Journal of the American Heart Association

ORIGINAL RESEARCH

Attendance at Supervised Exercise Sessions and Walking Outcomes in Peripheral Artery Disease: Results From 2 Randomized Clinical Trials

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BACKGROUND: Supervised exercise therapy (SET) is the first-line therapy for walking impairment in peripheral artery disease (PAD). This study evaluated the association between attendance at SET and improved walking performance, compared with a control group, in PAD.

METHODS AND RESULTS: Data from 2 randomized clinical trials of SET for PAD were combined. In each trial, participants were randomized to 3 times weekly supervised treadmill exercise or an attention control group for 6 months (maximum, 77 exercise sessions). Participants randomized to SET were categorized into tertiles, according to the proportion of exercise sessions they attended. Results adjusted for age, sex, race, baseline walking performance, comorbidities, and other potential confounders. A total of 272 participants with PAD (mean age, 67.9±9.3 years; 44% women; 61% Black race) were included. For participants randomized to SET, tertiles of attendance rates at exercise sessions were as follows: 11% to 68% (N=45), 69% to <85% (N=46), and ≥85% (N=46). Compared with control, mean improvement in 6-minute walk was significantly greater in each SET tertile: mean (95% CI) for tertile 1, 27.9 m (1.3–54.4 m; P=0.04), tertile 2, 38.2 m (12.2–64.2 m; P=0.001), and tertile 3, 56.9 m (29.9–83.8 m; P<0.0001). Among participants randomized to SET, greater SET attendance was associated with greater improvement in 6-minute walk distance (overall P for trend=0.025). Compared with control, improvement in maximal treadmill walking time was greater in each SET attendance tertile: tertile 1 (3.3 minutes [95% CI, 1.7–4.8 minutes]; P<0.0001), tertile 2 (3.8 minutes [95% CI, 2.3–5.3 minutes]; P<0.0001), and tertile 3 (5.4 minutes [95% CI, 3.9–7.0 minutes]; P:<0.0001). Among participants randomized to SET, greater attendance at SET was not significantly associated with greater improvement in maximal treadmill walking time (overall P for trend=0.064).

CONCLUSIONS: Among people with PAD randomized to SET, better attendance at exercise sessions was associated with significantly greater 6-minute walk improvement. Among all participants with PAD, even relatively low SET attendance was associated with significantly greater improvement in walking performance, compared with a control group who did not exercise.

REGISTRATION: URL: https://clinicaltrials.gov/ct2/show/NCT01408901. URL: https://clinicaltrials.gov/ct2/show/NCT00106327

Key Words: 6-minute walk ■ adherence ■ functional outcomes ■ peripheral artery disease ■ supervised exercise ■ walking outcomes

Supervised exercise therapy (SET) is the first-line therapy for improving walking impairment in people with lower extremity peripheral artery disease (PAD) and has been paid for by the Centers for Medicare and Medicaid Services (CMS) insurance since 2017.[1,2] CMS covers 36 supervised exercise sessions over 12 weeks.[2] If patients with PAD remain symptomatic after 12 weeks of SET, CMS pays for an additional 36 sessions of

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Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.122.026136

For Sources of Funding and Disclosures, see page 10.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- In combined data from 2 randomized clinical trials of supervised exercise therapy that included 272 people with lower extremity peripheral artery disease, better attendance at supervised exercise therapy was associated with significantly greater improvement in 6-minute walk distance among participants randomized to exercise.
- Even participants with peripheral artery disease who had poor adherence to exercise had better improvement in 6-minute walk than a control group who did not exercise.

What Are the Clinical Implications?

- Among people with peripheral artery disease, even relatively poor attendance to supervised exercise sessions was associated with significantly greater improvement in walking ability, compared with a control group who did not exercise.
- Among participants randomized to a supervised exercise intervention, attending a higher number of supervised exercise sessions was associated with greater improvement in walking performance.

Nonstandard Abbreviations and Acronyms

CMS	Centers for Medicare and Medicaid Services
PROPEL	Progenitor Cell Release Plus Exercise to Improve Functional Performance in Peripheral Artery Disease
SET	supervised exercise therapy
SILC	Study to Improve Leg Circulation

exercise.[2] However, few people with PAD participate in SET, and even when patients with PAD enroll in SET, attendance is poor.[3–5] A study of 129 699 Medicare beneficiaries with PAD and claudication showed that of 1735 patients who enrolled in SET between 2017 and 2018, the median number of SET sessions attended was 16 (interquartile range, 6–28).[3] The benefit of SET, when exercise session attendance is poor, remains unclear.

This study used data from 2 randomized clinical trials of SET in people with PAD to examine whether people with different degrees of attendance at supervised exercise had greater improvement in 6-minute walk distance and maximal treadmill walking time, compared with a control group who did not exercise. Among people with PAD, the association of attendance at exercise sessions with improvement in 6-minute walk and treadmill walking time was evaluated. Clinical characteristics associated with poorer attendance at supervised treadmill exercise in people with PAD were also studied. Study hypotheses were that participants with PAD randomized to supervised exercise would have significantly better improvement in outcomes, regardless of attendance, compared with a control group who did not exercise, and that greater attendance at supervised treadmill exercise therapy would be associated with greater improvement in 6-minute walk distance and maximal treadmill walking time.

METHODS

Study Population

This study reports post hoc analyses from 2 randomized clinical trials of supervised treadmill exercise in people with PAD: the SILC (Study to Improve Leg Circulation) and PROPEL (Progenitor Cell Release Plus Exercise to Improve Functional Performance in PAD) trials.[6–9] Details of the SILC and PROPEL trials have been described.[6–9] The institutional review board at Northwestern University and all participating institutions approved the study protocols. All participants provided written informed consent. The data that support the findings of this study may be available from the corresponding author upon reasonable request.

Overview of SILC and PROPEL Randomized Clinical Trials

The SILC clinical trial randomized 156 participants with PAD to lower extremity strength training, supervised treadmill exercise, or an attention control group and studied whether supervised treadmill exercise and lower extremity strength training significantly improved 6-minute walk distance, compared with a control group.[6,7] Because the current analyses focused on the association of supervised treadmill exercise attendance with change in walking performance, participants randomized to lower extremity resistance training were excluded from the present analyses. The PROPEL clinical trial randomized 210 participants with PAD to supervised treadmill exercise or granulocyte-macrophage colony-stimulating factor using a 2×2 factorial design to determine whether supervised treadmill exercise, with or without granulocyte-macrophage colony-stimulating factor, significantly improved 6-minute walk distance compared with an attention control group.[8,9] Because granulocyte-macrophage colony-stimulating factor did not have a significant effect on 6-minute walk distance, either alone or in combination with supervised exercise, participants randomized to granulocyte-macrophage colony-stimulating factor in the PROPEL trial were included in analyses reported herein.

Participant Recruitment

Recruitment methods included newspaper and radio advertisements, mailing recruitment postcards to older people in the Chicago, IL, area identified via purchased mailing lists, posted flyers, recruitment mailings to people diagnosed with PAD in the Lifeline of Screening program, community outreach, and mailing recruitment letters to patients with PAD identified from Northwestern Medical Center and other Chicago-area hospitals.[6–9]

Inclusion Criteria

In the SILC trial, the inclusion criterion was an ankle-brachial index (ABI) ≤0.95.[6,7] In the PROPEL trial, the inclusion criterion was an ABI ≤0.90.[8,9] In the PROPEL trial, participants with ABI ≥0.90 at baseline were eligible if there was vascular laboratory evidence of PAD from a hospital-affiliated vascular laboratory, and participants with ABI between 0.90 and 1.00 with prior lower extremity revascularization were eligible if they had a 20% decrease in ABI following a heel-rise test.[8–10]

Exclusion Criteria

Exclusion criteria in each trial have been reported and are summarized herein.[6–9] In both trials, potential participants with dementia, major lower extremity amputation, chronic limb-threatening ischemia, foot ulcers, and walking limitation from a cause other than PAD, those unable to walk on a treadmill, and those unable or unwilling to exercise at the medical center 3 times weekly were excluded. Potential participants with major surgery, revascularization, or a myocardial infarction within the past 3 months, or with major surgery planned in the next 6 months, were excluded. Participants involved in other clinical trials at the time of recruitment, those with baseline exercise behavior comparable with that offered in the exercise interventions, and those with abnormal baseline exercise stress test results were excluded.[6–9] In the SILC trial, participants with a baseline short physical performance battery score of 12 (the highest possible score) were excluded.[6,7] In the PROPEL trial, potential participants with Parkinson disease, those with significant visual or hearing impairment, and those recently treated for cancer, unless the prognosis was excellent, were excluded.[8,9]

Run-In

Potential participants who did not attend an exercise training session and 1 control group session over a 3-week period were excluded.[6,8]

Randomization

In the SILC trial, participants were randomized using a randomly permuted block design, stratified by the presence versus absence of intermittent claudication.[6] In the PROPEL trial, participants were randomized using block randomization, stratified by diabetes, with block sizes randomly selected from 8 and 12.[8,9]

ABI Measurement

A handheld Doppler probe (Nicolet Vascular Pocket Dop II, Golden, CO) was used to measure systolic blood pressures in the right brachial, posterior tibial, and dorsalis pedis arteries and left posterior tibial, dorsalis pedis, and brachial arteries. Measurements were performed twice. ABI was calculated by dividing mean pressures in each leg by the mean of the 4 brachial pressures.[11,12]

Supervised Treadmill Exercise Therapy

Typically, participants randomized to exercise had 72 exercise sessions scheduled. However, participants were scheduled for 6-month follow-up testing during a window of time beginning 2 weeks before and ending 2 weeks after the date that was 6 months after baseline. Some participants completed 6-month follow-up testing outside this window (eg, because of illness, travel, or to avoid follow-up testing during the holiday season). Therefore, the number of scheduled exercise sessions was not always 72. Participants began with ≈15 minutes of walking exercise per session and were helped to increase up to 40 to 50 minutes of walking exercise per session, not including rest.[6,9] Transportation to exercise sessions was available. Costs of parking and public transportation were covered by the study. Participant attendance was recorded.

Attention Control Group

In the SILC trial, participants in the attention control group were asked to attend 11 educational sessions over 6 months; these sessions provided information about healthy eating.[6] In the PROPEL trial, participants in the attention control group were asked to attend 1 educational session per week for 6 months. Lecture topics included nutritional supplements, hypertension, dementia, cancer screening, and medication safety.[8,9]

The 6-Minute Walk (Primary Outcome)

Participants were asked to walk back and forth along a 100-foot hallway, after receiving instructions via a script to cover as much distance as possible within 6 minutes. The total distance walked after 6 minutes was recorded.[13–15] In the PROPEL trial, 6-minute walk was measured at baseline and at 12-week and 6-month follow-up. In the SILC trial, 6-minute walk was measured at baseline and at 6-month follow-up. A clinically meaningful change in 6-minute walk has been defined as 8 to 20 m in people with PAD.[16,17]

Maximal Treadmill Walking Time

Change in maximal treadmill walking time was measured at baseline, 12-week follow-up (in the PROPEL trial), and 6-month follow-up using the Gardner-Skinner protocol.[6–9,18] The treadmill test began at a speed of 2.0 miles per hour with 0 grade. Grade was increased by 2% every 2 minutes until the participant could not continue walking. When participants were unable to walk at 2.0 miles per hour, the treadmill speed was started at 0.5 miles per hour and increased by 0.5 miles per hour every 2 minutes until the treadmill reached 2.0 miles per hour, after which the grade increased by 2% every 2 minutes. For maximum treadmill walking time, a small minimum clinically important difference has been defined as 38 seconds, and a large minimum clinically important difference has been defined as 152 seconds.[16]

Other Measures

Medical history, demographic characteristics, and comorbidities were obtained using an administered questionnaire, based on self-report.[6–9] Height and weight were measured at baseline. Body mass index (BMI) was calculated by dividing the weight in kilograms by the square of height in meters.[7,9]

Statistical Analysis

Data from the 2 clinical trials were combined. Baseline characteristics were compared between participants randomized to supervised treadmill exercise and those randomized to the control group using generalized linear models for continuous variables and χ^2 tests for categorical variables.

Participants randomized to the supervised treadmill exercise were categorized into tertiles of attendance based on the proportion of total available exercise sessions attended during the trial. Characteristics of participants across tertiles of attendance at exercise were compared using generalized linear models for continuous variables and χ^2 tests for categorical variables. Descriptive statistics were expressed as means with SDs for continuous variables and as frequencies and percentages for categorical variables.

General linear regression models were used to compare 6-month changes in 6-minute walk distance and maximal treadmill walking time between each supervised exercise attendance tertile and the control group, adjusting for age, sex, race, clinical trial (PROPEL versus SILC), ABI, smoking, diabetes, BMI, baseline walking performance (6-minute walk or maximal treadmill walking time), coronary artery disease, heart failure, myocardial infarction, cancer, pulmonary disease, and stroke. The Tukey-Kramer test was used to examine whether there were significant differences in 6-month change in 6-minute walk distance and 6-month change in maximal treadmill walking time, compared with the control group, for each tertile of exercise attendance. *P* values for overall trend were also calculated. Analyses were repeated among people randomized to supervised treadmill exercise alone. Because CMS initially covers 36 sessions of supervised exercise over 12 weeks, in a sensitivity analysis, participants randomized to the supervised treadmill exercise were categorized into tertiles of attendance based on the proportion of total available exercise sessions attended at 12-week follow-up for the PROPEL trial only, because 12-week follow-up 6-minute walk and treadmill walking time were available for the PROPEL trial but not for the SILC trial. The characteristics of participants across tertiles of exercise attendance were compared, and analyses of the association of attendance at exercise sessions over 12 weeks with 12-week change in 6-minute walk and maximal treadmill walking time were repeated using data available in the PROPEL trial only.

Because there was a wide range of attendance among people in the lowest tertile of attendance in those randomized to supervised exercise, additional sensitivity analyses were performed in which the lowest tertile of exercise attendance was further divided into 2 groups (above versus below the median attendance rate within the lowest tertile), and the associations of SET attendance with change in walking performance were examined. The performance with these newly defined groups was examined using methods described for the 3 tertiles of attendance and adjusted for age, sex, race, clinical trial, ABI, smoking, BMI, baseline maximal treadmill walking time, and comorbidities. Statistical analysis was performed using SAS statistical software (version 9.4; SAS Institute, Cary, NC), and a 2-sided $P<0.05$ was considered statistically significant.

RESULTS

A total of 366 participants with PAD were randomized, including 210 in the PROPEL trial and 156 in the SILC trial. Of these participants, 52 randomized to the resistance training group in the SILC trial were excluded, and 5 randomized into the PROPEL trial were excluded, because they had also participated in the SILC trial, leaving 309 participants. A total of 35 participants with missing data for both 6-minute walk test and treadmill testing at 6-month follow-up and 2 missing exercise attendance data were excluded, leaving 272 participants (Figure 1). Of the 272 participants (mean age, 67.9±9.3 years; 44% women; 61% Black race), 137 (50.4%) were randomized to supervised treadmill exercise and 135 (49.6%) were randomized to the control group. Baseline characteristics between the 2 groups were similar (Table 1).

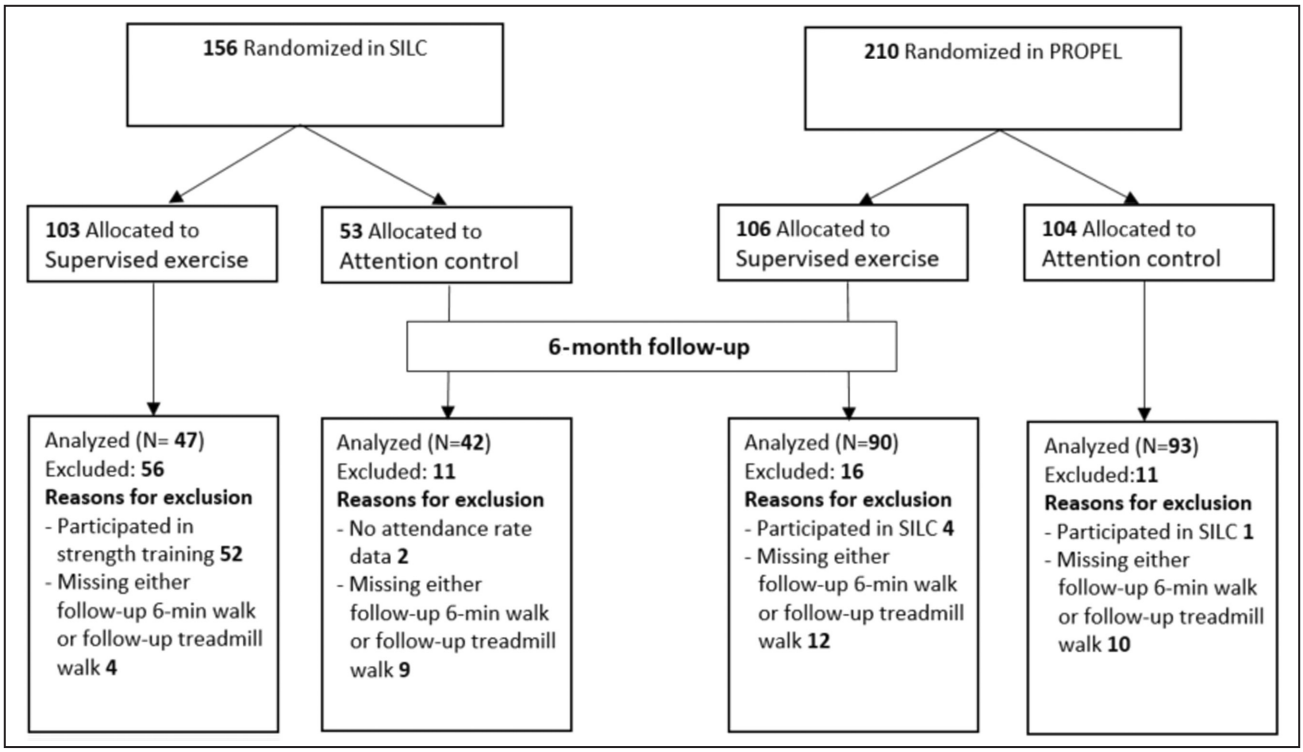

Figure 1. Study participant selection at 6-month follow-up.
PROPEL indicates Progenitor Cell Release Plus Exercise to Improve Functional Performance in Peripheral Artery Disease; and SILC, Study to Improve Leg Circulation.

Overall, mean attendance at supervised treadmill exercise sessions over 6 months was 74%±18%. Attendance rates by tertile over the 6-month intervention were 11% to 68% for tertile 1, 69% to <85% for tertile 2, and ≥85% for tertile 3. Reasons for nonattendance are shown in Table 2. In both clinical trials, the mean attendance rate over the first 12 weeks of the intervention was 72% (≈26 of 36 sessions) ±19%. Attendance rates by tertile during the first 12 weeks of the intervention for participants in the PROPEL trial were 3% to 67% (1–24 exercise sessions over 6 months) for tertile 1, 69% to 78% (25–28 sessions) for tertile 2, and ≥81% (29 sessions) for tertile 3.

Overall, at 6-month follow-up, supervised exercise improved 6-minute walk distance (27±61 m), whereas in the control group, it declined (–9±62 m) (mean difference, 36 m [95% CI, 22–51 m]; $P<0.0001$). At 6-month follow-up, the supervised exercise and control groups each improved maximal treadmill walk time by 4.5±4.2 and 0.5±2.8 minutes, respectively (mean difference, 4.0 minutes [95% CI, 3.2–4.9 minutes]; $P<0.0001$).

Participants with poorer attendance at supervised treadmill exercise sessions were significantly younger and had a higher prevalence of coronary artery disease, a lower prevalence of cancer, and poorer 6-minute walk and maximal treadmill walking time at baseline (Table 3).

Attendance at Exercise Sessions and 6-Month Change in 6-Minute Walk Distance

Mean improvement in 6-minute walk distance was significantly greater in each tertile of attendance at supervised exercise, compared with the control group (overall P for trend: <0.0001): tertile 1 (27.9 m [95% CI, 1.3–54.4 m]; $P=0.04$), tertile 2 (38.2 m [95% CI, 12.2–64.2 m]; $P=0.001$), and tertile 3 (56.9 m [95% CI, 29.9–83.8 m]; $P<0.0001$), adjusting for age, sex, race, clinical trial, ABI, smoking, BMI, baseline 6-minute walk, and comorbidities (Figure 2). In analyses limited to participants randomized to supervised treadmill exercise, there was a significant association between 6-month change in 6-minute walk distance and tertiles of exercise attendance (overall P for trend=0.025). In pairwise comparisons, there were no significant differences in 6-month change in 6-minute walk distance between the second or third tertiles of exercise attendance compared with tertile 1: tertile 3 (29.0 m [95% CI, –4.8 to 62.8 m]; $P=0.12$) and tertile 2 (10.3 m [95% CI, –22.1 to 42.7 m]; $P=0.84$), adjusting for age, sex, race, clinical trial, ABI, smoking, BMI, baseline 6-minute walk distance, and comorbidities (Figure 2). Tertile 3 did not significantly improve 6-month 6-minute walk distance compared with tertile 2 (18.7 m [95% CI, –13.8 to 51.2 m]; $P=0.45$), adjusting for age, sex, race, clinical trial,

Table 1. Baseline Characteristics of Participants With PAD Randomized Into 2 Clinical Trials of SET (N=272)

Characteristic	Supervised treadmill exercise (N=137)	Attention control (N=135)
Age, y	68.8 (9.2)	67.0 (9.4)
Women, n (%)	63 (46)	57 (42)
Black race, n (%)	78 (57)	87 (64)
Body mass index, kg/m^2	30.5 (6.1)	30.6 (6.9)
Ankle-brachial index	0.65 (0.17)	0.67 (0.18)
Current smokers, n (%)	43 (31)	38 (28)
Diabetes, n (%)	51 (37)	55 (41)
Coronary artery disease, n (%)	53 (39)	47 (35)
Heart failure, n (%)	10 (7)	19 (14)
Myocardial infarction, n (%)	29 (21)	29 (21)
Cancer, n (%)	26 (19)	22 (16)
Pulmonary disease, n (%)	12 (9)	18 (13)
Stroke, n (%)	24 (18)	25 (19)
Baseline 6-min walk, m	335.6 (96.4)	336.4 (93.8)
Baseline treadmill walking time, min	7.2 (4.7)	7.5 (3.9)

Data shown are means (SDs) unless otherwise indicated. PAD indicates peripheral artery disease; and SET, supervised exercise therapy.

ABI, smoking, BMI, baseline 6-minute walk distance, and comorbidities (Figure 2).

Attendance at Exercise Sessions and 6-Month Change in Maximal Treadmill Walking Time

Mean improvement in maximal treadmill walking time was significantly greater in each tertile of attendance at supervised treadmill exercise, compared with the control group (overall *P* for trend: <0.0001): tertile 1 (3.3 minutes [95% CI, 1.7–4.8 minutes]; *P*<0.0001), tertile 2 (3.8 minutes [95% CI, 2.3–5.3 minutes]; *P*<0.0001), and tertile 3 (5.4 minutes [95% CI, 3.9–7.0 minutes]; *P*<0.0001), adjusting for age, sex, race, clinical trial, ABI, smoking, BMI, baseline maximal treadmill walking time, and comorbidities (Figure 3). In analyses limited to participants randomized to supervised treadmill exercise, there was no significant association between 6-month change in maximal treadmill walking time and tertiles of exercise attendance (overall *P* for trend=0.064). In pairwise analyses, participants in tertile 3 (best attendance) had significantly greater improvement in maximal treadmill walking time compared with tertile 1 (2.1 minutes [95% CI, 0.2–4.1 minutes]; *P*=0.03) but not compared with tertile 2 (1.7 minutes [95% CI, −0.2 to 3.5 minutes]; *P*=0.11), adjusting for age, sex, race, clinical trial, ABI, smoking, BMI, baseline maximal treadmill walking time, and comorbidities (Figure 3). Compared with tertile 1, tertile 2 did not significantly improve 6-month maximal treadmill walking time (0.5 minutes [95% CI, −1.4 to 2.4 minutes]; *P*=0.91), adjusting for age, sex, race, clinical trial, ABI, smoking, BMI, baseline maximal treadmill walking time, and comorbidities (Figure 3).

Table 2. Reasons for Poor Attendance at Supervised Exercise (N=272)

Reason for poor attendance	No. (%) of people*
Staff not available to conduct visit, such as on holidays	134 (49)
Scheduled vacation or other appointment or obligation	119 (44)
Last minute work conflict, forgot appointment, or personal problem	113 (42)
Participant reported he/she was ill	107 (39)
Did not attend, unable to reach to provide reason why	40 (15)

One participant was suspended from exercise, but no additional details are available about the reason for suspension.

*Number of people who selected reason at least once.

Associations of Attendance During the First 12 Weeks of Exercise With Change in 6-Minute Walk and Treadmill Walking in the PROPEL Trial

A total of 187 participants from the PROPEL trial had baseline and 12-week follow-up data (Figure S1). Participants with poorer attendance at supervised treadmill exercise sessions were more likely to be women (Table S1). In sensitivity analyses of attendance at exercise in the first 12 weeks of the intervention, there was a significant association between 6-month change in 6-minute walk distance and tertiles of exercise attendance (overall *P* for trend: <0.0001). Mean improvement in 6-minute walk distance was significantly greater in tertiles 2 and 3 of

Table 3. Associations of Characteristics of Participants With PAD With Attendance at Supervised Exercise Sessions

Characteristic	Supervised treadmill exercise attendance Tertile 1 (N=45 [11%–68%])	Supervised treadmill exercise attendance Tertile 2 (N=46 [69%–<85%])	Supervised treadmill exercise attendance Tertile 3 (N=46 [≥85%])	*P* value for trend
Age, y	67.2 (10.4)	67.8 (8.5)	71.4 (8.2)	0.03
Women, n (%)	24 (53)	19 (41)	20 (43)	0.35
Black race, n (%)	30 (67)	26 (57)	22 (48)	0.07
Body mass index, kg/m^2	30.5 (6.2)	31.9 (5.6)	29.0 (6.3)	0.25
Ankle-brachial index	0.63 (0.15)	0.69 (0.18)	0.63 (0.17)	0.95
Current smokers, n (%)	15 (33)	15 (33)	13 (28)	0.60
Diabetes, n (%)	20 (44)	15 (33)	16 (35)	0.34
Coronary artery disease, n (%)	22 (49)	21 (46)	10 (22)	0.008
Heart failure, n (%)	5 (11)	3 (7)	2 (4)	0.21
Myocardial infarction, n (%)	12 (27)	14 (30)	3 (7)	0.02
Cancer, n (%)	5 (11)	8 (17)	13 (28)	0.04
Pulmonary disease, n (%)	4 (9)	6 (13)	2 (4)	0.44
Stroke, n (%)	7 (16)	10 (22)	7 (16)	1.00
Baseline 6-min walk, m	306.7 (89.7)	338.2 (93.9)	361.3 (99.3)	0.007
Baseline treadmill walking time, min	5.9 (3.6)	7.4 (4.7)	8.2 (5.4)	0.02

Data shown are means (SDs) unless otherwise indicated. PAD indicates peripheral artery disease.

exercise attendance, compared with the control group (41.9 m [95% CI, 11.0–72.8 m]; *P*=0.003; and 47.8 m [95% CI, 18.1–77.4 m]; *P*=0.0003, respectively), adjusting for aforementioned confounders (Figure S2). Participants in the first (poorest) tertile of exercise attendance did not have significantly greater improvement in 6-minute walk distance at 12-week follow-up, compared with the control group (11.2 m [95% CI, –18.8 to 41.2 m]; *P*=0.77), adjusting for aforementioned confounders (Figure S2). In analyses limited to participants randomized to supervised treadmill exercise, there were no significant differences in 12-week change in 6-minute walk distance by tertile of attendance (Figure S2).

In sensitivity analyses of the first 12 weeks of exercise or control in the PROPEL trial, mean improvement in maximal treadmill walking time was significantly greater in each tertile of attendance, compared with the control group (overall *P* for trend: <0.0001): tertile 1 (2.5 minutes [95% CI, 0.7–4.4 minutes]; *P*=0.003), tertile 2 (3.5 minutes [95% CI, 1.6–5.4 minutes]; *P*<0.0001), and tertile 3 (4.7 minutes [95% CI, 2.9–6.6 minutes]; *P*<0.0001), adjusting for age, sex, race, ABI, smoking, BMI, baseline maximal treadmill walking time, and comorbidities (Figure S3). In analyses limited to participants randomized to supervised treadmill exercise, there were no significant differences in 12-week change in maximal treadmill walking time by tertile of attendance, adjusting for confounders (Figure S3).

Sensitivity Analyses in Which Participants in the Lowest Tertile of Exercise Attendance Were Divided Into 2 Groups

In sensitivity analyses, in which participants in the lowest tertile of exercise attendance were further categorized according to whether their attendance was above or below the median attendance in the lowest tertile (ie, above or below an attendance rate of 57%), those with exercise attendance above the median had significantly greater improvement in 6-minute walk distance, compared with those with exercise attendance below the median (49.0 m [95% CI, 6.2–91.7 m]; *P*=0.02) and compared with the control group (51.2 m [95% CI, 19.2–83.3 m]; *P*=0.0006), adjusting for confounders (overall *P* for trend=0.0007; Figure S4). Compared with the control group, participants with exercise attendance below the median attendance (ie, <57%) did not significantly improve 6-minute walk distance (2.2 m [95% CI, –31.1 to 35.6 m]; *P*=0.99), adjusting for confounders (Figure S4).

In these sensitivity analyses, those with exercise attendance above the median and below the median each had significantly greater improvement in maximal treadmill walking time, compared with the control group (3.7 minutes for those with attendance above the median [95% CI, 2.1–5.3 minutes]; *P*<0.0001; and 2.8 minutes for those with attendance below the median [95% CI, 1.1–4.5 minutes]; *P*=0.0003), adjusting for age, sex, race, clinical trial, ABI, smoking, BMI,

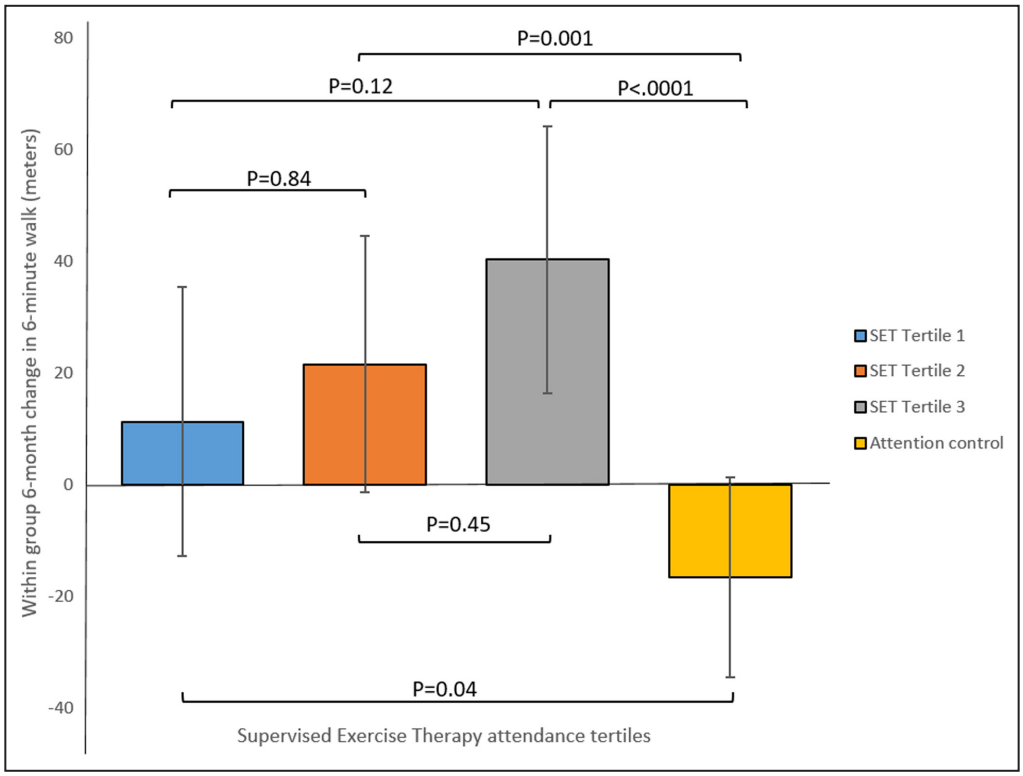

Figure 2. Effects of attendance at SET on 6-month change in 6-minute walk distance, in 272 randomized participants with peripheral artery disease.
Comparisons adjusted for age, sex, race, clinical trial, baseline ankle-brachial index, smoking, diabetes, baseline body mass index, baseline 6-minute walk, coronary artery disease, heart failure, myocardial infarction, cancer, pulmonary disease, and stroke. SET indicates supervised exercise therapy.

baseline maximal treadmill walking time, and comorbidities (overall *P* for trend: <0.0001; Figure S5). Within the lowest tertile of exercise attendance, there was no significant difference in improvement in maximal treadmill walking time between people with exercise attendance above the median attendance compared with those with exercise attendance below the median at 6-month follow-up (0.9 m [95% CI, –1.2 to 3.0 m]; *P*=0.58), adjusting for age, sex, race, clinical trial, ABI, smoking, BMI, baseline maximal treadmill walking time, and comorbidities (Figure S5).

DISCUSSION

In 2 randomized clinical trials of SET for people with PAD, participants randomized to exercise attended ≈74% of 72 supervised exercise sessions over 6 months and ≈72% of 36 supervised exercise sessions over 12 weeks. Better attendance to supervised exercise, measured by tertiles of attendance to exercise sessions, was associated significantly with greater improvement in 6-minute walk distance and maximal treadmill walking time, compared with the control group who did not exercise. Although participants in the lowest tertile of exercise attendance significantly improved both 6-minute walk distance and maximal treadmill walking time, compared with the control group, the range of exercise attendance rates within this tertile was wide (ie, 11%–69%), and results suggested that benefits in the lowest tertile of exercise attendance may primarily have been attributable to those with the greatest exercise session attendance within the lowest tertile.

The CMS provides medical insurance coverage for 36 supervised exercise sessions over 12 weeks for patients with symptomatic PAD. Patients with PAD who continue to report ischemic leg symptoms after 12 weeks of exercise may be referred for an additional 36 exercise sessions.[1,2] However, among 1735 patients covered by Medicare who enrolled in supervised exercise between June 1, 2017, and December 31, 2018, the median number (proportion) of the 36 exercise sessions attended was 16 (ie, 44% attendance rate) (interquartile range, 6–28 [ie, 26.7%–77.8%]).[3] Only 89 (5.1%) of the 1735 referred for supervised exercise completed all 36 sessions.[3]

The 72% attendance rates at supervised exercise sessions reported herein were similar to the 75% attendance rates reported in a systematic review of people with PAD participating in randomized trials of SET.[4] However, rates of attendance at supervised exercise

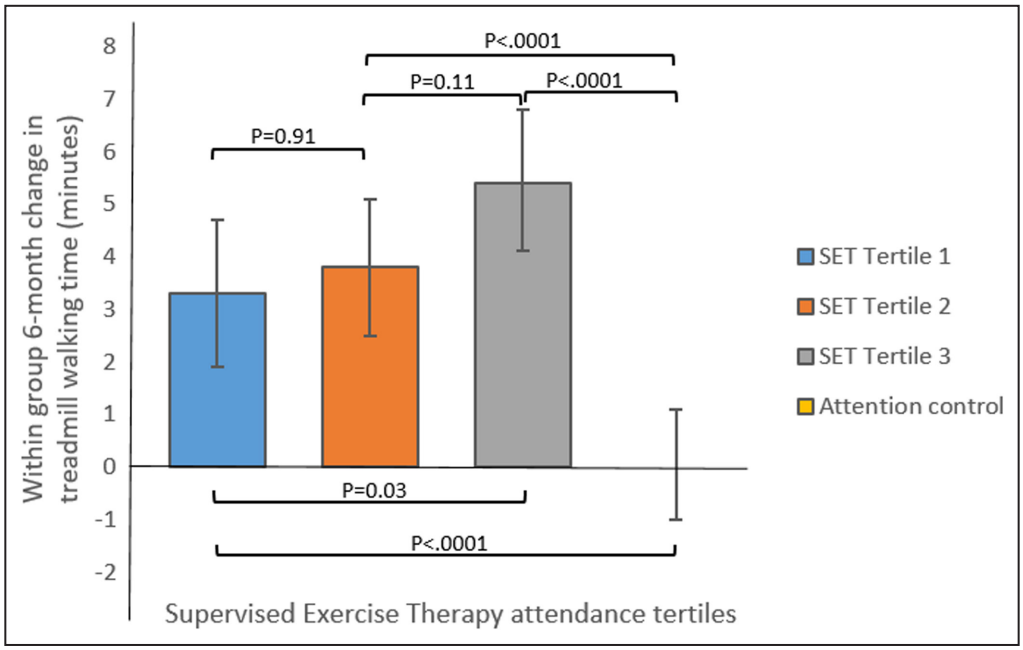

Figure 3. Effects of attendance at SET on 6-month change in maximal treadmill walking time, in 272 randomized participants with peripheral artery disease.
Comparisons adjusted for age, sex, race, clinical trial, baseline ankle-brachial index, smoking, diabetes, baseline body mass index, baseline treadmill walking time, coronary artery disease, heart failure, myocardial infarction, cancer, pulmonary disease, and stroke. SET indicates supervised exercise therapy.

sessions in people with PAD enrolled in clinical trials were substantially higher than the median SET attendance rate of 44% reported for patients with PAD participating in CMS covered SET.[3] The difference in attendance rates between patients with PAD participating in supervised exercise with CMS coverage and those in randomized trials reported herein may be attributable to greater motivation to exercise among participants in randomized trials, eligibility criteria for randomized trials of exercise (which may select for more adherent people), or clinical trial methods, which may include transportation to exercise sessions or payment for parking.

In analyses limited to participants randomized to exercise, greater attendance at supervised exercise sessions was associated with overall greater improvement in 6-minute walk distance at 6-month follow-up (*P* trend=0.025) but not with greater improvement in maximal treadmill walking distance at 6-month follow-up (*P* trend=0.064). In pairwise analyses, there were no statistically significant differences between tertiles of attendance and improvement in 6-minute walk distance. However, the differences in 6-minute walk distance between tertile 3 compared with tertiles 1 and 2 exceeded a clinically meaningful change for 6-minute walk.[16,17] It is therefore possible that the absence of statistically significant differences for these comparisons and for the overall association of adherence with improved treadmill walking performance was attributable to a lack of sufficient statistical power.

The finding reported herein that participants with greater walking impairment had poorer exercise attendance was unexpected and suggests that people with poorest exercise session attendance were more disabled than those with better attendance at SET. Among people with poorer baseline walking performance and lower attendance rates, it is possible that more severe ischemic leg symptoms induced by walking exercise in these participants made participation in supervised exercise more difficult. In addition, because almost 50% of participants with PAD listed scheduling conflicts as reasons for poor attendance at SET, it is possible that greater flexibility of the health care system to accommodate patient schedules may improve supervised exercise attendance in people with PAD.

This study has some limitations. First, participants were enrolled in randomized clinical trials of supervised exercise. Results may not be generalizable to people with PAD participating in supervised exercise outside of a clinical trial setting. Second, the exercise programs in the SILC and PROPEL trials were 6 months in duration, whereas CMS covers an initial 12 weeks (36 sessions) and requires a second referral for an additional 36 sessions. However, results were largely similar for attendance rates over 12 weeks of exercise compared with attendance rates over 6 months of exercise. Third,

analyses limited to participants randomized to exercise may have lacked statistical power to detect statistically significant differences in change in 6-minute walk distance and change in maximal treadmill walking time by attendance rates. Fourth, even participants in the lowest tertiles of attendance in the clinical trials described herein had higher rates of attendance than patients with PAD participating in CMS-covered supervised exercise.[3] Fifth, the results reported herein focused on objective measures of walking performance at 12-week and at 6-month follow-up. These results may not apply to other benefits of supervised exercise for PAD, such as favorable effects on cardiovascular risk factors or walking ability after 6-month follow-up.[19,20] Sixth, the lower 6-minute walk at baseline among participants in the poorest tertile of attendance may have facilitated greater improvement in 6-minute walk distance in this tertile, because of regression to the mean, even after adjusting for baseline 6-minute walk distance. Seventh, results reported herein were post hoc and exploratory and require confirmation.

CONCLUSIONS

Among people with PAD, better attendance at SET was significantly associated with greater improvement in walking performance, compared with a control group who did not exercise. In analyses limited to participants randomized to exercise, better attendance at exercise sessions was associated with greater overall 6-minute walk improvement, whereas lack of a statistically significant association of better attendance with greater overall improvement in treadmill walking performance may have been attributable to inadequate statistical power.

ARTICLE INFORMATION

Received March 17, 2022; accepted November 1, 2022.

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Sources of Funding

This work was funded by the American Heart Association (Strategically Focused Research Network grant 18SFRN339700097). The SILC (Study to Improve Leg Circulation) and PROPEL (Progenitor Cell Release Plus Exercise to Improve Functional Performance in Peripheral Artery Disease) trials were funded by the National Heart, Lung, and Blood Institute grants R01-HL73351 and R01-HL107510, respectively.

Disclosures

Dr McDermott has received research funding from Regeneron and Helixmith and has received other research support from Helixmith, Mars, ArtAssist, Chromadex, and ReserveAge. No other disclosures were reported.

Supplemental Material

Table S1
Figure S1–S5

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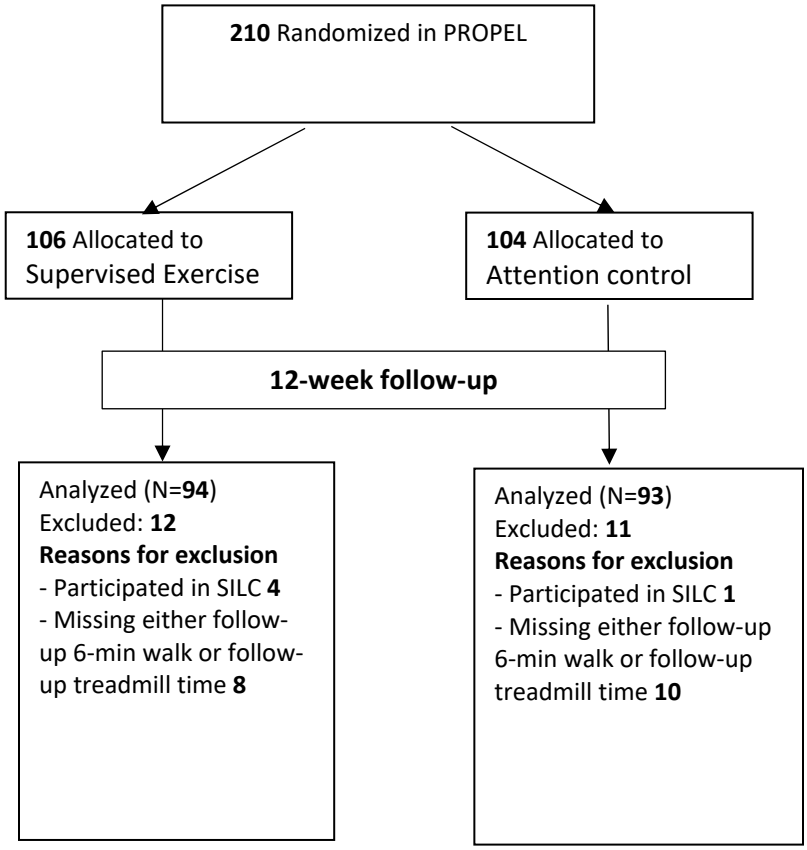
SUPPLEMENTAL MATERIAL

Table S1. Characteristics of participants with peripheral artery disease randomized to supervised treadmill exercise, according to supervised exercise attendance at 12-week follow-up

	Supervised treadmill exercise attendance Tertile 1 N=33 (3- 67%)	Supervised treadmill exercise attendance Tertile 2 N=29 (69 - 78%)	Supervised treadmill exercise attendance Tertile 3 N=32 (≥ 81%)	P-value for trend
Age (years)	64.7 (9.3)	67.0 (8.0)	68.2 (9.3)	0.12
Female n (%)	20 (61)	7 (24)	11 (34)	0.03
African American n (%)	23 (70)	18 (62)	19 (59)	0.39
Body mass index (kg/m^2)	30.9 (6.8)	32.3 (5.7)	30.8 (6.1)	0.94
Ankle brachial index	0.70 (0.21)	0.70 (0.18)	0.66 (0.15)	0.35
Current smokers n (%)	16 (48)	8 (28)	12 (38)	0.36
Diabetes mellitus n (%)	16 (48)	7 (24)	13 (41)	0.50
Coronary artery disease n (%)	13 (39)	10 (34)	10 (31)	0.49
Heart failure n (%)	3 (9)	1 (3)	4 (13)	0.63
Myocardial infarction n (%)	8 (24)	6 (21)	4 (13)	0.23
Cancer n (%)	4 (12)	5 (17)	7 (22)	0.30
Pulmonary disease n (%)	4 (12)	2 (7)	5 (16)	0.66
Stroke n (%)	8 (24)	2 (7)	3 (9)	0.08
Baseline 6-minute walk (meters)	323.2 (83.4)	352.3 (120.3)	346.2 (97.6)	0.36
Baseline treadmill walking time (minutes)	5.7 (3.5)	8.6 (5.9)	7.0 (5.3)	0.29

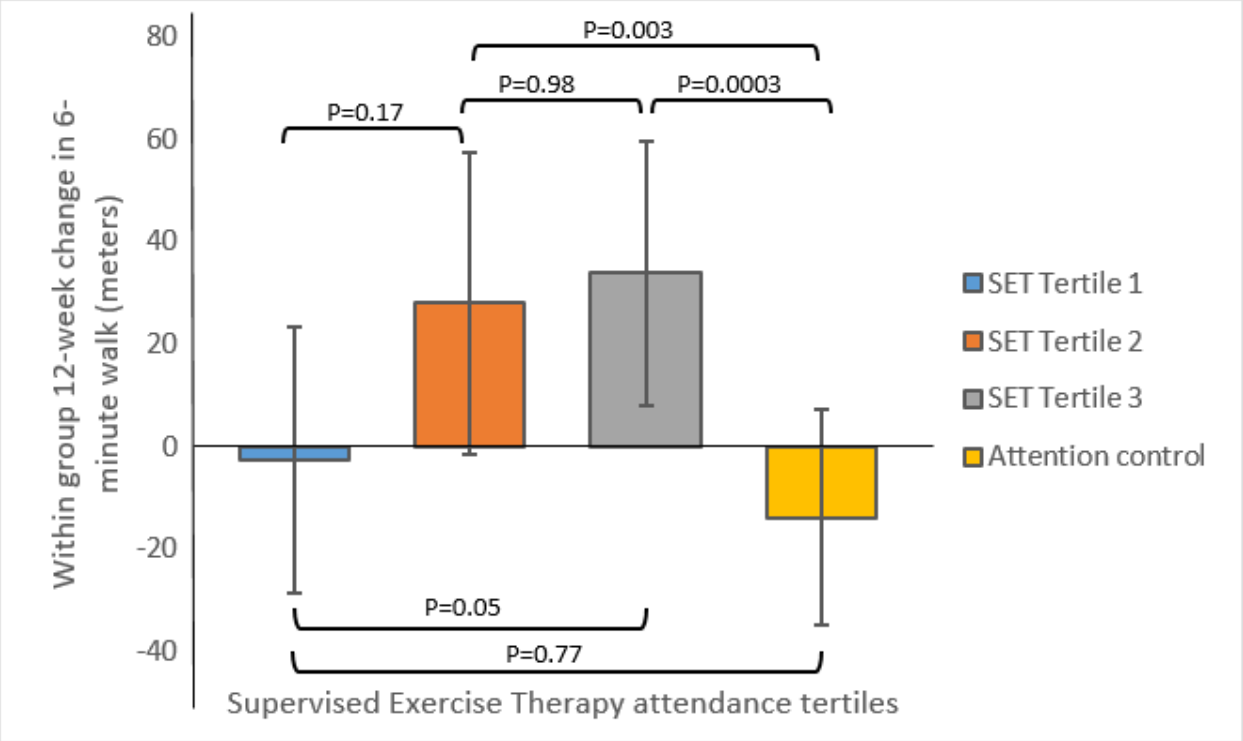
Data shown are means (standard deviation) unless otherwise indicated

Figure S1. Study participant selection at 12-week follow-up



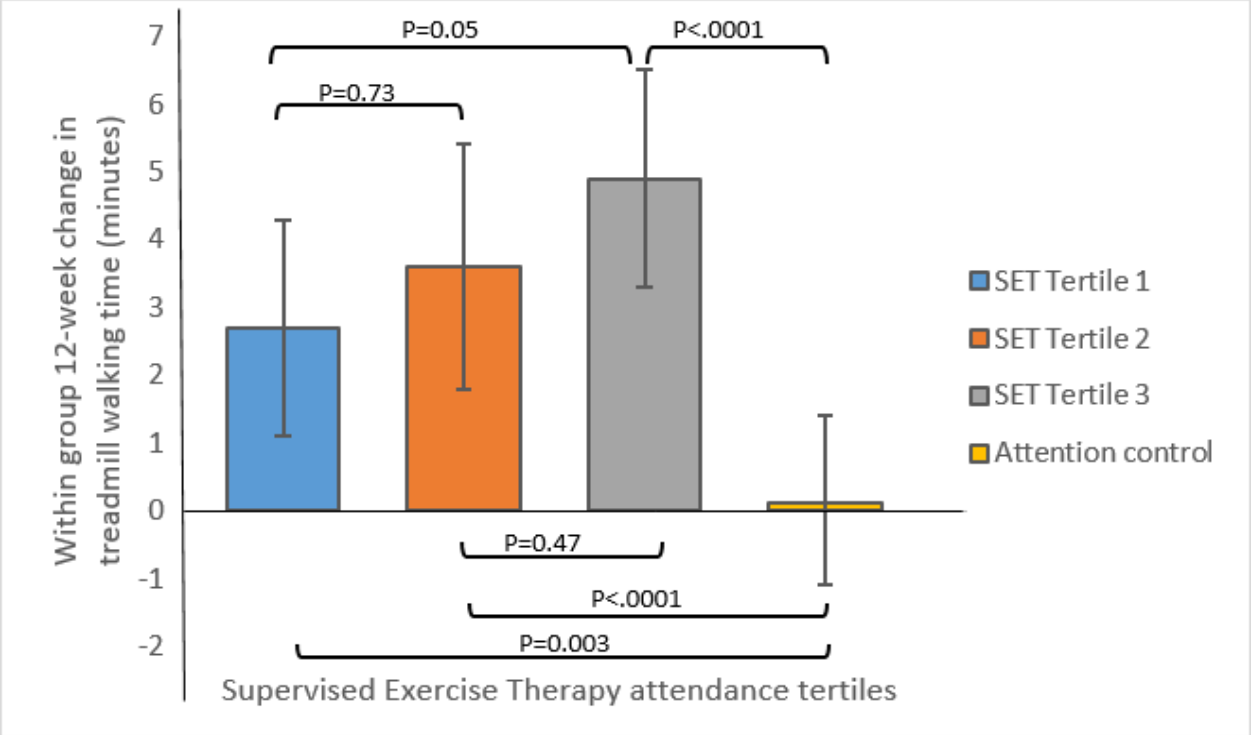
PROPEL: PROgenitor cell release Plus Exercise to improve functional performance in PAD
SILC: Study to Improve Leg Circulation

Figure S2. Effects of attendance at supervised exercise therapy on 12-week change in six-minute walk distance, in 187 randomized participants with peripheral artery disease



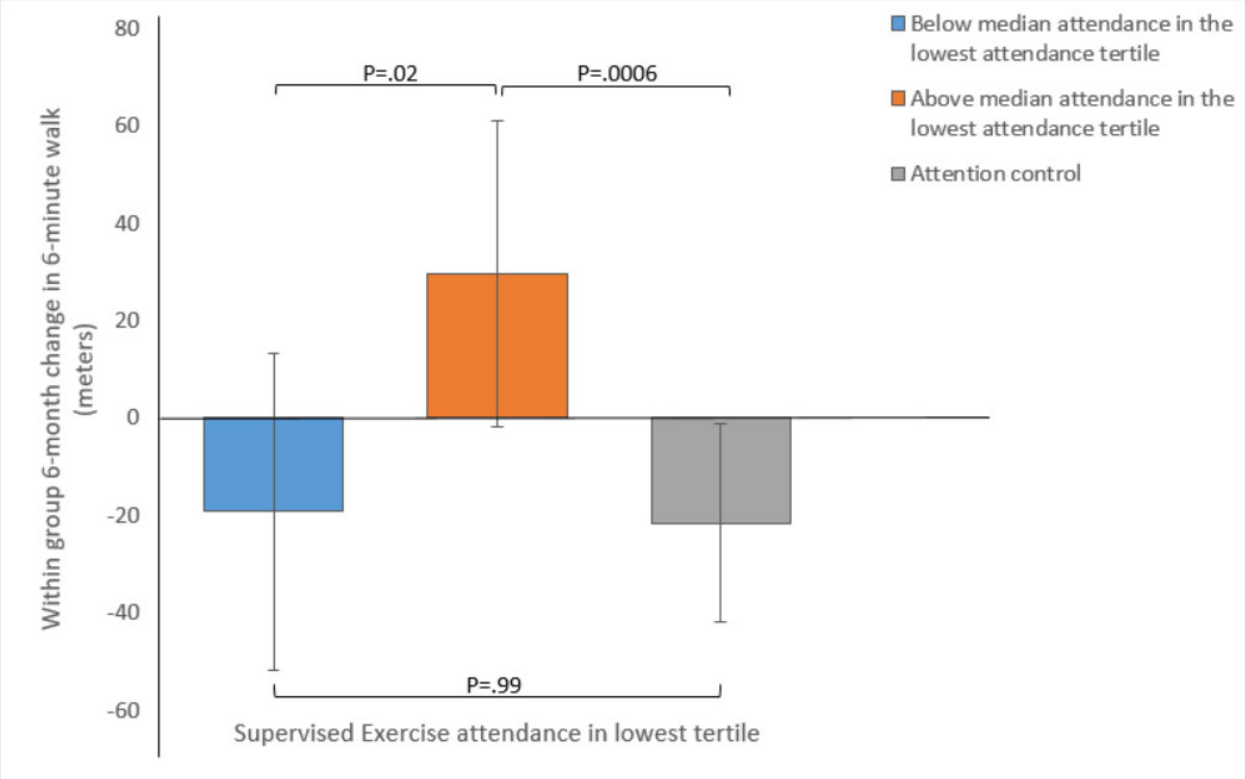
Comparisons adjusted for age, sex, race, baseline ankle brachial index, smoking, diabetes, baseline body mass index, baseline 6-minute walk, coronary artery disease, heart failure, myocardial infarction, cancer, pulmonary disease, and stroke

Figure S3. Effects of attendance at supervised exercise therapy on 12-week change in maximal treadmill walking time, in 187 randomized participants with peripheral artery disease



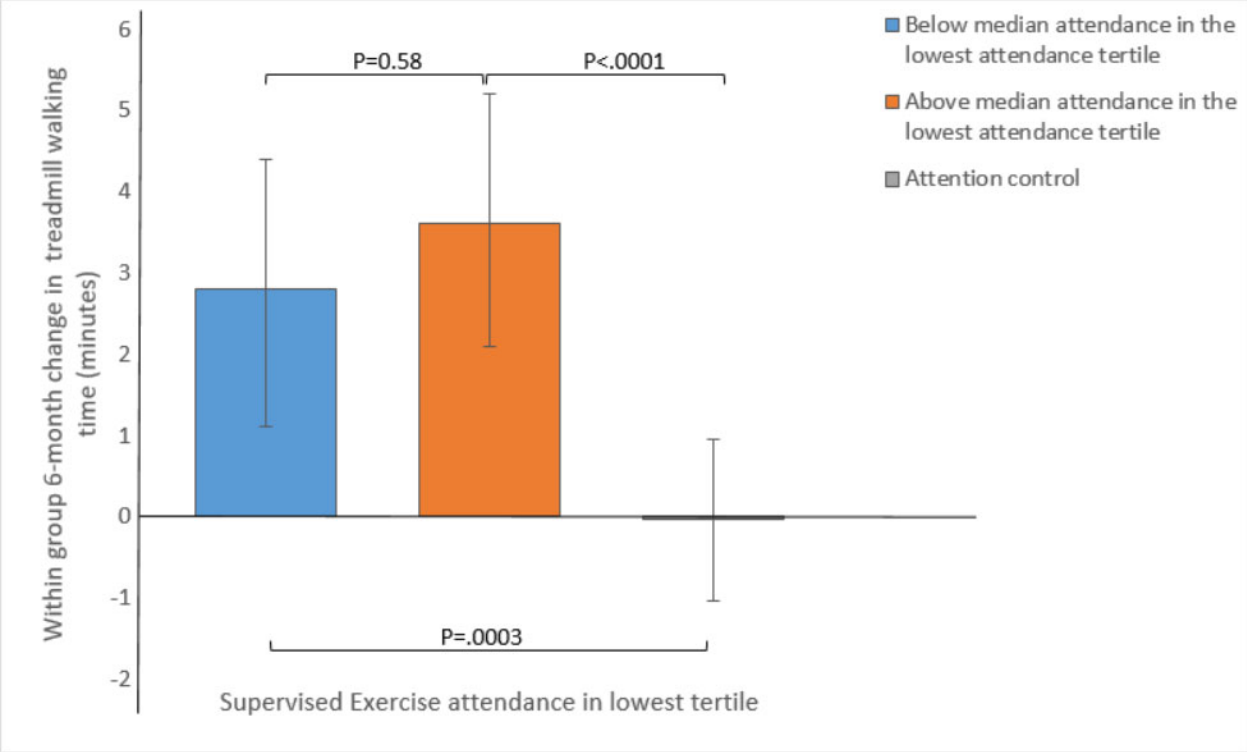
Comparisons adjusted for age, sex, race, baseline ankle brachial index, smoking, diabetes, baseline body mass index, baseline treadmill walking time, coronary artery disease, heart failure, myocardial infarction, cancer, pulmonary disease, and stroke

Figure S4. Effects of attendance at supervised exercise therapy on six month change in six-minute walk distance, within the lowest tertile of attendance



Comparisons adjusted for age, sex, race, clinical trial, baseline ankle brachial index, smoking, diabetes, baseline body mass index, baseline 6-minute walk, coronary artery disease, heart failure, myocardial infarction, cancer, pulmonary disease, and stroke

Figure S5. Effects of attendance at supervised exercise therapy on six month change in maximal treadmill walking time, within the lowest tertile of attendance



Comparisons adjusted for age, sex, race, clinical trial, baseline ankle brachial index, smoking, diabetes, baseline body mass index, baseline treadmill walking time, coronary artery disease, heart failure, myocardial infarction, cancer, pulmonary disease, and stroke