clinica Medica e Geriatria "Cesare Frugoni", University of Bari Aldo Moro, Bari, Italy; or Francesco Panza, MD, PhD, Unit of Research Methodology and Data Sciences for Population Health, National Institute of Gastroenterology "Saverio de Bellis" Research Hospital, Castellana Grotte, Bari, Italy.

E-mail addresses: f_panza@hotmail.com (F. Panza), vincenzo.solfrizzi@uniba.it (V. Solfrizzi).

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Although there is still no consensus on the definition of frailty and how frailty should be identified in clinical practice, most accepted screening and diagnostic tools are based on recognition of physical domains of the frailty phenotype.[5] Indeed, poorer physical performances, such as lower gait speed and muscle strength, are well-accepted indicators of physical frailty and strong predictors of adverse outcomes such as physical disability, falls, dementia, hospitalization, institutionalization, and mortality in older adults.[6-8] Conversely, a slight improvement on these parameters has been associated with health benefits and better overall quality of life.[9] Engaging in regular physical activity can help older adults to maintain and/or improve physical functioning and reverse frailty condition.[10,11] However, there is still uncertainty about the type and duration of physical activity interventions that are effective for maintenance of physical performance according to the frailty status of community-dwelling older adults.[12]

To date, no large randomized clinical trial (RCT) has examined the effect of a long-term multicomponent physical activity program, based on frailty status, with a notable exception.[13] The Lifestyle Interventions and Independence for Elders (LIFE) trial showed that a structured, moderate-intensity physical activity program reduced major mobility disability over 2.7 years among sedentary older adults.[14] Although this intervention neither reduced the risk of frailty nor was more effective in reducing risk of major mobility disability among frail compared with nonfrail individuals,[15] the effect of the interventions on gait speed measured over time accounting for frailty status of participants is not currently known. In this post hoc analysis, we examined whether a 24-month physical activity program had differential effectiveness on gait speed over short and long distance (4 and 400 meters, respectively) based on frailty status (frail, nonfrail) of sedentary community-dwelling older adults.

Methods and Material

Participants

The LIFE study was a multicenter, single-blind, parallel RCT designed to compare a long-term moderate-intensity physical activity program with a successful aging healthy educational intervention.[14] Between February 2010 and December 2013, 1635 sedentary older persons (aged 70 to 89 years) with mobility limitations were enrolled from 8 centers across the - -. Furthermore, participants were eligible it they had a sedentary lifestyle (defined in case of reporting <20 min/wk in the previous month of regular physical activity and <125 min/wk of moderate physical activity); lower extremity functional limitation assessed by Short Physical Performance Battery score ≤9; ability to walk 400 m in less than 15 minutes with no assistance; and absence of cognitive impairment, defined as a Modified Mini-Mental State Examination (3MSE) score 1.5 SDs below the education- and race-specific values. Written informed consent was obtained from all study participants. The study protocol was approved by the institutional review boards of all participating sites (clinicaltrials.gov identifier: NCT01072500). Further details of the study design and procedures were previously detailed elsewhere.[14]

Interventions

The interventions lasted approximately 2.0 to 3.5 years. The physical activity intervention combined both structured exercise and physical activity, including aerobic, strength, flexibility, and balance training. Indeed, the physical activity intervention consisted of 2 group sessions a week performed at the center combined with home-based activity 3 to 4 times a week. The physical activity sessions focused on 30 minutes of walking at a moderate intensity (at least 150 min/week), 10 minutes of primarily lower extremity strength training, 10 minutes of balance training, and 3 to 5 minutes of flexibility/stretching exercises. Specifically, leg strengthening activities included weight lifting using ankle weights and performing knee extension, knee flexion, squats, side leg raises, and toe raises. Using the Borg's scale of self-perceived exertion, participants were instructed to exercise at "somewhat hard" intensity during walking activity, and at "hard" intensity during strength training.[16] Participants in the physical activity intervention were also encouraged to reduce sedentary time, increasing all forms of physical activity throughout the day. The healthy educational intervention consisted of workshops on topics of interest for older adults (eg, travel safety, preventive services and screenings appropriate for different ages, nutritional advice) excluding purposefully the physical activity topic. Sessions were performed weekly in the first 26 weeks and then monthly or bimonthly at the discretion of each participant. At the end of every seminar, participants in the healthy educational intervention performed 5 to 10 minutes of light, upper extremity stretching.

Study of Osteoporotic Fractures Frailty Index

Physical frailty status was assessed at baseline by the Study of Osteoporotic Fractures frailty index.[17] The inability to rise from a chair 5 times without using arms was derived from the chair rise test component of the Short Physical Performance Battery.[18] Self-reported reduced energy level was defined by using the following statement of the Health-Related Quality of Life Questionnaire[19]: "During the past week, how often have you felt full of energy?" The criterion was considered as present if the participants answered "Some of the time," "A little bit of the time," or "None of the time." The criterion weight loss was based on the information at baseline if the participant reported a loss of appetite on the Health-Related Quality of Life Questionnaire.[19] Participants were considered "frail" if at least 2 of the 3 criteria were fulfilled, otherwise were deemed as "nonfrail."[17]

Four- and 400-Meter Gait Speed

Gait speed at usual pace was measured over a short distance (4 m) as well as a long distance (400 m). For the 400-m walk test, participants were instructed to walk 10 laps on a 20-m course (40 m/lap). Participants were able to use a cane or rest up to 1 minute, but they were not allowed to sit, lean against the wall, or get assistance from another person or walker. If the participant reported chest pain, tightness, or pressure; significant shortness of breath or difficulty breathing; or feeling faint, lightheaded, or dizzy, the test was stopped, marking the point at which the participant stopped and recording the total distance performed. Gait speed was calculated by dividing the meters walked before stopping by time walked in seconds.

Statistical Analysis

Baseline characteristics stratified by intervention group were summarized using means and SDs, or counts and percentages. We compared the intervention effects on 400-m and 4-m gait speed measurements, using separate repeated measures analysis with an unstructured parameterization matrix for longitudinal covariance. With this technique, to adjust for the differences at baseline between the physical activity and health education groups, the value of the intervention variable was not part of the model, but its interaction with time was included.

$$Y_{it} = \beta_0 + \beta_{1time1} + \beta_{2time2} + \beta_{3time3} + \beta_{4Intervention} \times time1 + \beta_{5Intervention} \times time2 + \beta_{6Intervention} \times time3 + \varepsilon_{it},$$

where Y_{it} is the observations for participant *i* at time *t*; $\beta_{1,2,3}$ are the regression coefficients for the time of the measurement at the first (6 months), second (12 months), and third follow-up (24 months); β_4 is the regression coefficient for the interaction between the intervention variable and time of measurement at 6 months, β_5 is the regression coefficient for the interaction between the intervention variable and time of measurement at 12 months, β_6 is the regression coefficient for the interaction between the intervention variable and time of measurement at 24 months, and ε_{it} is the "error" of individual *i* at time *t*. Because the intervention variable is not included in the model, the baseline values for healthy education and physical activity intervention groups are assumed to be equal and are reflected in the intercept of the model (β_0).[20] The advantage of this repeated measures analysis is that also individuals with only a baseline measurement are included in the analysis. All statistical models were adjusted for field center, gender, body mass index at baseline, and cumulative rate of falls and use of a straight cane during walking tests as time-dependent variables. Finally, we repeated these analyses based on the preserved (ie, not impaired) Study of Osteoporotic Fractures frailty index items/components (ie, inability to rise from a chair 5 times without using arms, reduced energy, and weight loss) in frail individuals. Contrasts were used to estimate the average effects over time. A sensitivity analysis was performed to verify differences in the estimates of average over time effect of interventions on 400 m in nonfrail participants by several statistical models adjusting for its baseline values and multiple imputations. The first statistical model was characterized by the outcome variable as the observed value at the different follow-up measurements and its baseline value as a covariate (analysis of covariance). The second statistical model was fully described in the first part of this section (alternative method to the analysis of covariance). The third statistical model was the analysis of covariance on the last value carried forward imputed dataset to estimate the treatment effects. Finally, we performed the longitudinal analysis of covariance on the multiple imputed data. All statistical analyses were performed using STATA 17 statistical software (StataCorp).

Results

Of the 1635 sedentary older adults originally randomized, this study included 1623 participants with available data for the Study of Osteoporotic Fractures frailty index assessment at baseline (99.3% of the total sample). Participants were assigned to the physical activity arm (n = 812) or the healthy educational arm (n = 811) (Figure 1). The

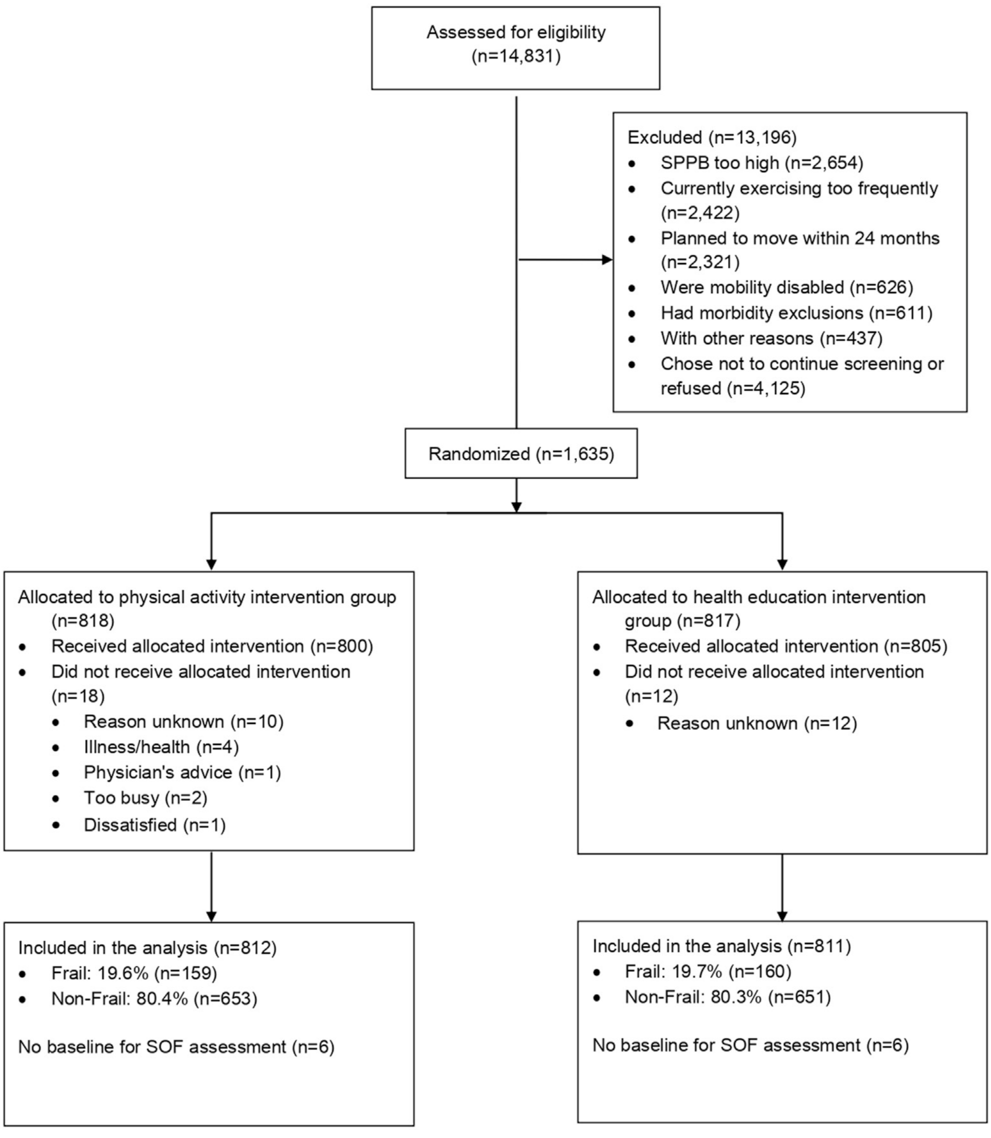

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Fig. 1. Flow of participants through the trial.

Table 1
Baseline Characteristics of Participants According to the Baseline Frailty Status and Intervention Group

Characteristic	Nonfrail (n = 1304)		Frail (n = 319)	
	Physical Activity (n = 653)	Healthy Education (n = 651)	Physical Activity (n = 159)	Healthy Education (n = 160)
Age, y	78.47 ± 5.11	78.84 ± 5.19	79.50 ± 5.65	79.99 ± 5.25
Female	431/653 (66.00)	428/651 (65.75)	114/159 (71.70)	118/160 (73.75)
Minority non-White	144/650 (22.15)	124/648 (19.14)	43/159 (27.0)	29/159 (18.2)
Education	3.90 ± 0.82	3.90 ± 0.84	3.80 ± 0.87	3.93 ± 0.81
Living alone	306/652 (46.93)	326/648 (50.31)	81/159 (50.94)	90/158 (56.96)
Smoking status	21/650 (3.2)	19/649 (2.9)	6/159 (3.8)	5/158 (3.2)
BMI, kg/m^2	30.01 ± 5.64	30.56 ± 6.19	30.38 ± 6.09	29.34 ± 6.37
Waist circumference, cm	101.55 ± 15.43	102.75 ± 15.74	101.78 ± 15.59	98.75 ± 15.16
Number of comorbidities >2	150/574 (26.1)	138/560 (24.6)	39/142 (27.5)	45/132 (34.1)
Hypertension	407/580 (70.17)	415/572 (72.55)	100/145 (68.97)	95/136 (69.85)
Type 2 diabetes mellitus	138/580 (23.79)	149/570 (26.14)	34/144 (23.61)	40/136 (29.41)
Myocardial infarction	47/580 (8.10)	41/569 (7.21)	6/144 (4.17)*	15/136 (11.03)
Stroke	43/580 (7.41)	32/572 (5.59)	11/145 (7.59)	13/136 (9.56)
Cancer	130/579 (22.45)	127/572 (22.22)	32/145 (22.07)	31/136 (22.79)
Congestive heart failure	16/578 (2.77)	26/568 (4.58)	6/144 (4.17)	9/134 (6.72)
3MSE	91.73 ± 5.44	91.67 ± 5.26	90.89 ± 5.62	91.46 ± 5.70
CESD	6.99 ± 6.44	7.63 ± 7.04	14.19 ± 9.67	13.99 ± 9.18
Overall SPPB	7.66 ± 1.42	7.56 ± 1.45	6.53 ± 1.90	6.32 ± 1.84
Chair Stand, score	1.73 ± 0.93	1.72 ± 0.95	1.17 ± 1.17*	0.88 ± 1.14
Balance, score	2.83 ± 1.05	2.78 ± 1.06	2.50 ± 1.05	2.57 ± 1.11
4-m walk, score	3.09 ± 0.77	3.06 ± 0.76	2.86 ± 0.82	2.87 ± 0.82
SPPB, score <8	150/574 (26.1)	138/560 (24.6)	99/159 (62.3)	107/160 (66.9)
Grip strength, kg	25.49 ± 10.51	24.92 ± 9.79	21.91 ± 8.01	22.45 ± 8.98
400-m gait speed, m/s	0.84 ± 0.16	0.83 ± 0.16	0.75 ± 0.16	0.76 ± 0.17
4-m gait speed, m/s	0.78 ± 0.16	0.77 ± 0.16	0.73 ± 0.17	0.74 ± 0.17
Cane use	49/651 (7.5)	62/648 (9.6)	30/158 (19.0)	26/160 (16.3)
SOF criteria				
Poor muscle strength in lower limbs	48 (7.4)	51 (7.8)	67 (42.1)*	87 (54.4)
Reduced energy level	263 (40.3)	277 (42.6)	152 (95.6)	150 (93.8)
Weight loss	38 (5.8)	37 (5.7)	111 (69.8)	112 (70.0)

BMI, body mass index; CESD, Center for Epidemiologic Studies Depression; SOF, Study of Osteoporotic Fractures; SPPB, Short Physical Performance Battery.
*$P < .05$ for comparison between physical activity and health education groups within frailty category.

mean age was 78.9 (SD 5.23) years and 67.2% were women. Prevalence of frailty and nonfrailty, according to the Study of Osteoporotic Fractures frailty definition, was similar between 2 intervention groups, with 19.6% and 19.7% of frail older adults and 80.4% and 80.3% of nonfrail individuals, respectively, in the physical activity and healthy educational group (Figure 1). Intervention groups stratified by frailty condition were almost similar in terms of socio-demographic, physical, and cognitive characteristics at baseline (Table 1). The frail participants in the physical activity group had lower prevalence of chair stand inability compared with those in the health education intervention (42.1% vs 54.4%, $P = .033$) (Table 1). At baseline, Study of Osteoporotic Fractures frailty index was significantly and inversely correlated with 400-m gait speed (ρ: −0.219, $P < .001$) as well as 4-m gait speed (ρ: −0.119, $P < .001$).

Intervention Adherence

There was no difference in the median overall (71% vs 72%, $P = .59$), and 6-months (79% vs 83%, $P = .23$), 12-months (75% vs 79%, $P = .21$), and 24-months (72% vs 74%, $P = .28$) attendance at physical activity sessions between frail and nonfrail participants, excluding medical leaves.

Intervention Effect on Gait Speed in Frail, Prefrail, and Robust Older Adults

Among nonfrail older participants, significant predicted mean differences between physical activity and healthy educational program on 400-m gait-speed were estimated at 6 months (0.029; 95% CI 0.017–0.041; $P < .001$), 12 months (0.023; 95% CI 0.011–0.035; $P < .001$), and up to 24 months (0.023; 95% CI 0.010–0.035; $P < .001$) (Figure 2A). On the other hand, we did not observe any intervention effect on change differences of 4-m gait-speed at different follow-ups (at 6 months: −0.004; 95% CI −0.018 to 0.011; $P = .62$; at 12 months: −0.002; 95% CI −0.016 to 0.013; $P = .80$; at 24 months: −0.001; 95% CI −0.014 to 0.016; $P = .94$) (Figure 2B).

In frail older participants, we did not estimate significant predicted mean differences between the intervention groups, on 400-m gait-speed both at 6 months (0.027; 95% CI −0.001 to 0.055; $P = .06$), at 12 months (0.014; 95% CI −0.015 to 0.042; $P = .35$), and 24 months (0.010; 95% CI −0.020 to 0.039; $P = .51$) (Figure 3A). No benefit was estimated on 4-m gait speed of Short Physical Performance Battery among frail participants across time (at 6 months: −0.011; 95% CI −0.041 to 0.018; $P = .46$; at 12 months: −0.008; 95% CI −0.039 to 0.012; $P = .61$; at 24 months: −0.010; 95% CI −0.022 to 0.41; $P = .54$) (Figure 3B).

Intervention Effect on Gait Speed by Preserved Study of Osteoporotic Fractures Frailty Index Components Among Frail Older Adults

Considering the characteristics of frail individuals, and specifically the preserved Study of Osteoporotic Fractures frailty index items/components, we found that those able to rise from a chair 5 times without using arms showed significant predicted mean differences between the intervention groups, favoring physical activity, on 400-m gait-speed at 6 months (0.055; 95% CI: 0.016–0.094; $P = .005$), but not at 12 months (0.037; 95% CI: −0.002 to 0.077; $P = .062$) and 24 months (0.032; 95% CI: −0.009 to 0.073; $P = .132$), and not for 4-m gait-speed at any times (Table 2). By contrast, no significant difference between interventions was found for 4- and 400-m gait-speed at all timepoints whether the preserved Study of Osteoporotic Fractures frailty index

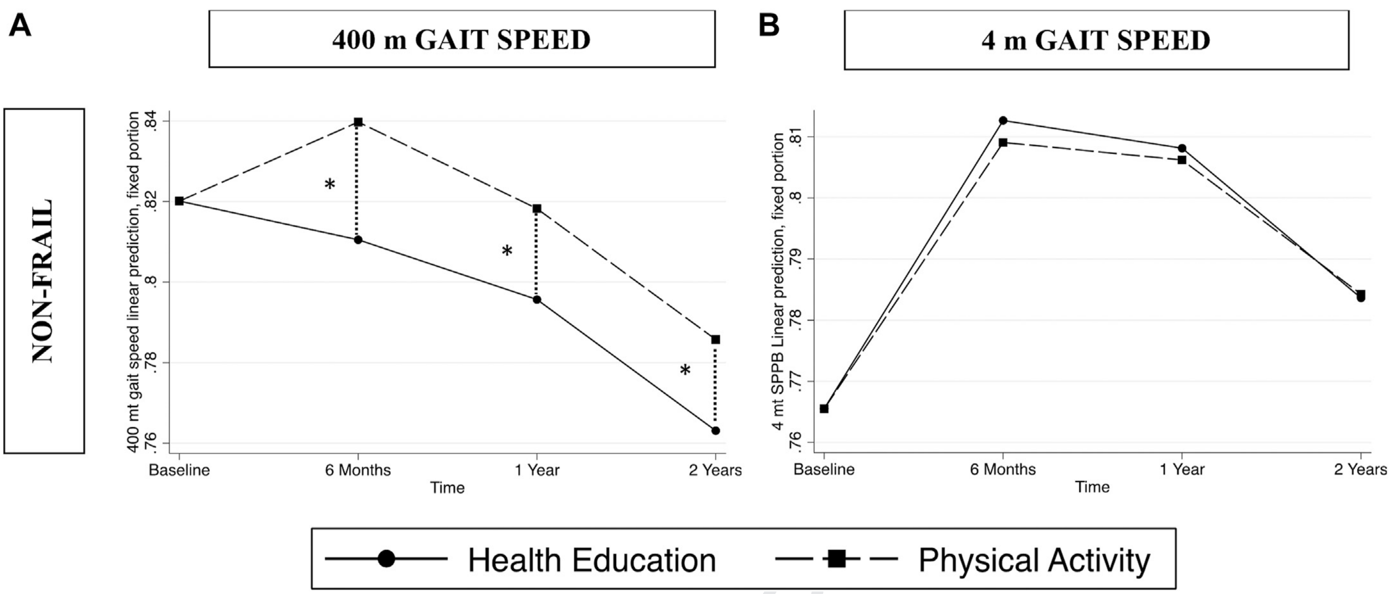

Fig. 2. Predicted mean difference values of the interventions on 400-m and 4-m gait speed in nonfrail (A and B) older adults across time. Predicted mean difference values between arms adjusted for gender, field center, body mass index at baseline, and cumulative rate of falls and use of a straight cane during walking tests as time-dependent variables.*$P < .001$.

items/components, in frail participants, were the energy levels and stable body weight (Table 2).

Sensitivity Analysis

Mean and SD estimates regarding the baseline values of 400 m for the 54 participants without follow-up measurement were 547.54 and 142.58, respectively, and for the 1581 participants with at least 1 follow-up measurement were 507.57 and 122.79, respectively. Approximately 3% of the participants had only a baseline value and that baseline 400-m gait-speed performance was slightly higher for the participants with only a baseline value compared with the participants with at least 1 follow-up measurement. According to the results of the longitudinal analysis of covariance, the regression coefficient for participants in the physical activity group (0.023; 95% CI 0.013–0.034) revealed a more strong and statistically significant effect on 400-m gait speed compared with those in the healthy educational intervention. In the alternative repeated measures analysis, 24-month physical activity intervention showed a statistically significant beneficial effect on 400-m gait speed compared with healthy educational intervention (0.031; 95% CI 0.014–0.048; $P < .001$). In the longitudinal analysis of covariance performed on the last value carried forward imputed dataset, no statistically significant difference was observed between physical activity and healthy educational interventions (−1.18; 95% CI −11.13 to 8.77). Finally, in the longitudinal analysis of covariance on the multiple imputed datasets, a statistically significant difference on average 400-m gait speed over time was found between physical activity and healthy educational interventions (0.023; 95%

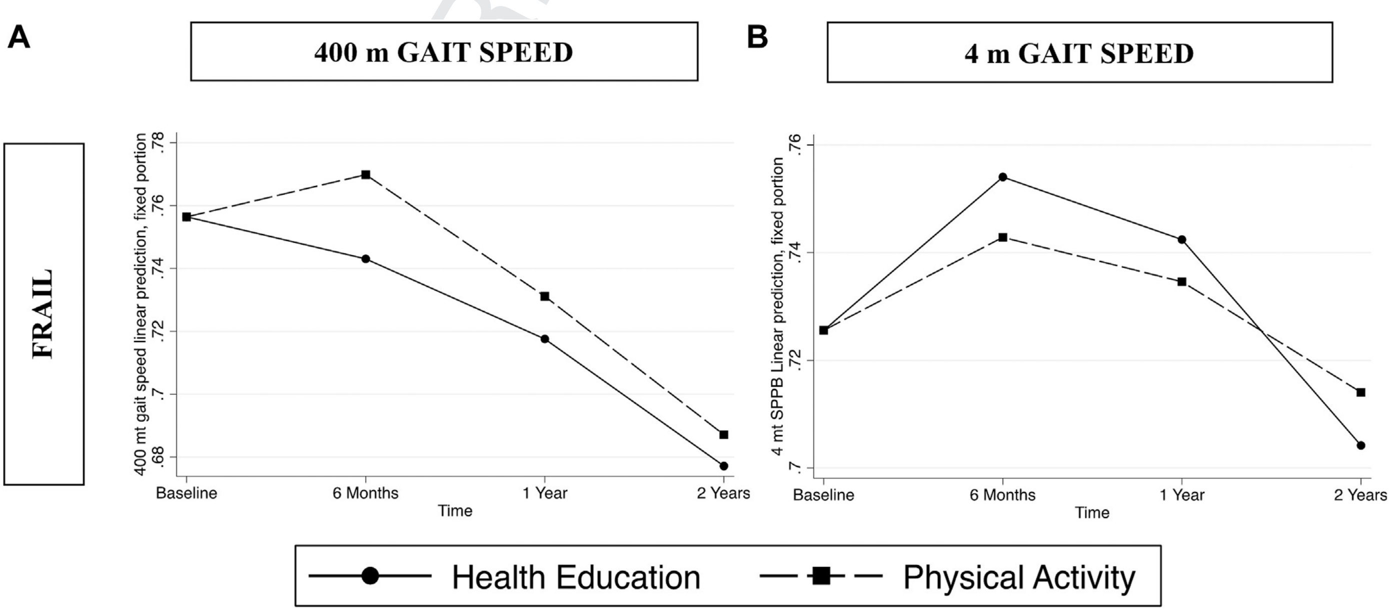

Fig. 3. Predicted mean difference values of the interventions on 400-m and 4-m gait speed in frail (A and B) older adults across time. Predicted mean difference values between arms adjusted for gender, field center, body mass index at baseline, and cumulative rate of falls and use of a straight cane during walking tests as time-dependent variables.

CI 0.012–0.033; $P < .001$). In all statistical models, the interpretation of the effect estimates was the difference on average over time (24 months) in the outcome of interest between physical activity and healthy educational interventions.

Discussion

In the present post hoc evaluation of the LIFE study, we observed that a 24-month structured, moderate-intensity, multicomponent physical activity intervention was associated with a short-term clinically meaningful faster 400-m gait speed among frail participants with preserved muscle strength in lower limbs only, based on the chair rise subtest of the Short Physical Performance Battery. In addition, a significant and sustained effect of the physical activity intervention on 400-m gait speed in nonfrail older adults was observed. Conversely, no intervention benefit was observed on 4-m gait speed regardless of frailty status.

To date, the optimal intervention for older adults of varying frailty status is currently unknown. In particular, there is poor-quality evidence about the influence of frailty status on the responsiveness to physical activity.[10] Although many studies support the safety of these approaches in frail patients,[21,22] these interventions have not been translated to clinical practice, because of poor guidelines and too many concerns. Moreover, in frail participants, data concerning the efficacy of physical activity are still mixed.[12,23] Very recently, in the Sarcopenia and Physical fRailty IN older people: multi-componenT Treatment strategies (SPRINTT) trial, an intervention based on physical activity with technological support and nutritional counseling in participants with physical frailty and sarcopenia and a Short Physical Performance Battery score ranging from 3 to 7 was associated with a reduction in the risk of incident mobility disability during 36 months of follow-up, compared with an intervention comprising lifestyle education.[13]

In the present study, we included sedentary community-dwelling older adults at risk for mobility disability. A well-designed physical activity intervention performed in the community could be able to modify the trajectories of frailty toward disability and prevent the key frailty-related adverse events, such as hospitalization and istituzionalization.[24] Systematic reviews suggest that physical activity intervention might be more effective in improving physical performance among frail participants rather than nonfrail individuals.[10] Specifically, a meta-analysis by Giné-Garriga and colleagues,[25] including trials on community-dwelling frail individuals, showed a significant benefit of physical activity on gait speed at usual pace of approximately 0.06 m/s, but only 1 study had a follow-up longer than 6 months,[26] and measures of frailty, even though based on frailty phenotype, were very heterogeneous.

The LIFE study showed that physical activity intervention may produce greater benefits on physical performance among lower-functioning individuals at baseline,[27] suggesting that physical activity may reduce incidence and reverse frailty condition, but in frail individuals physical activity did not reduce risk of major mobility disability.[15] This may mean that frail individuals are intrinsically at higher risk of mobility disability, but because frailty is a potentially reversible condition, they can still revert or slow-down under physical activity intervention. Two other post hoc analyses of the LIFE study, using a deficit accumulation approach to operationalize frailty, showed that each 1-unit increase in a 75-item frailty index increased the hazard of major mobility disability by 4%,[28] while, using a 44-item frailty index, both physical activity and healthy educational groups had similar frailty trajectories and clinically meaningful frailty changes, but those who were frailer benefited more from the physical activity intervention regarding major mobility disability and death.[29] Santanasto and colleagues[27] already found a significant, even though small, effect of physical activity

Table 2
Predicted Estimates of the Intervention Among Frail Participants According to the Preserved Physical Frailty Components Assessed at Baseline by the Study of Osteoporotic Fractures Frailty Index

Outcome	Months	Able to Rise From a Chair			Good Energy Level			No Weight Loss		
		Predicted Mean Difference Values Between Arms*	(95% CI)	P Value	Predicted Mean Difference Values Between Arms*	(95% CI)	P Value	Predicted Mean Difference Values Between Arms*	(95% CI)	P Value
400-m gait speed, m/s	6	0.055	0.016 to 0.094	.005	−0.007	−0.102 to 0.087	.876	0.009	−0.046 to 0.065	.740
	12	0.037	−0.002 to 0.077	.062	0.054	−0.041 to 0.149	.264	−0.005	−0.062 to 0.052	.873
	24	0.032	−0.009 to 0.073	.132	−0.021	−0.122 to 0.080	.684	−0.013	−0.071 to 0.046	.670
4-m gait speed, m/s	6	−0.004	−0.045 to 0.036	.831	0.001	−0.133 to 0.134	.994	−0.005	−0.062 to 0.050	.848
	12	0.010	−0.032 to 0.051	.648	−0.002	−0.135 to 0.131	.977	−0.011	−0.069 to 0.047	.707
	24	0.030	−0.014 to 0.073	.179	−0.018	−0.161 to 0.124	.801	−0.023	−0.083 to 0.036	.439

*Adjusted for gender and field center, body mass index at baseline, and cumulative rate of falls and use of a straight cane during walking tests as time-dependent variables.

intervention compared with the healthy educational arm only on 400-m gait speed (ranging between 0.02 and 0.03 m/s based on time point) rather than on other physical performance, and more pronounced in lower-functioning individuals based on Short Physical Performance Battery score. Moreover, 400-m gait speed explained a considerable proportion of the effect of physical activity intervention, compared with healthy educational intervention, on the prevention of mobility disability.[27] Changes in gait speed of 0.04 to 0.06 m/s have been associated with clinically meaningful modifications in functional limitation.[30] Here, we found a significant short-term (at 6 months) benefit on 400-m gait speed, of 0.05 m/s in physical activity compared with the healthy educational group, only among frail participants who had preserved muscle strength in lower limbs. Trombetti and colleagues[15] already demonstrated in the LIFE study population that among the Study of Osteoporotic Fractures frailty index items, the ability to rise from a chair 5 times without using arms was the parameter most affected by the intervention, and was also the one that showed the strongest correlation with the risk of major mobility disability. Thus, the frail individuals with chair stand still preserved, might be those who get more benefit from physical activity in terms of slower reduction of 400-m gait speed. Consistently, another previous observational study showed that frail individuals with higher lower-limb muscle strength, assessed by chair stand test, had higher degree of functional independence compared with frail or prefrail individuals with poorer lower-limb muscle strength.[31] Overall, these findings may further support the heterogeneity of a frailty phenotype, which should be interpreted not merely as a dichotomous condition, but rather as a continuum with different degrees of severity also within the frail individuals.

In the present analysis, we also found small, but significant and prolonged benefit on 400-m gait speed, in nonfrail older adults. The LIFE study population as selected among community-dwelling sedentary older adults could be considered as a prefrail population based on the physical frailty phenotype.[32] Previous evidence demonstrated a benefit of physical activity interventions on physical performance in prefrail older adults.[12,33] For example, Faber and colleagues[33] showed that 2 different exercise programs (ie, multicomponent physical activity and Tai Chi–based) performed for 20 weeks, significantly improved physical performance in prefrail participants, but not in frail participants. However, in that study, different outcome measures were used and participants in the control group were only asked not to change their usual pattern of activities not receiving any educational program.[33] Among nonfrail older adults, the physical activity intervention may promote beneficial effect on physical performance likely because of greater intrinsic capacity of these participants compared with frail individuals, but the benefits would be small and of scarse clinical relevance. In this study, no difference in adherence to the prescribed physical activity program were observed between frail and nonfrail participants.[15]

This study has several limitations that deserve to be mentioned. First, the included individuals were selected among those at risk for mobility-disability based on higher sedentarity and lower levels of physical performance on the Short Physical Performance Battery, and thus also the nonfrail participants might already have some degree of physical frailty. Therefore, the results may not be generalizable to all the community-dwelling older adults. Second, the selection, as control, of a health educational program (workshops and stretching exercises) could have underestimated the effect size of our intervention. Third, the LIFE study was not specifically designed to understand the differences in responsiveness to exercise intervention. Therefore, potential biological effect modifiers of gait speed were not assessed. Among outcomes, we only considered gait speed measures, and not muscle strength in upper and lower limbs and accelerometer-based measures of physical activity level. Moreover, for the Study of Osteoporotic Fractures frailty index, the criterion of weight loss was based on a proxy such as loss of appetite, with a possible impact on the frailty status identified in the present study. The prevalence of chair stand inability at baseline among frail participants was slightly different across the 2 interventions (lower in the physical activity group), thus might potentially have an impact on final findings. Last, but not least, given the post hoc nature of this analysis, our results do not allow understanding of the function and the target of each component of the exercise program.

Despite the aforementioned limitations, the present study has important strengths. First of all, this is one of the largest RCTs designed with the goal to evaluate the effects of a multicomponent physical activity intervention in community-dwelling older adults at risk for mobility disability. Moreover, the long duration of the intervention with good adherence[15] and the prolonged follow-up with outcome assessment must be mentioned. In the sensitivity analysis, the results obtained from the longitudinal analysis of covariance in this situation were comparable to those obtained from the alternative repeated measures analysis and the multiple imputations, except for the effect estimates obtained from the analysis of covariance performed on the last value carried forward imputation method, which were remarkably lower than then effect estimates obtained from the other 3 methods. The present results may have important implications both in clinical research, for a better design of future clinical trials, and in clinical practice, for the development of more efficient and feasible preventive strategies of mobility disability. There is an urgent need of larger well-designed RCTs including older adults with different states of frailty, able to evaluate all the potential effect modifiers of physical activity responsiveness, and to compare the efficacy of different types of interventions in each subgroup. Moreover, a deeper knowledge about the pathobiological mechanisms of each type of physical activity intervention and the related targeted frailty component could allow us to define the most useful multitarget intervention for each patient and to choose the proper outcome measure with the purpose of a more appropriate assessment and monitoring of the intervention long-term efficacy.[10,34]

Conclusions and Implications

Physical activity may have a key role in preventing physical disability in nonfrail, and specific subgroups of frail older adults. The results from the present study provide increased knowledge on the potential benefits of a well-designed multicomponent physical activity intervention on 400-m gait speed among community-dwelling physically frail older adults with preserved strength in lower limbs. Our findings should encourage refinement of selection criteria for a tailored physical activity–based intervention, with the final goal of achieving the optimal benefit from exercise therapy.

Supplementary Data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jamda.2023.01.023.

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