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Effect of structured physical activity on prevention of serious fall injuries in adults aged 70-89: randomized clinical trial (LIFE Study)

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ABSTRACT

OBJECTIVE
To test whether a long term, structured physical activity program compared with a health education program reduces the risk of serious fall injuries among sedentary older people with functional limitations.

DESIGN
Multicenter, single blinded randomized trial (Lifestyle Interventions and Independence for Elders (LIFE) study).

SETTING
Eight centers across the United States between February 2010 and December 2013.

PARTICIPANTS
1635 sedentary adults aged 70-89 years with functional limitations, defined as a short physical performance battery score ≤9, but who were able to walk 400 m.

INTERVENTIONS
A permuted block algorithm stratified by field center and sex was used to allocate interventions. Participants were randomized to a structured, moderate intensity physical activity program (n=818) conducted in a center (twice a week) and at home (3-4 times a week) that included aerobic, strength, flexibility, and balance training activities, or to a health education program (n=817) consisting of workshops on topics relevant to older people and upper extremity stretching exercises.

MAIN OUTCOME MEASURES
Serious fall injuries, defined as a fall that resulted in a clinical, non-vertebral fracture or that led to a hospital admission for another serious injury, was a prespecified secondary outcome in the LIFE Study. Outcomes were assessed every six months for up to 42 months by staff masked to intervention assignment. All participants were included in the analysis.

RESULTS
Over a median follow-up of 2.6 years, a serious fall injury was experienced by 75 (9.2%) participants in the physical activity group and 84 (10.3%) in the health education group (hazard ratio 0.90, 95% confidence interval 0.66 to 1.23; P=0.52). These results were consistent across several subgroups, including sex. However, in analyses that were not prespecified, sex specific differences were observed for rates of all serious fall injuries (rate ratio 0.54, 95% confidence interval 0.31 to 0.95 in men; 1.07, 0.75 to 1.53 in women; P=0.043 for interaction), fall related fractures (0.47, 0.25 to 0.86 in men; 1.12, 0.77 to 1.64 in women; P=0.017 for interaction), and fall related hospital admissions (0.41, 0.19 to 0.89 in men; 1.10, 0.65 to 1.88 in women; P=0.039 for interaction).

CONCLUSIONS
In this trial, which was underpowered to detect small, but possibly important reductions in serious fall injuries, a structured physical activity program compared with a health education program did not reduce the risk of serious fall injuries among sedentary older people with functional limitations. These null results were accompanied by suggestive evidence that the physical activity program may reduce the rate of fall related fractures and hospital admissions in men.

TRIAL REGISTRATION
ClinicalsTrials.gov NCT01072500.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Serious fall injuries are some of the most dreaded and debilitating conditions experienced by older people

Data on whether serious fall injuries can be prevented are lacking from randomised trials

WHAT THIS STUDY ADDS

A structured physical activity program, compared with a health education program, did not reduce the risk of serious fall injuries among sedentary older persons

These null results were accompanied by suggestive evidence that the physical activity program may reduce the rate of fall related fractures and hospital admissions in men

Introduction

Each year, 30% of community living older people fall, and 20-30% of those who fall experience moderate to severe injuries.[1-4] Among those aged 70 and older, falls are the leading cause of fatal and non-fatal injuries.[5] In 2010, 2.3 million non-fatal fall injuries were treated in US emergency departments, and more than 662000 of these patients were admitted to the hospital.[5] Falls among older people cost $28.2b (£19.5b; €26b) each year in the USA, and most of this cost is incurred by injurious falls leading to hospital admission.[6] Fall injuries are independently associated with subsequent disability in important activities, such as bathing and shopping, and with increased risk of long term admissions to nursing homes.[7 8]

Despite the cost and morbidity associated with serious fall injuries, data on prevention of these events are lacking from randomized trials. Several exercise based interventions have shown a reduction in falls,[9-11] but none had sufficient statistical power to show a reduction in serious fall injuries.

The Lifestyle Interventions and Independence for Elders (LIFE) study recently reported that a structured

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moderate intensity physical activity program significantly reduced the primary outcome of major mobility disability compared with a health education program, among 1635 sedentary men and women aged 70-89 with functional limitations.[12] The LIFE Study is the largest trial to evaluate the benefits of physical activity in older people. Serious fall injury was included in the LIFE Study as one of the prespecified secondary outcomes. By improving gait, balance, and lower extremity strength,[13] physical activity may reduce the likelihood of falling and sustaining a serious injury, but it may also increase opportunities to fall and incur a serious injury. Here we report results associated with our hypothesis that a long term physical activity program compared with a health education program reduces the risk of serious fall injuries among sedentary older people with functional limitations. We also report results for additional analyses that were not prespecified. The results of several other secondary outcomes from the LIFE Study have been published elsewhere.[12 14 15]

Methods

Trial design and participants

The LIFE Study was a multicenter, single blinded randomized trial conducted at eight field centers across the USA between February 2010 and December 2013. Details of the methods are published elsewhere.[16] Men and women aged 70-89 were eligible if they were sedentary (reported <20 min/week in past month performing structured physical activity (that is, exercise), and <125 min/week of moderate physical activity); had functional limitations, as evidenced by a short physical performance battery score 9 or less out of 12 (the short physical performance battery is an integrative measure of gait, balance and lower extremity strength);[17] could walk 400 m in 15 minutes or less without the help of someone or a walker; had no major cognitive impairment (modified mini-mental state examination[18] score 1.5 standard deviations below education specific and race specific norms); and could safely participate in the intervention as determined by medical history, physical exam, and electrocardiography. The primary recruitment strategy was targeted mass mailings to the community.[19] The methods and procedures of the LIFE Study were refined based on the results and participant input from an earlier pilot study.[13]

The institutional review boards at all participating sites approved the study protocol, available on request at www.thelifestudy.org/public/index.cfm. We obtained written informed consent from all participants.

Randomization

Participants were randomized to a physical activity or health education program (see appendix figure 1) through a secure web based data management system using a permuted block algorithm (with random block lengths) stratified by field center and sex.

Interventions

The two interventions, which lasted 24 to 42 months depending on the time of enrollment, are described elsewhere.[16] The physical activity intervention consisted of walking, with a goal of 150 min/week; strength; flexibility; and balance training.[16] The intervention included two center based visits a week and home based activity 3-4 times a week. The physical activity sessions were individualized and progressed toward a goal of 30 minutes of walking at moderate intensity, 3-5 minutes of large muscle group flexibility exercises, 10 minutes of primarily lower extremity strength training by means of ankle weights (two sets of 10 repetitions), and 10 minutes of balance training. The participants began with light intensity and gradually increased intensity over the first two to three weeks of the intervention. On average the physical activity group attended 63% of the scheduled sessions: median 71% (interquartile range 50-83%).[12]

The health education group attended weekly workshops during the first 26 weeks and monthly sessions thereafter. Workshops covered topics of relevance to older people, such as negotiating the healthcare system, traveling safely, and preventive services. The program also included a five to 10 minute instructor led program of stretching exercises. On average the health education group attended 73% of the scheduled sessions: median 82% (63-90%).[12]

Data collection

Participants returned every six months for follow-up. Assessment staff were blinded to the intervention. Race and ethnicity were reported by the participants and were collected according to the requirements of the National Institutes of Health. The short physical performance battery was reassessed at 6, 12, 24, and 36 months, and physical activity at 6, 12, and 24 months. Self reported physical activity was assessed with the community healthy activities model program for seniors questionnaire (CHAMPS),[20] administered by unblinded staff, and objective physical activity was assessed by accelerometry over seven days (Actigraph; Pensacola, FL).[12]

For the purpose of safety monitoring, unblinded staff recorded falls and serious fall injuries occurring during intervention sessions. These events were not included in the outcomes assessment unless ascertained by blinded staff.

Outcomes assessment

We defined serious fall injury as a fall resulting in a clinical, non-vertebral fracture or that led to hospital admission for an injury. A fall was defined as an unexpected event in which the participant came to rest on the ground, floor, or lower level.[11]

Potential serious fall injuries were ascertained every six months through three questions: Since (last visit date), did a doctor tell you that you fractured or broke a bone? (If yes) Did you break a bone as a result of a fall? and Other than the conditions we just asked you about, were you admitted to a hospital overnight for any other reasons since (last visit date)? Two experts blinded to group randomization subsequently reviewed and adjudicated independently relevant

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medical records, including those from all hospital admissions. If the reviewers disagreed, they discussed the case. If they still disagreed, the information was forwarded to the adjudication committee, which arrived at consensus.

A definite fall related fracture required the fulfillment of four criteria:[21] radiologic evidence of a non-vertebral, non-stress fracture;[11] report of a fall within one week of injury; absence of major trauma or periprosthetic fracture; and no evidence of pathologic fracture. The non-fracture serious fall injuries required hospital admission and one of the following: non-fracture head injury with loss of consciousness, bleeding by neuroimaging, major facial trauma, or other comparable sequela; consequences of a long lie, such as rhabdomyolysis, dehydration or volume depletion, or hypothermia; or other fall injury, such as a severe sprain.

As an additional outcome, which was not prespecified, we evaluated falls that led to persistent restricted activity, defined as affirmative responses to two questions: Since (last visit date), have you fallen? and, Did this fall result in an inability to leave home for at least one week? The inclusion of this outcome allowed us to ascertain fall related events that were likely clinically important but did not meet the operational definition of a serious fall injury.

Patient involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for recruitment, design, or implementation of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to study participants or the relevant patient community.

Statistical analysis

We based the sample size for the LIFE Study on power for the primary outcome of major mobility disability. Given this sample size, the power required for detecting differences between the two intervention groups in serious fall injuries was based on preliminary data from the LIFE pilot study.[13] Adopting a two sided type 1 error of 0.05, assuming a 3% annual incidence rate of serious fall injuries in the health education group and 8% annual loss to follow-up, the planned sample size of 800 participants for each group yielded 80% and 90% power to detect relative hazard ratios of 0.54 and 0.49, respectively.

We tested the effect of the intervention on time until the first post-randomization serious fall injury based on a two tailed significance of 0.05 using the intention to treat approach. Event times were defined as the time from randomization until the adjudicated fall date, and censoring times were defined as the time from randomization until the last fall assessment or death. We used the Nelson-Aalen estimator to obtain cumulative incidence curves by intervention group. To compare interventions, we estimated hazard ratios with 95% confidence intervals and used likelihood ratio tests from Cox proportional hazards regression models, with the baseline hazard stratified by sex. We chose a priori not to stratify by field center owing to the relatively small number of anticipated serious fall injuries. Using Fine and Gray's approach for fitting proportional subdistribution hazard models to survival data with competing risks, we performed a sensitivity analysis considering death as a competing risk.[22]

The types of serious fall injuries were enumerated for the two intervention groups, with the unit of measurement as people and injury. To compare the number of fractures, hospital admissions, and fractures or hospital admissions between groups, we calculated rate ratios (95% confidence intervals) using a negative binomial model, with log transformed total follow-up time as an offset. A Lagrange multiplier test was used to evaluate whether the scale variable in this model was equal to 0.

For serious fall injuries, we entered interaction terms into the Cox model (that is, separate models for each subgroup analysis) and used likelihood ratio tests to assess the consistency of the intervention effect across levels of four prespecified subgroups (age, sex, race/ethnicity, and physical performance) and one post hoc subgroup (self reported fall in the year before randomization). When analyzing the sex interaction, we did not stratify the baseline hazard by sex. Because a clinically meaningful, although non-significant, interaction was observed for sex, we completed several post hoc analyses including calculating cumulative incidence curves separately by sex; including all prespecified subgroup factors in the model when evaluating the effect of sex on the incidence of serious fall injuries; and evaluating the interaction between sex and the intervention for all serious fall injuries, fall related fractures, and fall related hospital admissions.

We calculated the proportion of participants with at least one fall leading to persistent restricted activity by intervention group. Risk ratios (95% confidence intervals) and a test for an interaction between intervention group and sex were obtained using Poisson regression, with log transformed follow-up time as an offset. We also used these methods to compare the risk of any fall over the entire follow-up period.

To understand better the sex specific results, we compared self reported and objectively measured physical activity between men and women by intervention group during the first two years of follow-up, which was the minimum duration of the intervention. For the self reported measure, we focused on walking and strength training activities. For the objective measure, we evaluated moderate activity based on accelerometry, using a definition of 760 counts/min.[23] We compared short physical performance battery scores between men and women by intervention group during follow-up. For each outcome, we used linear contrasts within the framework of mixed effects models to compare the average visit specific intervention effect for men versus women.

Finally, we calculated rates for falls and serious fall injuries that occurred during the physical activity and health education sessions.

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Table 1 | Baseline characteristics of participants by intervention group. Values are numbers (percentages) unless stated otherwise

Characteristics	Physical activity (n=818)	Health education (n=817)
Mean (SD) age (years)	78.7 (5.2)	79.1 (5.2)
Age ≥80	341 (41.7)	362 (44.3)
Women	547 (66.9)	551 (67.4)
Race/ethnicity:		
White, non-Hispanic	604 (73.8)	635 (77.7)
Black, non-Hispanic	163 (19.9)	125 (15.3)
Hispanic	31 (3.8)	30 (3.7)
Other	20 (2.4)	27 (3.3)
Education beyond high school	544 (66.6)	550 (67.7)
Mean (SD) No of chronic conditions	2.0 (1.2)	2.0 (1.2)
Hypertension	573 (70.5)	578 (71.5)
Diabetes	199 (24.4)	216 (26.6)
Myocardial infarction	60 (7.4)	69 (8.5)
Stroke	57 (7.0)	52 (6.4)
Chronic pulmonary disease	130 (16.0)	123 (15.2)
Cancer	178 (21.9)	192 (23.6)
Mean (SD) No of prescription drugs	5.3 (3.4)	5.4 (3.3)
Fall in past year	412 (50.4)	404 (49.4)
Fall receiving medical attention in past year	106 (26.0)	83 (20.6)
Mean (SD) body mass index	30.1 (5.7)	30.3 (6.2)
Mean (SD) 3MSE score	91.5 (5.5)	91.6 (5.3)
SPPB score:		
Mean (SD) score	7.4 (1.6)	7.3 (1.6)
Score ≤7	353 (43.2)	378 (46.3)

3MSE=modified mini-mental state examination (0-100 scale); SPPB=short physical performance battery.

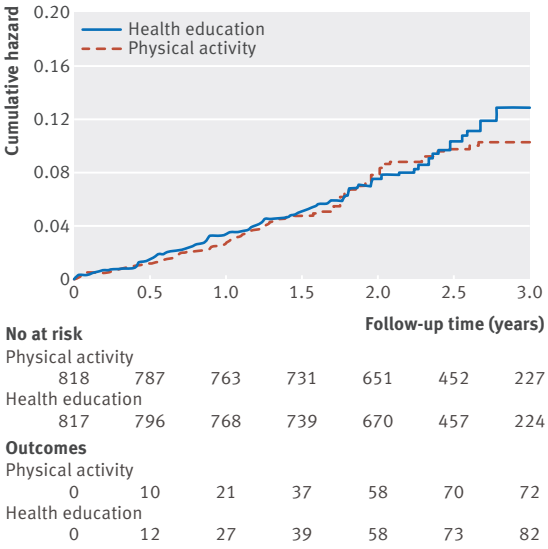

Fig 1 | Effect of a moderate physical activity intervention on time to first serious fall injury. Outcomes represent the cumulative number of participants with a serious fall injury. The adjusted hazard ratio was obtained from a proportional hazards regression model that stratified the baseline hazard by sex. Curves were truncated at three years because of the small number of subsequent outcomes and people at risk. See table 2 for numbers of all outcomes through the end of follow-up (3.5 years). Duration of follow-up differed because participants were recruited over a 21 month period, but follow-up ended for all participants in December 2013

We did not control for the increased risk of type I error resulting from multiple testing of the secondary and exploratory endpoints, instead viewing them as providing useful information that can potentially bolster interpretation of results for the primary endpoint, a position that has previously been expressed as reasonable in clinical trials.[24] All analyses were performed in SAS (SAS Institute), version 9.4.

Results

Baseline characteristics of the two intervention groups were comparable (table 1). About half of the participants reported at least one fall in the past year. A larger proportion in the physical activity group reported a fall that required medical attention.

Over a median follow-up of 2.6 years, a serious fall injury was experienced by 75 (9.2% of 818) participants in the physical activity group and 84 (10.3% of 817) in the health education group (hazard ratio 0.90, 95% confidence interval 0.66 to 1.23; P=0.52) (fig 1). The results were unchanged when death (n=42 in physical activity group and n=37 in health education group) was accounted for as a competing outcome. Table 2 provides the types of serious fall injuries. No significant differences were observed in rates of all serious fall injuries (rate ratio 0.87, 95% confidence interval 0.65 to 1.18), fall related fractures (0.87, 0.63 to 1.19), or fall related admissions to hospital (0.78, 0.51 to 1.20) for the physical activity group compared with the health education group.

In subgroup analyses, hazard ratios for time to first serious fall injury did not differ significantly according to age, sex, race/ethnicity, fall in past year, or baseline physical performance (fig 2). However, a clinically meaningful quantitative difference was observed for sex, with a hazard ratio of 0.62 (95% confidence interval 0.34 to 1.12) in men and 1.05 (0.72 to 1.52) in women (fig 3). Over the entire follow-up period, 6.6% (18 of 271) of the men in the physical activity group versus 10.5% (28 of 266) in the health education group experienced at least one serious fall injury; the corresponding values for women were 10.4% (57 of 547) and 10.2% (56 of 551). When factors for all prespecified subgroups were included as covariates in the model containing the interaction term with sex, results were consistent with the more parsimonious model (men: 0.58, 0.31 to 1.04; women: 1.17, 0.81 to 1.70). Significant sex differences were observed for rates of all serious fall injuries (risk ratio 0.54, 95% confidence interval 0.31 to 0.95 in men; 1.07, 0.75 to 1.53 in women; P=0.043 for interaction), fall related fractures (0.47, 0.25 to 0.86 in men; 1.12, 0.77 to 1.64 in women; P=0.017 for interaction), and fall related admissions to hospital (0.41, 0.19 to 0.89 in men; 1.10, 0.65 to 1.88 in women; P=0.039 for interaction). Appendix table 1 provides the types of serious fall injuries for men and women.

A fall leading to persistent restricted activity occurred in 47 (5.7% of 818) participants in the physical activity group and 71 (8.7% of 817) in the health education group, yielding a risk ratio of 0.66 (95% confidence interval 0.46 to 0.94). The reduction in fall related restricted activity did not differ (P=0.53 for

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Table 2 | Types of serious fall injuries by intervention group. Values are numbers (percentages) unless stated otherwise

Types of injuries	Physical activity (n=818)		Health education (n=817)	
	People*	Injury	People*	Injury
All serious fall injuries	75 (9.2)	81	84 (10.3)	94
Fall related fractures:	66 (8.1)	71	76 (9.3)	84
Facial	3 (4.5)	3 (4.2)	6 (7.9)	6 (7.1)
Hand or finger	5 (7.6)	5 (7.0)	8 (10.5)	8 (9.5)
Lower arm or wrist	15 (22.7)	15 (21.1)	12 (15.8)	12 (14.3)
Elbow	3 (4.5)	3 (4.2)	6 (7.9)	6 (7.1)
Upper arm	6 (9.1)	6 (8.5)	12 (15.8)	13 (15.5)
Rib	10 (15.2)	10 (14.1)	8 (10.5)	8 (9.5)
Pelvis	2 (3.0)	2 (2.8)	5 (6.6)	5 (6.0)
Hip	13 (19.7)	13 (18.3)	15 (19.7)	17 (20.2)
Upper or lower leg	3 (4.5)	3 (4.2)	1 (1.3)	1 (1.2)
Knee	2 (3.0)	2 (2.8)	6 (7.9)	6 (7.1)
Ankle	5 (7.6)	5 (7.0)	3 (3.9)	3 (3.6)
Foot or toe	4 (6.1)	4 (5.6)	4 (5.3)	4 (4.8)
Other	4 (6.1)	4 (5.6)	3 (3.9)	3 (3.6)
Fall related admissions to hospital:	36 (4.4)	37	44 (5.4)	48
Fracture	27 (75.0)	27 (73.0)	35 (79.5)	38 (79.2)
Head injury	5 (13.9)	5 (13.5)	7 (15.9)	7 (14.6)
Consequence of long lie	2 (5.6)	2 (5.4)	3 (6.8)	3 (6.3)
Other serious injury	4 (11.1)	4 (10.8)	6 (13.6)	6 (12.5)

*For all serious fall injuries, fall related fractures, and fall related admissions to hospital, the denominator includes all participants randomized to the specific intervention group.
†Denominator includes all injuries for specific injury subtype. Some participants had more than one serious fall injury event, and some events included more than one type of injury.
‡The rates per 100 person years were 3.83 for all serious fall injuries, 3.36 for fall related fractures, and 1.75 for fall related hospital admissions.
§Rates per 100 person years were 4.38 for all serious fall injuries, 3.92 for fall related fractures, and 2.24 for fall related admissions to hospital.

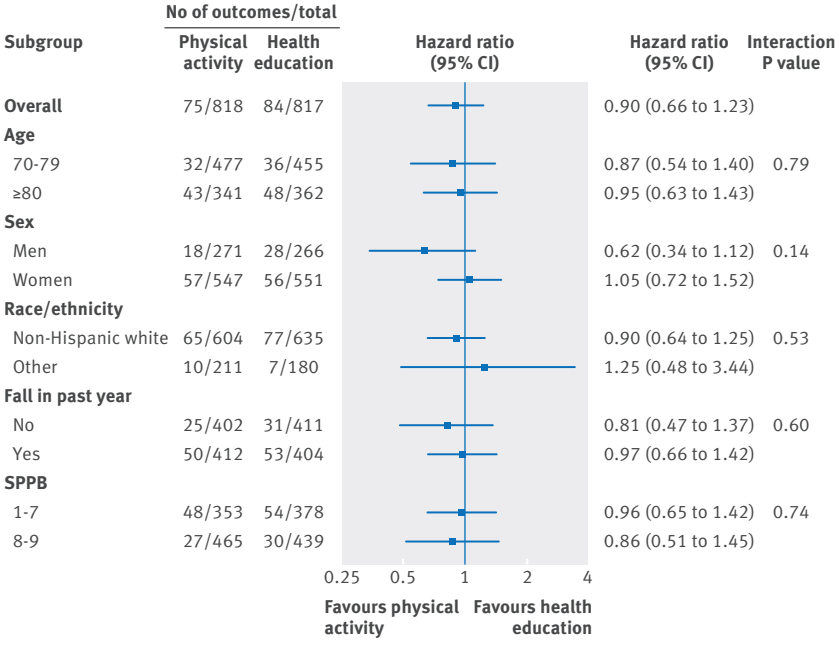

Fig 2 | Hazard ratios for time to first serious fall injury for physical activity versus health education according to subgroups. Age, sex, ethnicity/race, and baseline physical performance were prespecified in the analysis plan, whereas fall in past year was not. With the exception of the analysis for the sex subgroup effect, the adjusted hazard ratios were obtained from proportional hazards regression models that stratified the baseline hazard by sex. SPPB=short physical performance battery. P values were obtained from likelihood ratios tests of the interaction terms added to the proportional hazards regression model

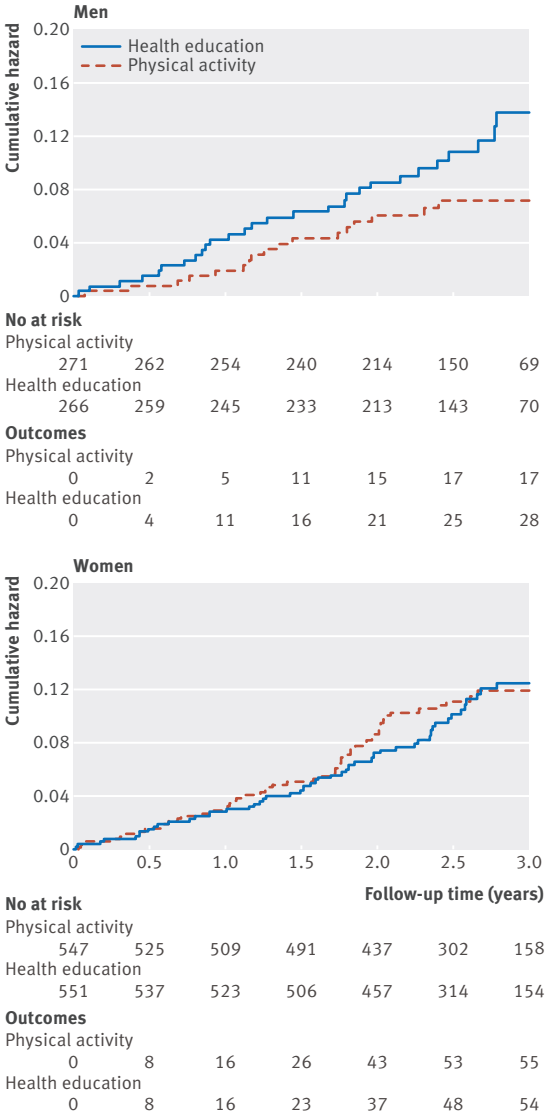

Fig 3 | Effect of a moderate physical activity intervention on time to first serious fall injury in men and women. Outcomes represent the cumulative number of participants with a serious fall injury. Adjusted hazard ratios were obtained from proportional hazards regression models that included sex, intervention, and sex×intervention terms (that is, sex was not used as a factor to stratify the baseline hazard). The curves were truncated at three years because of the small number of subsequent outcomes and persons at risk. The numbers of all outcomes through the end of follow-up (3.5 years) are reported in appendix table 1

interaction) between men (0.54, 0.26 to 1.10) and women (0.71, 0.47 to 1.07). The difference in the percentage of participants reporting any fall between the physical activity (59.9%) and health education (61.2%) groups was small (0.98, 0.91 to 1.06) and did not differ by sex: 56.8% and 63.5% in men and 61.4% and 60.1% in women, respectively.

Based on mixed effects models fit to the CHAMPS questionnaire, the physical activity group averaged 104 more minutes (per week) in walking and strength training activities than the health education group. Although not statistically significant (P=0.06 for interaction),

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this differential was greater in men (120 minutes, 95% confidence interval 100 to 140) than in women (96 minutes, 82 to 110). Based on accelerometry, the physical activity group averaged 40 more minutes (per week) in moderate physical activity than the health education group; this differential was greater in men (59 minutes, 39 to 80) than in women (31 minutes, 16 to 45; P=0.02 for interaction). The follow-up short physical performance battery scores, adjusted for baseline scores, were greater for the physical activity group than for the health education group in men (0.43, 0.09 to 0.73) but not in women (0.04, –0.21 to 0.29), although the test for statistical interaction was not significant (P=0.06). Discontinuation of the physical activity intervention did not differ significantly between men (17.0%) and women (13.2%) (P=0.14).

Thirty falls and three serious fall injuries were reported during 114 100 physical activity sessions, yielding rates per 100 000 sessions of 26.3 and 2.6; and three and one, respectively, occurred during 37 180 health education sessions, yielding rates of 8.1 and 2.7.

Discussion

The LIFE Study found no difference in the risk of serious fall injuries for a physical activity intervention versus a health education program among sedentary older people with functional limitations. The results were consistent across several subgroups, including sex. In analyses that were not prespecified, the physical activity program was more effective in reducing the rate of all serious fall injuries, including fall related fractures and admissions to hospital, in men than in women.

Despite being the largest and longest trial of physical activity in older people,[19] the LIFE Study only had sufficient power to detect relatively large reductions in serious fall injuries. For the comparison of physical activity versus health education, the hazard ratio was 0.90 for serious fall injuries, which was a prespecified secondary outcome in the LIFE Study, and the rate ratio was 0.87. These null results were accompanied by a statistically significant 34% reduction in falls leading to persistent restricted activity, a finding that did not differ significantly between men and women.

In contrast to women, who showed no benefit, men randomized to physical activity experienced a 46% reduction in all serious fall injuries, including a 53% reduction in the rate of fall related fractures and a 59% reduction in the rate of fall injuries leading to admission to the hospital. Because the analyses were not prespecified, these sex specific results should be interpreted with caution and warrant replication in future studies. For comparisons between the two intervention groups, we found much larger differential increases in self reported and objectively measured physical activity in men than in women, providing one possible explanation for these results. Another possible explanation is that, in response to the physical activity program, men had greater improvements than women in their gait, balance, and muscle strength, as evidenced by their marginally greater benefit on short physical performance battery scores over time.

Comparison with other studies

A recent systematic review and meta-analysis of seven exercise based clinical trials reported a pooled rate ratio of 0.57 (95% confidence interval 0.36 to 0.90) for serious fall injuries.[25] Inconsistency across trials was deemed to be moderately large, with effect sizes ranging from 0.15 (0.02 to 1.16) to 0.94 (0.60 to 1.49).[25] In contrast to interventions in these previous trials, the LIFE intervention was not designed specifically to prevent falls or serious fall injuries and may not have focused sufficiently on balance, a factor deemed to be important to the success of previous trials.[25] None the less, the LIFE intervention has previously been shown to improve scores on the short physical performance battery,[13] an integrative measure of gait, balance, and strength. Although an earlier systematic review and meta-analysis had raised concerns that increasing physical activity without adequate attention to balance might increase the risk of falling,[26] we found no difference in the percentage of participants experiencing any fall between the physical activity and health education groups, despite large differences in physical activity between the groups, suggesting that balance training may have been adequate.

Limitations and strengths of this study

In addition to being underpowered to detect small, but possibly important reductions in the hazard of the prespecified outcome of first serious fall injury, our study has several other limitations. Firstly, the injurious fall outcome was limited to fractures and other serious fall injuries leading to hospital admission. These fall related injuries are associated with the greatest morbidity and costs.[27] Furthermore, less severe injuries, such as bruises, cuts, and persistent pain, are more difficult to adjudicate since they may not receive medical attention or may be poorly documented in the medical record. Given the significant differences that were observed for falls leading to persistent restricted activity, it is possible that the physical activity program reduces the risk of any fall injury (serious and less severe). Secondly, the six month assessment interval may have led to under-ascertainment of fall related outcomes. Serious fall injuries, however, are much less susceptible to poor recall than are other falls.[28] To enhance the ascertainment of serious fall injuries, medical records from all hospital admissions were reviewed and adjudicated. Thirdly, men represented only about a third of the study population, a value that is consistent with census estimates. Had a larger number of men been enrolled, the power to detect sex specific differences in the risk of a first serious fall injury by intervention group would have been enhanced. Fourthly, study participants were not recruited because of their fall risk, possibly leading to a diminished benefit of the intervention for the prevention of serious fall injuries. However, the physical activity program was no more effective among higher risk participants who reported a fall in the year before randomization or those

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who had more severe functional limitations. Finally, we did not control for type I error in this analysis of a prespecified secondary outcome and related outcomes that were not prespecified. This approach is consistent with the views of others, as the estimated effects sizes are trustworthy and useful even in the presence of an inflated type I error.[24]

Study strengths include the large and racially diverse sample of vulnerable older people from eight field centers spanning the USA, the rigorous methods to ascertain and adjudicate serious fall injuries, excellent retention, and adherence rates to the physical activity intervention that were similar or higher than those achieved in other shorter studies involving older people.[29] In addition, because fewer than 5% of age eligible people were excluded on the basis of an underlying medical condition, our results should be broadly applicable to our target population of sedentary older people with functional limitations who do not already have major mobility disability.

Clinical implications

Our results should be interpreted in the context of the primary results from the LIFE Study, which showed an 18% reduction in the risk of major mobility disability, defined as loss of ability to walk 400 m, and a 28% reduction in the risk of persistent mobility disability.[12] Given the morbidity and costs associated with serious fall injuries, demonstrating a concomitant reduction in this distinct and clinically meaningful outcome would further enhance the public health relevance of the LIFE physical activity intervention. Results from the current study are mixed, with no overall reduction in the prespecified outcome of time to first serious fall injury, but a substantial decrease in the rate of all serious fall injuries, an outcome that was not prespecified, in men. As a recurrent event, the outcome of all serious fall injuries may have greater clinical relevance than that of time to first serious fall injury. The safety of the LIFE intervention is evidenced by the low rate of serious fall injuries during the physical activity sessions, a rate that was comparable to that during the health education sessions.

Conclusions

Our results do not support the benefit of structured moderate intensity physical activity in reducing the risk of serious fall injuries among sedentary older people with functional limitations. None the less, the safety and demonstrated benefit of the LIFE physical activity program in reducing major mobility disability,[12] coupled with suggestive evidence from the current study for reduction of fall related fractures and hospital admissions in men, support continued evaluation of the program for possible widespread implementation in the community.

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Contributors: MEM had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors participated in designing the analyses, interpreting the results, and writing the manuscript. All authors had full access to the data and are guarantors for the study.

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Ethical approval: Each participating centers' institutional review board approved this study; all participants provided informed consent.

Transparency: TMG and MEM affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Data sharing: Information is available at www.thelifestudy.org/public/index.cfm under the LIFE coded dataset access link.

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Appendix: figure showing flow of participants through study
Appendix: footnote to accompany appendix figure
Appendix: research investigators for the LIFE Study
Appendix: types of serious fall injuries by intervention group for men and women

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