

A multicomponent frailty intervention for socioeconomically vulnerable older adults: a designed-delay study

Il-Young Jang^{1,2}
 Hee-Won Jung³
 Hyelim Park^{1,2}
 Chang Ki Lee⁴
 Sang Soo Yu²
 Young Soo Lee¹
 Eunju Lee¹
 Robert J Glynn^{5,6}
 Dae Hyun Kim^{6,7}

¹Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; ²PyeongChang Health Center & County Hospital, Pyeongchang, Gangwon-Do, Republic of Korea; ³Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Republic of Korea; ⁴Goldman Urology Clinic, Seoul, Republic of Korea; ⁵Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA; ⁶Division of Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA; ⁷Division of Gerontology, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA

Correspondence: Eunju Lee
 Department of Internal Medicine,
 Asan Medical Center, University
 of Ulsan College of Medicine, 88,
 Olympic-ro 43-gil, Songpa-gu,
 Seoul 05505, Republic of Korea
 Tel +82 2 3010 3308
 Fax +82 2 476 0824
 Email eunjulee@amc.seoul.kr

Purpose: The primary aim of this study was to evaluate the effectiveness of a 6-month multicomponent intervention on physical function in socioeconomically vulnerable older adults in rural communities. As secondary aims, we evaluated the effectiveness of the intervention on frailty and other geriatric syndromes, sustained benefit at 12 months, and baseline characteristics associated with poor response.

Patients and methods: This designed-delay study was conducted in 187 adults (mean age: 77 years; 75% women) who were living alone or on a low income in three rural regions of Korea. A 24-week multicomponent program that consisted of group exercise, nutritional supplementation, depression management, deprescribing medications, and home hazard reduction was implemented with a planned 6-month interval from August 2015 through January 2017. The primary outcome was physical function, measured using the Short Physical Performance Battery (SPPB) score (range: 0–12; minimum clinically important difference ≥ 1) at 6 months. Secondary outcomes included frailty phenotype, sarcopenia, Mini Nutritional Assessment-Short Form score (range: 0–14), Center for Epidemiologic Studies-Depression Scale score (range: 0–60), and falls.

Results: At 6 months, the SPPB score increased by 3.18 points (95% CI: 2.89, 3.48) from baseline. The program improved frailty (odds ratio: 0.06; 95% CI: 0.02, 0.16), sarcopenia (odds ratio: 0.32; 95% CI: 0.15, 0.68), Mini Nutritional Assessment-Short Form score by 1.67 points (95% CI: 1.28, 2.06), and Center for Epidemiologic Studies-Depression Scale score by –3.83 points (95% CI: –5.26, –2.39), except for fall (rate ratio: 0.99; 95% CI: 0.69, 1.43). These beneficial effects were sustained at 12 months. Body mass index ≥ 27 kg/m² and instrumental activities of daily living disability at baseline were associated with poor improvement in the SPPB score.

Conclusion: This 24-week multicomponent program had sustained beneficial effects up to 1 year on physical function, frailty, sarcopenia, depressive symptoms, and nutritional status in socioeconomically vulnerable older adults in rural communities. ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02554994), NCT 02554994)

Keywords: clinical trial, exercise, frailty, geriatric assessment, malnutrition, public health practice

Introduction

The prevalence of frailty is disproportionately high in older adults who have limited social support or who live in rural areas.^{1,2} Due to limited access to health care facilities and resources in rural area, these older adults may be at greater risk for functional decline. A community-based public health intervention may be needed to reduce the risk of frailty and its consequences.

Several randomized controlled trials have tested the effect of interventions targeting major risk factors for functional decline, such as physical inactivity, nutritional status, depression, or falls, in older adults. Some studies showed that exercise and nutritional supplementation improved physical function and frailty,^{3–6} whereas others found limited benefits.^{7–9} This heterogeneity is possibly due to differences in the intervention (exercise alone vs multicomponent, individual vs group, or center-based intervention vs home-based intervention), adherence, loss to follow-up, or target populations. In particular, the effectiveness and feasibility of these interventions in a resource-limited rural setting have not been well studied. Because designing a public health intervention with sustained benefit is a high priority for rural communities, it is useful to learn how long the benefit can be maintained once the intervention is completed. In addition, identifying the characteristics of people who are unlikely to improve from this intervention is important as they may need personalized case management, instead of a group intervention.

In this paper, we report the results of a designed-delay intervention study to evaluate the effectiveness of a 6-month multicomponent program that comprises group exercise training, nutritional supplementation, depression management, deprescribing medications, and home hazard reduction in older adults who live alone or are on low income in rural communities in Korea. The primary aim was to test the hypothesis that our multicomponent program would improve physical performance in 6 months. As secondary aims, we evaluated the effectiveness of the intervention on frailty and other geriatric syndromes, sustained benefit at 12 months, and baseline characteristics associated with poor response to our program.

Patients and methods

Study design

We conducted a designed-delay study wherein the intervention was rolled out sequentially in three geographic regions with a planned 6-month interval (see Figure 1).

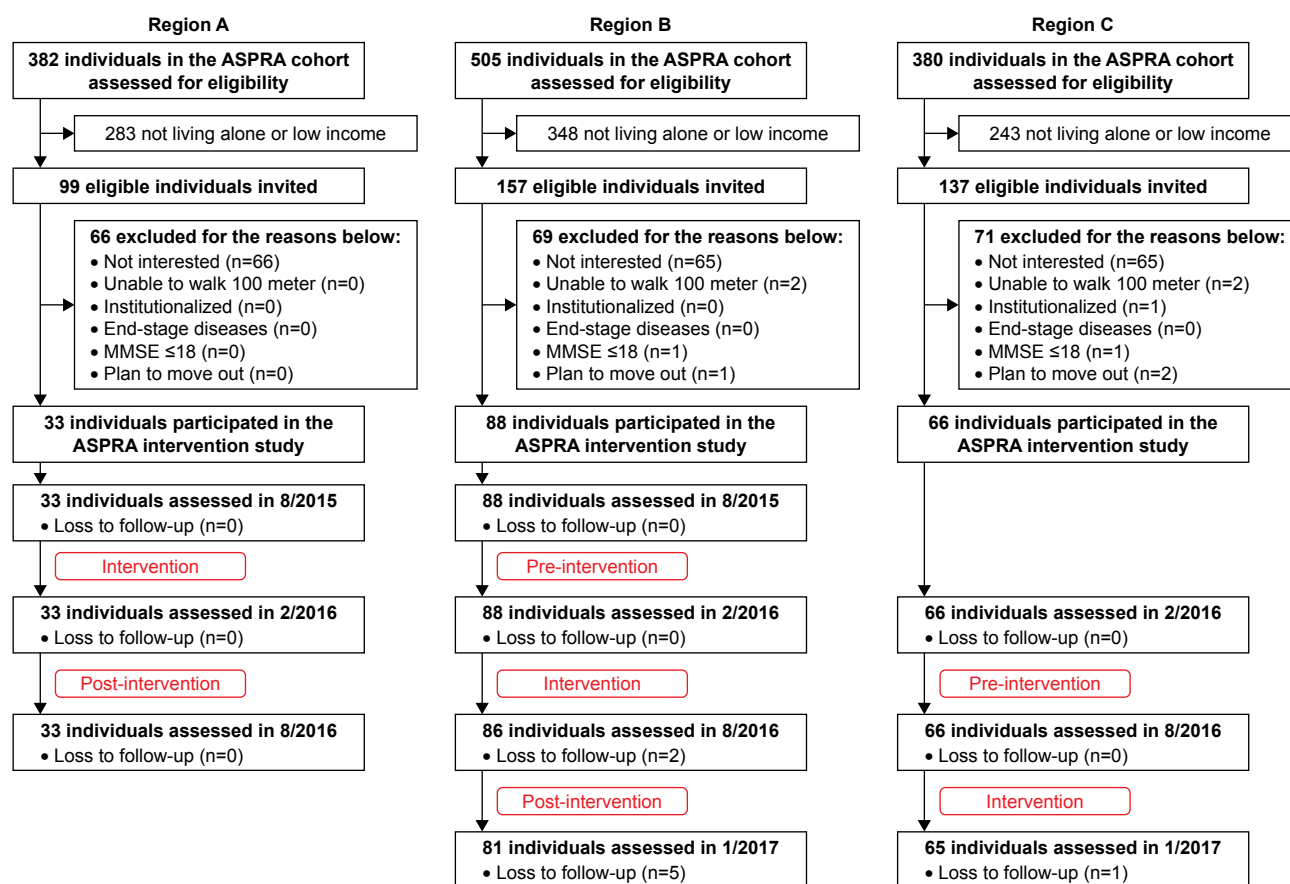


Figure 1 Study design and population of the Aging Study of Pyeongchang Rural Area, an intervention study.

Notes: Participants for this study were selected from the Aging Study of Pyeongchang Rural Area, a population-based, prospective cohort study of aging in 1,267 adults aged 65 years or older who live in three regions of Pyeongchang County, Gangwon Province, Korea. The 24-week intervention was delivered in one geographic region at a time. Enrolled individuals in region A participated in the multicomponent intervention program from August 2015 through January 2016; those in region B did so from February 2016 through July 2016; and those in region C participated from August 2016 through January 2017. All participants were assessed every 6 months for physical function.

Abbreviation: ASPRA, Aging Study of Pyeongchang Rural Area.

This pragmatic design was chosen after consulting regional and local public health workers and town representatives, who expressed concerns about the limited resources at the public health centers to conduct a randomized controlled trial and unfamiliarity of public health workers and town residents with random treatment assignment. A designed-delay study allowed efficient use of the existing infrastructure and limited resources by implementing the program in one region at a time, while residents in all three regions received the intervention after a prespecified delay during the study period. The effectiveness of an intervention can be evaluated by comparing the outcome with a historical (pre-intervention period) comparison group as well as a concurrent (non-intervention region) comparison group. Based on these results from the three regions, the public health center can decide whether or not to adopt this intervention for the entire county. The study protocol was approved by the Institutional Review Board of the Asan Medical Center (Research Protocol 2015-0706) and was registered with [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study?term=NCT02554994) (NCT 02554994).

Study population

This study was conducted between August 2015 and January 2017 in Pyeongchang County, a rural area located 180 km east of Seoul. The study population was recruited from the Aging Study of Pyeongchang Rural Area (ASPRA), a population-based, prospective cohort study of 1,267 adults aged ≥ 65 years who lived in Pyeongchang County.¹⁰ The cohort included over 90% of older adults living in the study area. Individuals were included if they 1) were currently living in the three regions; 2) were aged 65 years or older; 3) were living alone or receiving medical aid services; and 4) signed informed consent. The exclusion criteria were as follows: 1) unable to walk 100 m; 2) institutionalized in the past 6 months; 3) diagnosed with end-stage heart failure, end-stage renal disease, or metastatic cancer; 4) cognitively impaired (Mini-Mental State Examination score ≤ 18); and 5) planning to move out of the study area in the next 6 months. All participants provided written informed consent.

A multicomponent program

A 24-week multicomponent program was implemented in one geographic region at a time: region A in August 2015–January 2016, region B in February 2016–July 2016, and region C in August 2016–January 2017. During the pre-intervention period, participants received usual care from the local public health centers. Usual care consists of ambulatory visit every month or as needed for medical management of chronic conditions from local public health centers without

receiving any component of the intervention (described later). During the intervention period, they received group exercise training, nutritional supplements, depression management, deprescription of medications, and home hazard reduction (Table 1). Our intervention team comprised two part-time exercise trainers (equivalent to 15% of weekly working hours), three part-time physicians (5% of weekly working hours), and two nurses or social workers (30% of weekly working hours). A 60-minute group exercise session was held twice weekly by licensed exercise trainers at a local town hall. Each session focused on resistance, balance, and aerobic capacity for ~20 minutes each. Participants were given a written guide for exercises and were encouraged to exercise for 60 minutes daily on their own. In addition, all participants received two 125 mL nutritional supplement packs (ready to drink) per day. The nutritional supplement was provided free of charge by Maeil Dairies Co., Ltd (Seoul, Korea). Individuals with high depressive symptoms were evaluated monthly by a geriatrician or a psychiatrist and received pharmacologic management or supportive psychotherapy as indicated. Individuals taking ≥ 5 prescription drugs were evaluated monthly by a geriatrician for the discontinuation or reduction of potentially inappropriate medications according to the 2012 Beers criteria.¹¹ Visiting nurses and social workers made home visits to identify and fix anything that could lead to home hazards using the Home Fall Prevention Checklist by Centers for Disease Control and Prevention.¹²

Outcome assessment

Our primary outcome was change in physical function over 6 months, measured using the Short Physical Performance Battery (SPPB) that comprised repeated chair stands, standing balance, and gait speed.¹³ The minimal clinically important change in SPPB was a change of 1 point.¹⁴ Secondary outcomes were 1) frailty phenotype,¹⁵ 2) sarcopenia,^{16,17} 3) nutritional risk,¹⁸ 4) depressive mood,¹⁹ 5) number of falls, and 6) number of emergency room visits and hospitalizations (see Table S1). Assessments of SPPB, frailty, sarcopenia, nutritional risk, and depressive symptoms were performed every 6 months by a team of seven to eight trained nurses who were not aware of the participation status in the intervention study. Self-reported falls and health care utilization were assessed on a monthly basis during the intervention period to ensure the safety of participants; they were assessed every 3 months during the non-intervention period.²⁰

Other measurements

Trained nurses collected sociodemographic information and assessed multimorbidity, polypharmacy, activities of daily

Table I Description of multicomponent intervention program

Focus	Description of intervention
Exercise	<ul style="list-style-type: none"> Intervention: 60-minute group exercise session led by licensed exercise focusing on the following types. The intensity was increased every month <ol style="list-style-type: none"> Resistance (20 minutes): squat, plank, side plank, straight leg raises Balance (20 minutes): one-leg standing, shifting from side to side, heel-to-toe walk Aerobic/endurance (20 minutes): step up and down, quick pace, dancing Target: all participants Frequency: twice weekly
Nutrition	<ul style="list-style-type: none"> Intervention: administration of 125 mL commercial liquid formula containing 200 kcal of energy, 24.5 g carbohydrate, 13 g protein, 5.63 g essential amino acid, and 7 g fat Target: all participants Frequency: twice daily
Depression	<ul style="list-style-type: none"> Intervention: evaluation by a geriatrician or a psychiatrist and administration of supportive psychotherapy or antidepressant medication as clinically indicated Target: participants with the CES-D score >20 points at baseline Frequency: monthly
Polypharmacy	<ul style="list-style-type: none"> Intervention: medication review by a geriatrician, and dose reduction or discontinuation of potentially inappropriate medications according to the 2012 Beer's criteria Target: participants taking ≥ 5 prescription medications at baseline Frequency: monthly
Home hazards	<ul style="list-style-type: none"> Intervention: evaluation of home environment by a visiting nurse and a social worker using the Home Fall Prevention Checklist by Centers for Disease Control and Prevention and modification of the environment to eliminate any identified hazard Target: all participants with any identified home hazard at baseline Frequency: trimonthly

Abbreviation: CES-D, Center for Epidemiologic Studies Depression Scale.

living (ADL), and instrumental activities of daily living (IADL), as shown in Table S1. During the intervention period, we calculated the attendance to the group exercise sessions and the number of nutritional supplements consumed on a weekly basis; in addition, we assessed the attendance to monthly evaluation and management for depression and polypharmacy in those who were eligible for the respective intervention at the beginning of the intervention (baseline). The adherence rate was calculated by the number of sessions attended divided by the total number of sessions for each intervention component (or the number of nutritional supplement packs consumed divided by the total packs distributed) during the intervention period. A standardized questionnaire was used to assess severe adverse events requiring emergency room visit or hospitalization.

Statistical analysis

We estimated that at least 78 participants would be needed to detect a 1-point change in the SPPB score over 6 months, assuming the SD of the change score to be 2.1 points and 10% loss to follow-up.^{4,14} There were no planned interim analyses or stopping rules. Using two-sample *t*-test and chi-squared test, we examined how the characteristics of participants in the intervention study differed from those who declined to participate.

To assess the effectiveness of our multicomponent intervention program, we assessed the change in the mean SPPB score before and after the intervention for each geographic region. For continuous outcome measures, including SPPB, Center for Epidemiologic Studies Depression Scale (CES-D), and Mini Nutritional Assessment-Short Form scores, we used linear mixed-effects models that included a random intercept term for each participant and fixed-effect terms for time indicators (using the beginning of the intervention as baseline) and indicators for geographic regions. We used logistic mixed-effects models for frailty and sarcopenia with the same random- and fixed-effect terms and negative binomial mixed-effects model for the number of falls with log follow-up time as an offset. From these models, we estimated the program's immediate and sustained effects on the outcomes and its 95% CIs. As a post hoc secondary analysis, we included time indicators-by-subgroup interaction terms in the mixed-effects model to evaluate effect modification by baseline characteristics. In addition, we applied random forests²¹ to identify baseline characteristics that predict good responders to the program. Good response was defined as an increase in the SPPB score >1 point or the total SPPB score >10 (out of 12 points) by the end of the intervention. Important baseline variables were selected by inspecting the mean decrease in accuracy due to exclusion of each variable

in the “out-of-bag” sample which was not used to develop the decision rule.²¹ We calculated the proportion of good vs poor responders according to these characteristics. All analyses were performed using R software version 3.3.3,²² and a two-sided *P*-value <0.05 was considered statistically significant.

Results

Study population

Of the 1,267 ASPRA cohort participants, 393 (31.0%) were eligible (Figure 1). After excluding 206 who declined the intervention (*n*=196) or met the exclusion criteria (*n*=10), we enrolled 187 individuals. Compared with the excluded individuals, the included individuals were older (mean age, 77.4 vs 76.0 years) and had a poorer health status, as evidenced by higher prevalence of multimorbidity (61.0% vs 42.2%), polypharmacy (53.5% vs 22.8%), ADL disability (24.6% vs 16.0%), sarcopenia (49.2% vs 35.9%), undernutrition (78.1% vs 41.3%), and fall history (26.7% vs 14.1%), as shown in Table S2. Although the prevalence of geriatric conditions varied across the three regions, multimorbidity, polypharmacy, sarcopenia, and undernutrition were common (Table 2). The mean SPPB score ranged from 7.0 to 7.8 points; 25.8%–43.2% met the frailty phenotype criteria and 33.3%–46.5% had gait speed <0.6 m/s.

Adherence and follow-up

On average, participants attended 83.7% of the group exercise sessions during the 24-week period and consumed 87.8% of nutrition packs provided during the intervention period (Table 3). Those with greater depressive symptoms (*n*=33) and polypharmacy (*n*=100) attended 88% of evaluations which were conducted by a geriatrician or a psychiatrist. Home hazards were reduced in 91% of individuals who were identified as having a greater risk for home hazards at baseline. During the intervention period, six serious adverse events were reported: one distal radius fracture, one heart failure exacerbation, one coronary artery revascularization, one peptic ulcer, one metastatic lung cancer, and one fatal hemorrhagic stroke. Seven participants in region B (five refused due to health-related reasons and two moved out of the area) and one participant in region C (refused follow-up due to health-related reasons) were lost to follow-up.

Effectiveness of a multicomponent program

The multicomponent program had a sustained positive effect on physical function (Figure 2). Since we repeated outcome assessment 6 months after the conclusion of intervention in regions A and B, we were able to assess the sustained effectiveness of our intervention at 12 months. The SPPB score

Table 2 Characteristics of the participants in Aging Study of Pyeongchang Rural Area, an intervention study

Characteristics	Total population	Region A intervention: August 2015–January 2016	Region B intervention: February 2016–July 2016	Region C intervention: August 2016–January 2017
Sample size, <i>n</i>	187	33	88	66
Age, years, mean±SD	77.4±5.1	78.1±4.9	76.4±5.2	78.3±4.9
Female, <i>n</i> (%)	141 (75.4)	29 (87.9)	59 (67.0)	53 (80.3)
Education, years, mean±SD	2.1±3.8	2.5±3.8	2.1±3.8	1.8±3.9
Low income, <i>n</i> (%)	49 (26.2)	8 (24.2)	31 (35.2)	10 (15.2)
Living alone, <i>n</i> (%)	151 (80.7)	26 (78.8)	62 (70.5)	63 (95.5)
Height, cm, mean±SD	150.5±8.1	148.7±7.5	151.6±8.2	149.9±7.9
Weight, kg, mean±SD	55.8±10.2	55.0±9.7	55.4±9.8	56.8±11.1
BMI, kg/m ² , mean±SD	24.6±3.8	24.7±3.4	24.0±3.7	23.8±4.1
Multimorbidity, <i>n</i> (%)	114 (61.0)	22 (66.7)	51 (58.0)	41 (62.1)
Polypharmacy, <i>n</i> (%)	100 (53.5)	21 (63.6)	47 (53.4)	32 (48.5)
Gait speed <0.6 m/s, <i>n</i> (%)	68 (36.4)	15 (46.5)	31 (35.2)	22 (33.3)
ADL disability, <i>n</i> (%)	46 (24.6)	7 (21.2)	32 (36.4)	7 (10.6)
IADL disability, <i>n</i> (%)	68 (36.4)	20 (60.6)	24 (27.3)	24 (36.4)
SPPB score, mean±SD	7.4±2.2	7.1±2.7	7.8±2.1	7.0±2.1
Frailty, <i>n</i> (%)	66 (35.3)	11 (33.3)	38 (43.2)	17 (25.8)
Sarcopenia, <i>n</i> (%)	92 (49.2)	16 (48.5)	43 (48.9)	33 (50.0)
MNA-SF score ≤11, <i>n</i> (%)	146 (78.1)	31 (93.9)	64 (72.7)	51 (77.2)
CES-D score >20, <i>n</i> (%)	33 (17.6)	4 (12.1)	21 (23.9)	8 (12.1)
Fall in the past year, <i>n</i> (%)	50 (26.7)	5 (15.2)	27 (30.7)	18 (27.3)

Abbreviations: ADL, activities of daily living; BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale; IADL, instrumental activities of daily living; MNA-SF, Mini Nutritional Assessment-Short Form; SPPB, Short Physical Performance Battery.

Table 3 Adherence to multicomponent intervention program

Focus	Definition of adherence	Eligible participants n (%)	Adherence (%)			
			Total population	Region A intervention: August 2015–January 2016	Region B intervention: February 2016–July 2016	Region C intervention: August 2016–January 2017
Exercise	Attendance to group exercise sessions	187 (100)	83.7	80.0	86.9	81.2
Nutrition	Proportion of supplements consumed	187 (100)	87.8	90.7	79.1	97.8
Depression	Attendance to monthly visits	33 (17.6)	88.4	87.5	88.9	87.5
Polypharmacy	Attendance to monthly visits	100 (53.5)	88.5	88.1	91.5	84.4
Home hazards	Correction of any home hazards	149 (79.7)	91.3	85.7	91.3	93.8

did not change before the intervention; however, it increased with the intervention and changed minimally after the intervention. Compared with the baseline score, the SPPB score increased by 3.18 points (95% CI: 2.89, 3.48) at 6 months and by 3.24 points (95% CI: 2.88, 3.60) at 12 months (Table 4). The program substantially reduced frailty (odds ratio: 0.08 at 6 months and 0.06 at 12 months) and sarcopenia (odds ratio: 0.21 at 6 months and 0.32 at 12 months). The Mini Nutritional Assessment-Short Form score improved by 1.67 points at 12 months (95% CI: 1.28, 2.06); the CES-D score improved at 6 months (−3.36 points; 95% CI: −4.55, −2.17) and at 12 months (−3.83 points; 95% CI: −5.26, −2.39). However, the rate of falls did not significantly reduce (rate ratio: 0.99 at 6 months and 1.18 at 12 months).

Post hoc analysis

Female gender, multimorbidity, gait speed <0.6 m/s, frailty, CES-D score >20 points, and ADL disability at baseline

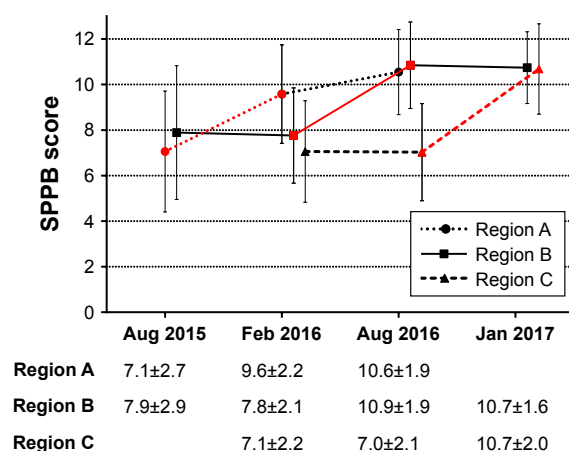


Figure 2 Physical function before and after multicomponent intervention program. **Notes:** The mean (node) and SD (vertical bar) of the SPPB score are presented for participants in the three geographic regions before and after the multicomponent intervention program. The intervention period is denoted in red. The table below the graph presents the mean±SD for each region.

Abbreviation: SPPB, Short Physical Performance Battery.

were associated with greater improvements in the SPPB score after the program (P -value for interaction <0.05), as shown in Figure S1. When we examined the baseline variables for predicting >1-point SPPB improvement or >10 points at the end of the intervention, we found body mass index and IADL disability as the two most important baseline characteristics (Figure 3). Body mass index <27 kg/m² and the absence of IADL disability at baseline were associated with good response to the intervention; the proportion of good responders decreased from 92% (84 of 91) to 53% (10 of 19) when patients with body mass index ≥27 kg/m² and IADL disability were considered.

Discussion

This designed-delay intervention study found that our 24-week intervention program resulted in a clinically meaningful improvement in terms of physical function, frailty, sarcopenia, nutritional risk, and depression symptoms in older adults who were living alone or had low income in the rural community. Except for falls, the benefit was sustained for most outcomes at 6 months after the intervention. As such, a consistent level of improvement across the three different regions and three different periods provides strong evidence for the effectiveness of our intervention. In addition, the design and protocol of our study demonstrate that the effectiveness of a public health program can be evaluated in a resource-limited setting without randomization.

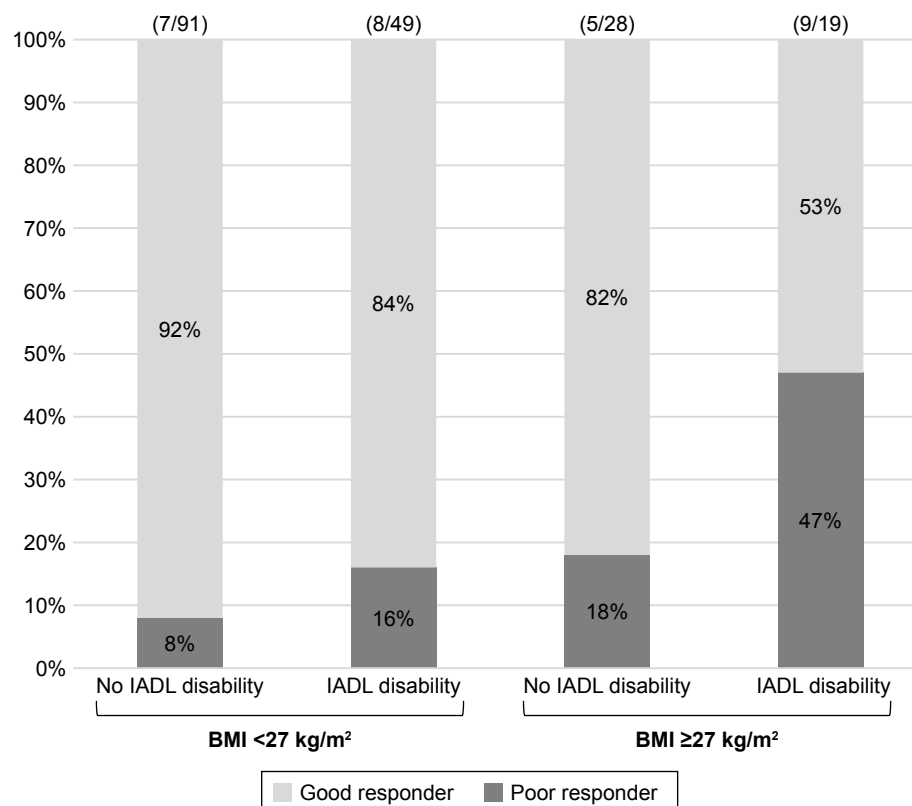
The results of our trial are consistent with the benefit of exercise alone or multicomponent interventions on objective measures of physical function reported in the literature (Table 5). Four studies showed a modest improvement in physical function^{3,7,8,23} (eg, SPPB score 0.6²³–1.0 point⁸) with exercise alone. Five studies of multicomponent interventions that included exercise, nutritional supplementation, and other

Table 4 Effects of multicomponent program on physical function, frailty, and other geriatric conditions

Outcome	Time ^a (months)	N _{total} ^b	N _{drop-out} ^c	Summary statistics	Effect size (95% CI) ^d
SPPB, mean±SD	0	187	0	7.4±2.2	Reference
	6	184	3	10.6±2.0	MD: 3.18 (2.89, 3.48)
	12	114	5	10.7±1.7	MD: 3.24 (2.88, 3.60)
Frailty, n (%)	0	187	0	66 (35.3)	Reference
	6	184	3	12 (6.5)	OR: 0.08 (0.03, 0.18)
	12	114	5	7 (6.1)	OR: 0.06 (0.02, 0.16)
Sarcopenia, n (%)	0	187	0	92 (49.2)	Reference
	6	184	3	57 (31.0)	OR: 0.21 (0.11, 0.41)
	12	114	5	40 (35.1)	OR: 0.32 (0.15, 0.68)
MNA-SF, mean±SD	0	187	0	10.7±2.2	Reference
	6	184	3	11.9±1.9	MD: 1.20 (0.88, 1.53)
	12	114	5	12.5±1.8	MD: 1.67 (1.28, 2.06)
CES-D, mean±SD	0	187	0	10.8±9.6	Reference
	6	184	3	7.4±7.9	MD: -3.36 (-4.55, -2.17)
	12	114	5	7.3±9.0	MD: -3.83 (-5.26, -2.39)
No of falls per 100 person-days	0	187	0	0.47	Reference
	6	186	1	0.35	RR: 0.99 (0.69, 1.43)
	12	119	0	0.37	RR: 1.18 (0.77, 1.81)

Notes: ^aThe time between month 0 and month 6 represents the intervention period. ^bOnly participants from region A and region B were assessed at month 12. ^cThe rate of falls was calculated using data from all available person-time, even if some participants did not complete assessments at month 6 or month 12. ^dEffect sizes (MD, OR, or RR) were estimated from mixed-effects models that included a random intercept term for each participant and fixed-effect terms for time indicators (month 6 and month 12) and for geographic regions. The effect size comparing month 6 vs month 0 represents the immediate effect of the intervention. The effect size comparing month 12 vs month 0 represents the sustained effects of the intervention.

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; MD, mean difference; MNA-SF, Mini Nutritional Assessment-Short Form; OR, odds ratio; RR, rate ratio; SPPB, Short Physical Performance Battery.

**Figure 3** Prediction of response to multicomponent intervention program.

Notes: Good responders were defined as either those having an increase of > 1 point in the SPPB score over the 24-week intervention period compared with the baseline score, or those with a total SPPB score increase of > 10 points (range: 0–12 points; higher score indicates better physical function) at 6 months. Numbers on the top of the graph represent the number of poor responders/number of participants in each category.

Abbreviations: BMI, body mass index; IADL, instrumental activities of daily living; SPPB, Short Physical Performance Battery.

Table 5 Randomized controlled trials of exercise intervention in community-dwelling older adults at risk for functional decline

Study	Population	Intervention	Main findings
Binder et al, 2002 ³ USA	Total N=115 Mean age: 83 years Women: 52%	Intervention: supervised group exercise <ul style="list-style-type: none"> Three indoor exercises per week for 9 months Gradually increasing intensity of flexibility, resistance, balance, and endurance Comparison: low-intensity exercise instruction <ul style="list-style-type: none"> Two to three exercises per week at home for 9 months Nine flexibility exercises 	<ul style="list-style-type: none"> Physical function at 9 months 1. Modified PPT (range: 0–36): +3.4 vs +0.8^a 2. Peak VO₂ (mL/kg/min): +2.0 vs –0.4^a Loss to follow-up: 30% vs 16%
Gill et al, 2004 ⁷ USA	Total N=188 Mean age: 83 years Women: 80%	Intervention: home-based physical therapy <ul style="list-style-type: none"> Daily home exercise for 6 months, such as bed mobility, transfer, indoor gait, and outdoor mobility Progressive, competency-based exercise including range of motion, balance, and muscle strengthening Comparison: monthly home visit by a health educator	<ul style="list-style-type: none"> Physical function at 12 months 1. Timed rapid gait (seconds): +2.4 vs +6.0 2. Timed chair stand (seconds): –3.1 vs –1.2^a 3. Modified POMA (range: 0–12): –0.5 vs –0.8 4. Modified PPT (range: 0–12): +1.3 vs +0.2^a Loss to follow-up: 6% vs 4%
LIFE-P, 2006 ⁸ USA	Total N=424 Mean age: 77 years Women: 69%	Intervention: physical activity program <ul style="list-style-type: none"> First 2 months (adoption): weekly center-based sessions Next 4 months (transition): two center-based sessions per week plus ≥3 home-based sessions per week Final 6 months (maintenance): ≥3 home-based sessions per week plus optional 1–2 center-based sessions per week and monthly telephone follow-up Aerobics, strength, balance, and flexibility Comparison: group education	<ul style="list-style-type: none"> Physical function at 12 months 1. SPPB score (range: 0–12): +1.0 vs +0.4^a 2. 400 m walk test (m/s): –0.01 vs –0.03^a Loss to follow-up: 4% vs 9%
McAuley et al, 2013 ²³ USA	Total N=307 Mean age: 71 years Women: 77%	Intervention: DVD-delivered exercise program <ul style="list-style-type: none"> Three home-based programs per week for 6 months Two sets of 11–12 different exercises focusing on flexibility, balance, and toning Comparison: healthy aging DVD	<ul style="list-style-type: none"> Physical function 1. SPPB score (range: 0–12): +0.6 vs –0.1^a Loss to follow-up: 19% vs 11%
Cameron et al, 2013 ⁴ Australia	Total N=241 Mean age: 83 years Women: 68%	Intervention: individualized, multidisciplinary intervention targeting the CHS frailty domains <ul style="list-style-type: none"> Weakness, slowness, or low physical activity: up to ten home-based physiotherapy sessions and then three to five home exercise program per week over the course of 12 months (strength, balance, and endurance) Weight loss: home-delivered meals and additional high-energy protein supplements for 12 months if BMI <18.5 kg/m² or mid upper arm circumference <10th percentile Exhaustion: referred to a psychiatrist or psychologist Comparison: usual care <ul style="list-style-type: none"> General practitioner and medical specialist consultations Nursing and allied health interventions by community aged care services 	<ul style="list-style-type: none"> Frailty and physical function at 12 months 1. CHS score (range: 0–5): –0.80 vs –0.41 2. SPPB score (range: 0–12): +0.52 vs –0.98^a Loss to follow-up: 11% vs 10%

(Continued)

Table 5 (Continued)

Study	Population	Intervention	Main findings
Ng et al, 2015 ⁵ Singapore	Total N=246 Mean age: 70 years Women: 61%	Intervention: physical, nutritional, cognitive, and combination intervention (four intervention programs) <ul style="list-style-type: none"> Physical intervention: two group exercises per week for 12 weeks, followed by daily individualized home-based exercise for 12 weeks Nutritional intervention: daily commercial formula, iron, folate, and vitamin B6 and B12 supplements for 24 weeks Cognitive training intervention: weekly cognition-enhancing activity sessions for 24 weeks Combined intervention: all three components Comparison: usual health and aged care services from government or private clinics and hospitals <ul style="list-style-type: none"> Placebo supplement 	<ul style="list-style-type: none"> Frailty at 12 months in physical intervention group vs nutritional intervention group vs cognitive training group vs combined intervention group 1. CHS score (range: 0–5): –0.83 vs –0.63 vs –0.62 vs –0.92 vs –0.14^a Loss to follow-up: 8% vs 10% vs 4% vs 6% vs 8%
Tarazona-Santabalbina et al, 2016 ⁶ Spain	Total N=100 Mean age: 80 years Women: 54%	Intervention: a multicomponent exercise program with nutritional support <ul style="list-style-type: none"> Five supervised-facility exercises per week for 24 weeks; daily protein-calorie and vitamin D supplementation Proprioception, aerobics, strength, and stretching Comparison: nutritional supplementation alone <ul style="list-style-type: none"> Protein-calorie and vitamin D supplements 	<ul style="list-style-type: none"> Physical function and frailty at 6 months 1. SPPB score (range: 0–12): +0.9 vs –1.5^a 2. PPT score (range: 0–36): +4.2 vs –2.2^a 3. CHS score (range: 0–5): –2.0 vs 0.0^a Loss to follow-up: 20% vs 16%
Serra-Prat et al, 2017 ⁹ Spain	Total N=172 Mean age: 78 years Women: 56%	Intervention: nutritional assessment and physical activity program <ul style="list-style-type: none"> Four home-based exercises per week for 12 months Aerobics, resistance, and balance exercises Nutritional assessment and referral for dietary recommendations Comparison: usual care	<ul style="list-style-type: none"> Frailty at 12 months 1. Incident CHS frailty: +4.9% vs +15.3%^a Loss to follow-up: 24% vs 22%
Villareal et al, 2017 ²⁴ USA	Total N=160 Mean age: 70 years Women: 64%	Intervention: a multicomponent exercise program combined with dietary weight management and calcium and vitamin D supplementation (three intervention programs) <ul style="list-style-type: none"> Aerobic intervention: three individual exercises per week on flexibility, aerobics, and balance for 26 weeks Resistance intervention: three individual exercises per week on flexibility, resistance, and balance for 26 weeks Combined intervention: three individual exercises per week for flexibility, resistance, and balance, as well as aerobics for 26 weeks Comparison: education on a healthy diet <ul style="list-style-type: none"> Calcium and vitamin D supplementation 	<ul style="list-style-type: none"> Physical function at 6 months 1. PPT (range: 0–36): +3.9 vs +3.9 vs +5.5 vs +1.0^a 2. Peak VO₂ (mL/kg/min): +3.3 vs +1.3 vs +3.1 vs +0.1^a 3. One repetition maximal strength (kg): +5 vs +49 vs +48 vs +2%^a Loss to follow-up: 13% vs 13% vs 13% vs 10%

Note: ^aStatistical significance compared with the comparison group ($P<0.05$).

Abbreviations: BMI, body mass index; CHS, Cardiovascular Health Study; POMA, Performance Oriented Mobility Assessment; PPT, Physical Performance Test; SPPB, Short Physical Performance Battery.

interventions (eg, mental health provider referral,⁴ cognitive training⁵) showed a moderate improvement in physical function^{4,6,24} (eg, SPPB score 1.4⁴–2.0 points⁶) and frailty phenotype.^{4–6,9} These are possibly due to lower adherence, difference in the intervention (targeting fewer components), nutritional supplementation only in selected individuals, and choice of young and less frail target populations in other studies. The Sarcopenia and Physical Frailty IN older people: multi-component Treatment strategies (SPRINTT) trial will confirm the long-term benefits of a multicomponent intervention in preventing mobility impairment in 1,500 older adults with frailty and sarcopenia in nine European countries.²⁵

Our main objective was to evaluate the effectiveness of the intervention within the existing infrastructure of the regional public health center rather than establishing a clinical trial center. Therefore, our study design was influenced by the input from regional and local public health workers and town representatives. We enrolled residents who were living alone or on low income, because they had been identified by the local public health centers as high-priority individuals for various public health interventions. We previously found high burden of frailty and geriatric syndromes in these residents.¹⁰ Another advantage of targeting this population was that we were able to achieve efficient enrollment, high adherence, high retention, and more complete outcome assessment.

Although a randomized controlled trial is considered the gold standard to test the efficacy of an intervention, barriers to conducting a randomized controlled trial in rural areas have been well described.^{26–29} Previous research showed that older adults with low educational attainment or in rural communities might be unfamiliar with randomization.^{26–29} Public health officials are more interested in pragmatic implementation and evaluation of a program than scientific rigor; typically, the program evaluation is based on pre- vs post-intervention comparison. Such a design is subject to bias due to concurrent changes in clinical and public health practice that can result in an improvement in the outcome, unrelated to the intervention itself. Since most participants in our study received medical and preventive care through the local public health centers, we are certain that there were no major changes in usual care during the study period. Moreover, stable SPPB score in the pre-intervention period excludes the possibility of a practice effect or a spontaneous improvement. In summary, our study demonstrates that a designed-delay study can be an economically favorable alternative for testing the effectiveness of new therapies, programs, or policy changes in the routine care setting.^{30,31}

This study has several limitations that deserve mention. First, our results derived from socioeconomically vulnerable older Koreans living in rural areas may not be generalizable to other populations. However, we believe that the physiologic effects of our program would be similar across populations. Second, the adherence to individual components of the intervention was less than perfect. We were unable to distinguish the effect of individual components. Our exercise and nutritional interventions were not individualized according to the nutritional status or muscle condition of each individual, mainly for practical reasons. Nonetheless, our intervention was highly effective in improving the physical function, as shown in other multicomponent interventions for geriatric syndromes (eg, falls³² and delirium³³). Third, in a designed-delay study where the intervention was rolled out sequentially to different regions, any concurrent interventions outside our study may have affected the SPPB score. Given the nature of our intervention (eg, group exercise session, nutritional supplements, physician evaluation, and home safety evaluation) and the distance between the regions of intervention, we think that the chance of contamination across different regions is low. Fourth, we were unable to examine long-term clinical outcomes, such as mortality or institutionalization, because all participants received the intervention at some point. Fifth, in assessing falls and health care utilization, we interviewed participants on a monthly basis during the intervention period for safety monitoring and every 3 months during the non-intervention period. Higher surveillance frequency during the intervention period may have resulted in larger numbers of these outcomes at 6 months, which may have caused underestimation of the beneficial effect. Finally, further validation is needed to confirm whether obesity and IADL disability are predictors of poor response.

Conclusion

Our study shows that a 24-week multicomponent intervention program can effectively improve physical function, frailty, sarcopenia, depressive symptoms, and nutritional status in community-dwelling older populations. Most benefits seem to last at least 6 months after the intervention. A widespread adoption of our program as a public health intervention can potentially promote relatively healthy aging in older people.

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Author contributions

All authors participated in designing the study concept, performed statistical analysis, data analysis, and interpretation, and drafted the manuscript. The agreement is to be accountable for all aspects of the work in ensuring that the accuracy or integrity of any part of the work is appropriately investigated and

resolved. All authors read and revised this manuscript. This manuscript is the final approval of version from all authors. All authors have reviewed and agreed to be responsible for the process, accuracy, and integrity of all parts of this manuscript.

Disclosure

Dr Dae Hyun Kim is a consultant to Alosa Health, a nonprofit educational organization with no relationship to any drug or device manufacturer. The other authors declare that there is no potential conflict of interests regarding the publication of this article.

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Supplementary materials

Table S1 Details of outcome assessments and other measurements

Outcomes	Measurements	Range	Reference
Primary outcome			
Short Physical Performance Battery	Repeated chair stands, standing balance, and gait speed	0–12 ^a	1, 2
Secondary outcomes			
Frailty phenotype	According to the Cardiovascular Health Study criteria	0–5	3
Sarcopenia	According to the consensus report of the Asian Working Group for Sarcopenia	Yes or no	4, 5
	<ul style="list-style-type: none"> Weight loss, exhaustion, low activity, slowness, and weakness Low appendicular skeletal muscle mass measured using a bioimpedance analysis (Inbody 620; InBody, Seoul, Korea) Decreased physical performance 		
Nutritional risk	MNA-SF	0–14 ^b	6
Depressive symptoms	CES-D	0–60 ^c	7
Number of falls	Interview	Counts	8
Number of emergency room visits and hospitalization	Interview	Counts	
Other measurements			
Sociodemographic	Interview	NA	
Multimorbidity	Having ≥5 of the eleven physician-diagnosed conditions	Counts	9
	<ul style="list-style-type: none"> Angina, arthritis, asthma, cancer excluding minor skin cancer, chronic lung disease, congestive heart failure, diabetes, heart attack, hypertension, kidney disease, and stroke 		
Polypharmacy	Defined as taking ≥5 prescription medications	Counts	9
Disability	Requiring assistance in performing any of the ADLs and IADLs	Yes or no	10
	<ul style="list-style-type: none"> ADLs: bathing, continence, dressing, eating, toileting, transferring, and washing face and hands IADLs: food preparation, household chores, going out for short distances, grooming, handling finances, laundry, managing own medications, shopping, transportation, and using telephone 		

Notes: ^aHigher scores indicate better physical function. ^bHigher scores indicate better nutritional state. ^cHigher scores indicate greater depressive symptoms.

Abbreviations: ADL, activities of daily living; CES-D, Center for Epidemiologic Studies Depression Scale; IADL, instrumental activities of daily living; MNA-SF, Mini Nutritional Assessment-Short Form.

Table S2 Characteristics of individuals who were included or excluded from the Aging Study of Pyeongchang Rural Area, an intervention study

Characteristics	Older adults living alone or with low income		P-value
	Included	Excluded	
Sample size, n	187	206	
Age, years, mean±SD	77.4±5.1	76.0±6.5	0.025
Female, n (%)	141 (75.4)	142 (68.9)	0.154
Education, years, mean±SD	2.1±3.8	2.6±4.3	0.186
Low income, n (%)	49 (26.2)	34 (16.5)	0.019
Living alone, n (%)	151 (80.7)	184 (89.3)	0.017
BMI, kg/m ² , mean±SD	24.6±3.8	24.4±4.0	0.600
Multimorbidity, n (%)	114 (61.0)	87 (42.2)	0.001
Polypharmacy, n (%)	100 (53.5)	47 (22.8)	0.001
ADL disability, n (%)	46 (24.6)	33 (16.0)	0.034
IADL disability, n (%)	68 (36.4)	73 (35.4)	0.849
Gait speed <0.6 m/s, n (%)	68 (36.4)	63 (30.6)	0.226
Frailty, n (%)	66 (35.3)	62 (30.1)	0.273
Sarcopenia, n (%)	92 (49.2)	74 (35.9)	0.008
MNA-SF score ≤11, n (%)	146 (78.1)	85 (41.3)	0.001
CES-D score >20, n (%)	33 (17.6)	31 (15.0)	0.489
Fall in the past year, n (%)	50 (26.7)	29 (14.1)	0.002

Abbreviations: ADL, activities of daily living; BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale; IADL, instrumental activities of daily living; MNA-SF, Mini Nutritional Assessment-Short Form.

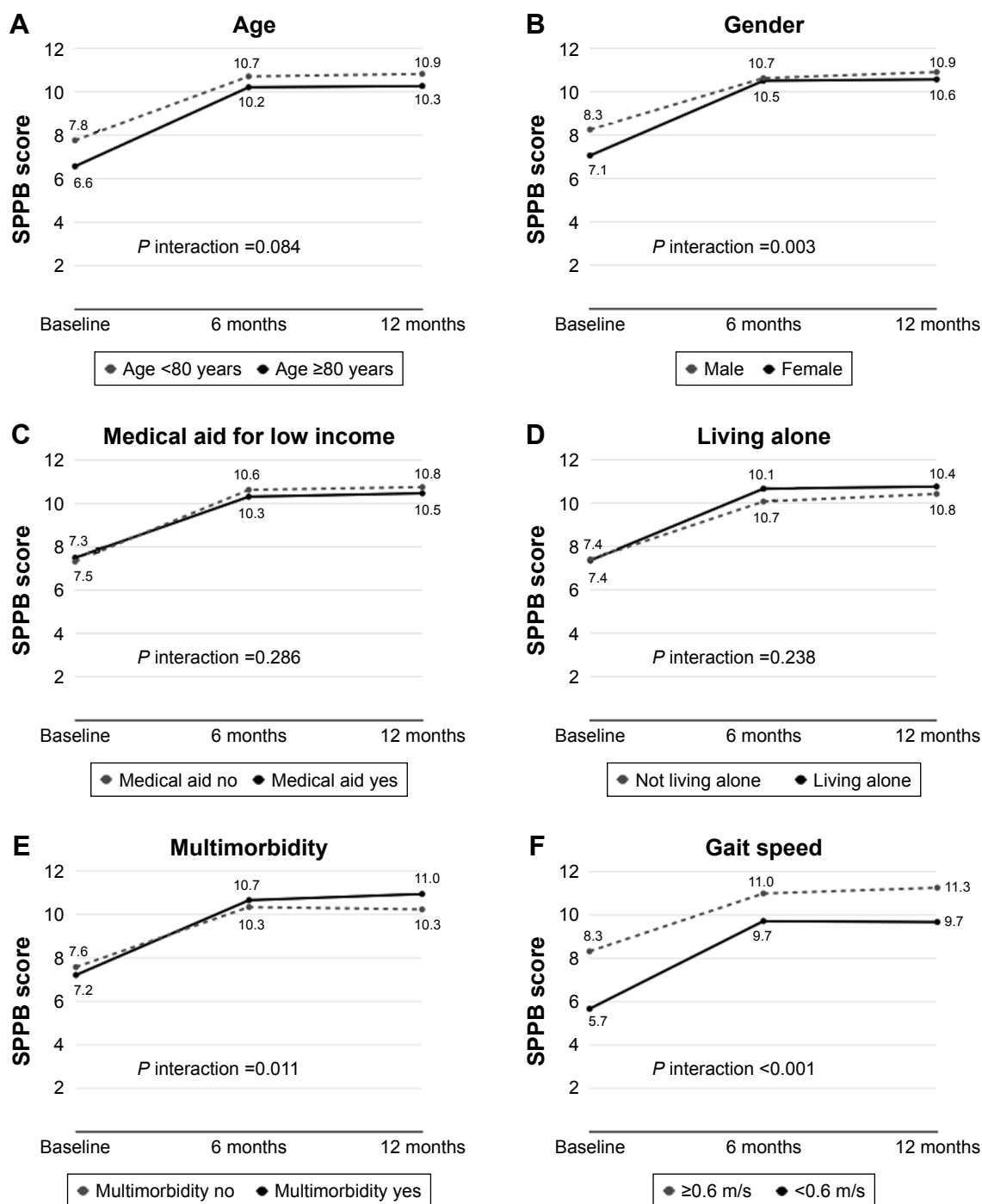


Figure S1 (Continued)

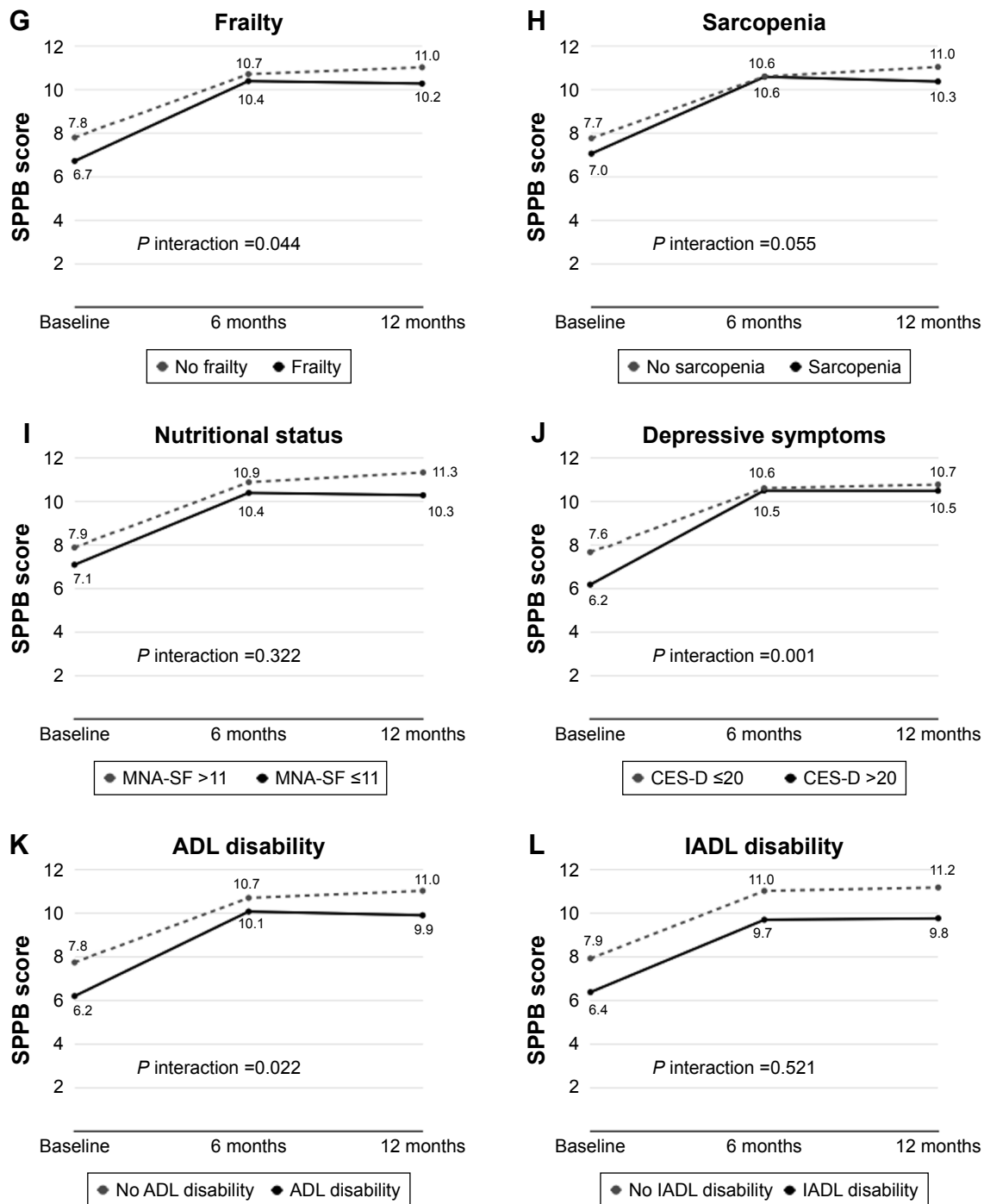


Figure S1 Effect of multicomponent program by subgroups defined by baseline characteristics.

Note: Female gender, multimorbidity, gait speed <0.6 m/s, frailty, CES-D score >20 points, and ADL disability at baseline were associated with greater improvements in the SPPB score after the program (P -value for interaction <0.05).

Abbreviations: ADL, activities of daily living; CES-D, Center for Epidemiologic Studies Depression Scale; IADL, instrumental activities of daily living; MNA-SF, Mini Nutritional Assessment-Short Form; SPPB, Short Physical Performance Battery.

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