

Changes in Physical Activity, Sedentary Time, and Risk of Falling: The Women's Health Initiative Observational Study

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ABSTRACT

Falling significantly affects quality of life, morbidity, and mortality among older adults. We sought to evaluate the prospective association between sedentary time, physical activity, and falling among post-menopausal women aged 50–79 y recruited to the Women’s Health Initiative Observational Study between 1993 and 1998 from 40 clinical centers across the United States. Baseline (B) and change in each of the following were evaluated at year 3 (Y3) and year 6 (Y6; baseline n=93,676; Y3 n=76,598; Y6 n=75,428): recreational physical activity (MET-h/wk), sitting, sleeping (min/d), and lean body mass by dual energy X-ray absorptiometry (subset N=6,475). Falls per year (0, 1, 2, ≥3) were assessed annually by self-report questionnaire and then dichotomized as ≤1 and ≥2 falls/year. Logistic regression models were adjusted for demographics, body mass index, fall history, tobacco and alcohol use, medical conditions, and medications. Higher baseline activity was associated with greater risk of falling at Y6 (18%; p for trend <0.0001). Increasing sedentary time minimally decreased falling (1% Y3; 2% Y6; p<0.05). Increasing activity up to ≥ 9 MET-h/wk (OR: 1.12, 95%CI: 1.03-1.22) or maintaining ≥ 9 MET-h/wk (OR: 1.20, 95% CI: 1.13-1.29) increased falling at Y3 and Y6 (p for trend <0.001). Adding lean body mass to the models attenuated these relationships. Physically active lifestyles increased falling among post-menopausal women. Additional fall prevention strategies, such as balance and resistance training, should be evaluated to assist post-menopausal women in reaching or maintaining levels of aerobic activity known to prevent and manage several chronic diseases.

Key Words: accidental falls; falls; exercise; menopause; sedentary lifestyle

Abbreviations: analysis of variance, ANOVA; body mass index, BMI; dual energy X-ray absorptiometry, DXA; metabolic equivalent of task, Hispanic Established Population for the Epidemiologic Study of the Elderly, H-EPESE; MET; standard deviation, SD; Women’s Health Initiative, WHI

INTRODUCTION

The propensity to fall increases with aging, often due to other age related issues, such as impaired vision, balance, and mental acuity (Rubenstein, 2006). Although many falls result in minor injuries, approximately 10% will result in fractures which are associated with significant morbidity and mortality in the aged (Gillespie et al., 2012). Reductions in falls among community dwelling older adults engaging exercise interventions offers hope (Gillespie et al., 2012), as does the protection against fracture with higher baseline physical activity demonstrated in the Women's Health Initiative (WHI) (Robbins et al., 2007), but overall, the association between physical activity and falls in the literature has been inconsistent (Clarke et al., 2015). Physical activity patterns over time may prove to be more predictive of falls than exercise interventions or assessment of physical activity at a single time point. Longitudinal changes in physical activity and body composition, which may mediate the falls benefit of physical activity through preservation of muscle mass (LaStayo et al., 2003), are needed to better understand their independent and joint roles in falls risk. However, because prospective studies on older adults typically do not have repeated prospective measures on these factors, they have yet to be fully explored with respect to incidence of falling.

In the United States, physical activity decreases dramatically in adulthood, stabilizing at relatively low levels in middle aged women (Caspersen et al., 2000). Low levels of physical activity have been associated with decreased muscle mass (Morley et al., 2001)._Meanwhile, sedentary time, distinctly different than insufficient moderate to vigorous physical activity (Owen et al., 2010), increases with aging (Clark et al., 2010). High sedentary time may also aid in skeletal muscle decline and has been shown to be a risk factor for falling in studies with 1-2 years follow-up (Thibaud et al., 2012).

We sought to determine whether prospectively assessed physical activity patterns, including sedentary time, are associated with_the risk of falling over several years and whether risk of falling is mediated by body composition. We hypothesized that decreasing physical activity over time would be associated with increased risk of falling among postmenopausal women (**Figure 1**). High sedentary time was also hypothesized to increase risk of falling.

METHODS

Study Population

The WHI Study recruited postmenopausal women aged 50-79 y at 40 WHI clinical centers across the United States between 1993 and 1998 to four clinical trials and an observational study (1998; Hays et al., 2003). Only women enrolled in the observational study were included in this analysis (N=93,676); body composition was measured in those enrolled at the Pittsburgh, PA; Birmingham, AL; and Tucson-Phoenix, AZ sites (N=6,475) (Chen et al., 2008). The protocol and consent forms were approved by each institutional review board at each site and all participants provided written informed consent. For the present study, measurements taken at baseline, year 3 and year 6 of follow-up were used. The average follow-up time for incident falls in this study was 54 months.

Physical Activity Assessment

The frequency, intensity, and duration of walking, as well as moderate and vigorous recreational physical activity, were assessed using a reliable and valid questionnaire. Test-retest reliability was 0.67 - 0.71 (weighted κ coefficient) for individual physical activity variables on the WHI questionnaire and the questionnaire assessed activity levels correlated well with accelerometry ($r=0.73$) in a subset of the WHI. (Eaglehouse et al., 2016; Johnson-Kozlow et al., 2007; Langer et al., 2003; Manson et al., 2002; Meyer et al., 2009; Nguyen et al., 2013). Energy expenditure (MET-h/wk) was computed, as previously published (Ainsworth et al., 2000; Sims et al., 2012).

Based on the continuous physical activity data, 4 categories of baseline physical activity were created: no physical activity (0 MET-h/wk), ≤ 3 MET-h/wk, 3.1 to 8.9 MET-h/wk, and ≥ 9 MET-h/wk. Participants were classified as physically inactive (0 MET-h/wk), insufficiently active (>0 to < 9 MET-h/wk), and active (≥ 9 MET-h/wk of moderate-vigorous intensity physical activity) in approximate alignment with recommended physical activity levels (2008). *Change* in physical activity from baseline to year 3 and year 6 was categorized as follows.

- a) change/inactive: remaining in the inactive or insufficiently active category at baseline and follow-up
- b) increased activity: inactive or insufficiently active at baseline, but increased to ≥ 9 MET-h/wk at follow-up
- c) active maintainer: maintained ≥ 9 MET-h/wk at baseline and follow-up

- d) decreased/inactive: decreased physical activity categories from sufficiently active to insufficiently active or inactive, or decreased from insufficiently active to inactive category

Sedentary time was quantified separately by two questions in the questionnaire that asked how much time was spent sitting per day and lying down per day (hrs/d). Sedentary time is not equivalent to the inactive or insufficiently active terms above.

Anthropometry and Body Composition Assessment

Height and weight were measured without shoes on a wall-mounted stadiometer to the nearest 0.1 cm and balance-beam scale to the nearest 0.1 kg, respectively. BMI was calculated as weight (kg)/height (m)². Body composition was determined by performing dual energy X-ray absorptiometry scans (DXA; QDR2000, 2000+, or 4500W; Hologic Inc, Bedford, MA) at 3 WHI clinical centers (Pittsburgh, PA; Birmingham, AL; and Tucson-Phoenix, AZ), each using the rigorous WHI quality assurance program (Chen et al., 2005). Measurements included both whole body and regional bone mineral density, lean body mass, and fat mass. Calibration equations were developed when an older DXA machine was replaced with a newer model (QDR2000 to QDR4500W) (Chen et al., 2005). Participants who completed the baseline and at least year 3 or year 6 follow-up visits were included in this analysis.

Assessment of Falls

A self-report medical history questionnaire that included the following question was collected at baseline and by mail annually: "During the past 12 months, how many times did you fall and land on the floor or ground: none, 1 time, 2 times, 3 or more times?" Participants were asked not to include falls due to sports activities such as snow- or water-skiing or horseback riding. (Anderson et al., 2003)

Assessment of Covariates

Years since menopause were determined by last reported menstrual bleeding, time of bilateral oophorectomy, or initiation of menopausal hormone therapy. Self-report questionnaires were used to obtain information on demographics, medical history, medications, smoking and alcohol use, and prior hormone therapy use at baseline. Diet and physical function were assessed by a validated food frequency questionnaire (Block et al., 1990) and the Medical Outcomes Study Scale (Ware and Sherbourne, 1992), respectively.

Statistical Analysis

Descriptive statistics were computed and tests for significant differences were performed using analysis of variance (ANOVA) for continuous variables and Chi Squared tests for categorical variables. Logistic regression models were developed to determine the odds of falling based on baseline physical activity category and sedentary time, as well as change in physical activity (categories and continuous) over three and six years. In alignment with a prior WHI publications, (Bea et al., 2011; Cauley et al., 2007; Chen et al., 2004) a binary variable of ≥ 2 falls per year was used for risk of falling in all models. A history of ≥ 2 falls per year is a significant predictor of a recurrent faller (Stalenhoef et al., 2002) and higher fall rates are associated with frailty related fractures (Schwartz et al., 2005). Factors that have been associated with falling and body composition in the literature were selected *a priori* as covariates, including age, BMI, ethnicity, education, years since menopause, tobacco and alcohol use, number of falls at baseline, diabetes, hypertension, fainting, general health, physical function, and medication use including hormone therapy, beta blocker, antianxiety agent, hypnotic, narcotic, and sedative use. Geographic region, by latitude of the responsible clinical center at the time of enrollment, waist circumference, and total body fat did not significantly affect the models, so were not included. Exclusions included those with prior stroke, peripheral artery disease, multiple sclerosis, and Parkinson's Disease, or missing covariates. Change in activity models were stratified by body mass index ($\text{BMI} \geq 30\text{kg/m}^2$) due to previous associations with falls (Beck et al., 2009).

RESULTS

Overall, the mean physical activity level for the cohort was 13.7 (± 14.4) MET-h/wk at baseline, 13.6 (± 14.6) MET-h/wk at year 3, and 13.1 (± 14.2) MET-h/wk at year 6. The change in physical activity across the cohort was -0.4 (± 12.4) MET-h/wk from baseline to year 3 and -0.9 (± 13.5) MET-h/wk from baseline to year 6. Total sedentary time (hrs/d spent sitting or sleeping) was 15.0 (± 4.2) hrs/d at baseline, 14.7 (± 3.7) hrs/d at year 3 and 14.7 (± 3.8) hrs/d at year 6. Inactive time was reduced by -0.38 (± 3.9) from baseline to year 3 and remained stable at year 6.

Baseline activity levels varied by race/ethnicity, highest level of education, years postmenopausal, and baseline fall history. There were more obese individuals in the inactive group. The less-active and non-active groups were more likely to report medical conditions,

medication use, smoking, and lower alcohol consumption compared to others. Women in the highest category of physical activity had the highest lean mass at baseline (**Table 1**) and follow-up, however, they decreased physical activity and lost greater absolute appendicular lean mass over time compared to others (**Table 2**).

Overall, the risk of falling was significantly increased (18%) over six, but not three years of follow up among those with ≥ 9 MET-h/wk of physical activity at baseline compared to being inactive at baseline (p for trend < 0.001 ; **Table 3**). However, when stratified on BMI, the non-obese women were at 12% greater risk of falling over three years if they were active as compared to their inactive counterparts (p for trend = 0.04).

The odds of falling increased by 1% with increased walking at both three and six years ($p=0.02$) and increased vigorous activity at three, but not at six years, when evaluating change in activity as a continuous variable. Increased sitting slightly decreased falls over 6 years (OR: 0.98, 95%CI: 0.98-0.99, $p<0.001$), while time spent lying down decreased odds of falling by 2% and 3% at three and six years, respectively ($p<0.001$). Stratification by obesity did not significantly affect these results (data not shown).

In categorical analyses, increased or maintained adequate physical activity (≥ 9 MET-h/wk) significantly increased odds of falling, by 12% and 20%, respectively, compared to those that remained inactive between baseline and year three (**Table 4**; p for trend < 0.001). Models stratified by obesity were consistent with results from the entire cohort. After 6 years, the odds of falling increased to 30% for those that maintained a physically active lifestyle overall (p for trend < 0.001), but 36% among the non-obese (p for trend < 0.001).

When adjusted for change in lean mass, the pattern of increased odds of falling with increasing physical activity was similar to that of the entire cohort for the first three years (p for trend = 0.01), while decreased physical activity appeared to have a protective effect against falling when adjusting for changes in lean mass. Those with a BMI < 30 kg/m² drove the relationship between decreases in physical activity and falling over 3 years. This relationship did not persist over six years.

DISCUSSION

Contrary to our hypothesis, we found that active lifestyles and increases in physical activity over time were associated with increased fall risks among postmenopausal women aged 50-79 at baseline. Although reduction in falls has been supported by several exercise interventions (Gillespie et al., 2012), the positive studies tended to include multifactorial interventions (i.e. combination of physical activity, balance training, home hazards assessment, medication assessment, technical aids, etc.) and were typically limited to adults older than those in the WHI and those at high risk of falling. Community dwelling adults often do not employ multifactorial activity programs or activities designed to improve physical function (Lewis et al., 2015). Large longitudinal studies examining physical activity associations with falls in community dwelling older adults have suggested that physical activity may increase fall risk, although the risk is likely modified by type of activity and level of physical function or mobility (Jefferis et al., 2015; Lewis et al., 2015; Mertz et al., 2010; Peeters et al., 2010). Walking, in particular, the physical activity often selected by older women (Booth et al., 1997; Garcia et al., 2015; Sorkin et al., 2015), has been problematic for older adults in other studies (Mertz et al., 2010; Nikander et al., 2011 [Feb 15 2011 Epub ahead of print]). Postmenopausal women who spent greater time walking (>3hrs/wk) in a large, five-year study (N=2780) experienced more fractures, which authors suggest may be attributable to increased falls (Nikander et al., 2011 [Feb 15 2011 Epub ahead of print]).

In spite of these results, the benefits of physical activity for prevention and management of most of the prevalent chronic diseases in the United States, including osteoporosis, diabetes, cardiovascular disease, and some cancers (2008), likely outweigh the risks of falling. Further, exercise has been shown to reduce the risk of injury given a fall (Uusi-Rasi et al., 2015) and those who are more mobile prior to injury tend to have better outcomes (Thorngren et al., 2005). The minimal protection against falls due to greater sedentary time herein should be interpreted with caution, as well, as cardiovascular and other health benefits would be sacrificed with reduced activity. The distribution of medical conditions, medications, and falls across physical activity categories at baseline imply that the women self-limited physical activity if balance impairing medications, chronic conditions, or prior falls were present, as noted by others (2011; Bruce et al., 2002).

The results support the notion that aerobic activity alone among older adults is not enough to prevent falling in older populations (Clarke et al., 2015; Voukelatos et al., 2015). The increased

opportunities for interaction with environmental hazards, and therefore greater opportunities for falling (Feldman and Chaudhury, 2008), need to be counterbalanced by the ability to adapt to these challenges. We would suggest that the complimentary strength and balance activities recommended by both the Physical Activity Guidelines for Americans (2008) and the Clinical Practice Guideline for Prevention of Falls in Older Persons (2011) be further publicized and evaluated. The adoption rate and efficacy of these multifactorial recommendations *longitudinally* (Clarke et al., 2015), along with suggested environmental strategies in older adults (Feldman and Chaudhury, 2008) requires further exploration, though early pilot work suggests an effective multifactorial fall prevention strategy can be habituated (Fleig et al., 2016).

The similarity in results with and without lean mass adjustment aligns with the lack of association between change in lean mass and physical activity demonstrated in the WHI previously (Sims et al., 2013) and further supports the need for activities beyond aerobic training to enhance physical function and potentially muscle quality, rather than lean mass per se. In support of this assertion, the Hispanic Established Population for the Epidemiologic Study of the Elderly (H-EPESE; N=1011 aged ≥ 75 yrs) recently demonstrated that participants with high physical activity and low physical function had a greater fall risk than those with high physical activity and high physical function (Lewis et al., 2015). However, in The British Regional Heart Study (N=3137) those with initial low mobility participating benefited from increasing activity, while those without mobility limitations did not (Jefferis et al., 2015), suggesting the need to better understand the utility of initial mobility screening and activity planning in older adults.

Limitations

Statistical adjustment for potential confounding factors, may not fully account for differences between activity groups. Additionally, self-report physical activity measures, although validated herein and practical in large cohorts, have limitations. We could not separate falls occurring during activity from other falls which might be differentially related with physical activity and sedentary time. Objective measures of physical function were not available across this subset of WHI and fall data collection did not fully conform to Prevention of Falls Network Europe recommendations due to study completion prior to the consensus statement (Lamb et al., 2005). The study is not generalizable to younger women or men.

CONCLUSION

Physically active lifestyles increased falling among post-menopausal women. Additional fall prevention strategies, such as balance and resistance training, should be evaluated to assist post-menopausal women in reaching or maintaining the level of aerobic activity known to prevent and manage several chronic diseases.

DISCLOSURE STATEMENT

The authors have declared no conflicts of interest.

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REFERENCES

1998. Design of the Women's Health Initiative clinical trial and observational study. The Women's Health Initiative Study Group. *Controlled clinical trials* 19:61-109.
2008. Physical Activity Guidelines Advisory Committee Report, in: Services, U.S.D.o.H.a.H. (Ed.). *Physical Activities Guidelines Advisory Committee*, Washington (DC).
2011. Summary of the Updated American Geriatrics Society/British Geriatrics Society clinical practice guideline for prevention of falls in older persons. *J Am Geriatr Soc* 59:148-57.
- Ainsworth, B.E., Haskell, W.L., Whitt, M.C., Irwin, M.L., Swartz, A.M., Strath, S.J., O'Brien, W.L., Bassett, D.R., Jr., Schmitz, K.H., et al., 2000. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc* 32:S498-504.
- Anderson, G.L., Manson, J., Wallace, R., Lund, B., Hall, D., Davis, S., Shumaker, S., Wang, C.Y., Stein, E., et al., 2003. Implementation of the Women's Health Initiative study design. *Ann Epidemiol* 13:S5-17.
- Bea, J.W., Zhao, Q., Cauley, J.A., LaCroix, A.Z., Bassford, T., Lewis, C.E., Jackson, R.D., Tyllavsky, F.A., Chen, Z., 2011. Effect of hormone therapy on lean body mass, falls, and fractures: 6-year results from the Women's Health Initiative hormone trials. *Menopause* 18:44-52.
- Beck, T.J., Petit, M.A., Wu, G., Leboff, M.S., Cauley, J.A., Chen, Z., 2009. Does Obesity Really Make the Femur Stronger? Bone Mineral Density, Geometry and Fracture Incidence in the Women's Health Initiative-Observational Study. *J Bone Miner Res*.
- Block, G., Woods, M., Potosky, A., Clifford, C., 1990. Validation of a self-administered diet history questionnaire using multiple diet records. *J Clin Epidemiol* 43:1327-35.
- Booth, M.L., Bauman, A., Owen, N., Gore, C.J., 1997. Physical activity preferences, preferred sources of assistance, and perceived barriers to increased activity among physically inactive Australians. *Prev Med* 26:131-7.
- Bruce, D.G., Devine, A., Prince, R.L., 2002. Recreational physical activity levels in healthy older women: the importance of fear of falling. *J Am Geriatr Soc* 50:84-9.
- Caspersen, C.J., Pereira, M.A., Curran, K.M., 2000. Changes in physical activity patterns in the United States, by sex and cross-sectional age. *Med Sci Sports Exerc* 32:1601-9.
- Cauley, J.A., Wu, L., Wampler, N.S., Barnhart, J.M., Allison, M., Chen, Z., Jackson, R., Robbins, J., 2007. Clinical risk factors for fractures in multi-ethnic women: the Women's Health Initiative. *J Bone Miner Res* 22:1816-26.
- Chen, Z., Bassford, T., Green, S.B., Cauley, J.A., Jackson, R.D., LaCroix, A.Z., Leboff, M., Stefanick, M.L., Margolis, K.L., 2005. Postmenopausal hormone therapy and body

- composition--a substudy of the estrogen plus progestin trial of the Women's Health Initiative. *Am J Clin Nutr* 82:651-6.
- Chen, Z., Beck, T.J., Cauley, J.A., Lewis, C.E., LaCroix, A., Bassford, T., Wu, G., Sherrill, D., Going, S., 2008. Hormone therapy improves femur geometry among ethnically diverse postmenopausal participants in the Women's Health Initiative hormone intervention trials. *J Bone Miner Res* 23:1935-45.
- Chen, Z., Kooperberg, C., Pettinger, M.B., Bassford, T., Cauley, J.A., LaCroix, A.Z., Lewis, C.E., Kipersztok, S., Borne, C., et al., 2004. Validity of self-report for fractures among a multiethnic cohort of postmenopausal women: results from the Women's Health Initiative observational study and clinical trials. *Menopause* 11:264-74.
- Clark, B.K., Sugiyama, T., Healy, G.N., Salmon, J., Dunstan, D.W., Shaw, J.E., Zimmet, P.Z., Owen, N., 2010. Socio-demographic correlates of prolonged television viewing time in Australian men and women: the AusDiab study. *J Phys Act Health* 7:595-601.
- Clarke, C.L., McMurdo, M.E., Witham, M.D., 2015. Falls research: stumbling or striding? *Age Ageing* 44:350-2.
- Eaglehouse, Y.L., Talbott, E.O., Chang, Y., Kuller, L.H., 2016. Participation in Physical Activity and Risk for Amyotrophic Lateral Sclerosis Mortality Among Postmenopausal Women. *JAMA Neurol* 73:329-36.
- Feldman, F., Chaudhury, H., 2008. Falls and the physical environment: a review and a new multifactorial falls-risk conceptual framework. *Can J Occup Ther* 75:82-95.
- Fleig, L., McAllister, M.M., Chen, P., Iverson, J., Milne, K., McKay, H.A., Clemson, L., Ashe, M.C., 2016. Health behaviour change theory meets falls prevention: Feasibility of a habit-based balance and strength exercise intervention for older adults. *Psychol Sport Exerc* Volume 22:114-22.
- Garcia, D.O., Wertheim, B.C., Manson, J.E., Chlebowski, R.T., Volpe, S.L., Howard, B.V., Stefanick, M.L., Thomson, C.A., 2015. Relationships between dog ownership and physical activity in postmenopausal women. *Prev Med* 70:33-8.
- Gillespie, L.D., Robertson, M.C., Gillespie, W.J., Sherrington, C., Gates, S., Clemson, L.M., Lamb, S.E., 2012. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 9:CD007146.
- Hays, J., Hunt, J.R., Hubbell, F.A., Anderson, G.L., Limacher, M., Allen, C., Rossouw, J.E., 2003. The Women's Health Initiative recruitment methods and results. *Ann Epidemiol* 13:S18-77.

- Jefferis, B.J., Merom, D., Sartini, C., Wannamethee, S.G., Ash, S., Lennon, L.T., Iliffe, S., Kendrick, D., Whincup, P.H., 2015. Physical Activity and Falls in Older Men: The Critical Role of Mobility Limitations. *Med Sci Sports Exerc* 47:2119-28.
- Johnson-Kozlow, M., Rock, C.L., Gilpin, E.A., Hollenbach, K.A., Pierce, J.P., 2007. Validation of the WHI brief physical activity questionnaire among women diagnosed with breast cancer. *Am J Health Behav* 31:193-202.
- Lamb, S.E., Jorstad-Stein, E.C., Hauer, K., Becker, C., 2005. Development of a common outcome data set for fall injury prevention trials: the Prevention of Falls Network Europe consensus. *J Am Geriatr Soc* 53:1618-22.
- Langer, R.D., White, E., Lewis, C.E., Kotchen, J.M., Hendrix, S.L., Trevisan, M., 2003. The Women's Health Initiative Observational Study: baseline characteristics of participants and reliability of baseline measures. *Ann Epidemiol* 13:S107-21.
- LaStayo, P.C., Ewy, G.A., Pierotti, D.D., Johns, R.K., Lindstedt, S., 2003. The positive effects of negative work: increased muscle strength and decreased fall risk in a frail elderly population. *J Gerontol A Biol Sci Med Sci* 58:M419-24.
- Lewis, Z.H., Markides, K.S., Ottenbacher, K., Al Snih, S., 2015. The Role of Physical Activity and Physical Function on the Risk of Falls in Older Mexican Americans. *J Aging Phys Act*.
- Manson, J.E., Greenland, P., LaCroix, A.Z., Stefanick, M.L., Mouton, C.P., Oberman, A., Perri, M.G., Sheps, D.S., Pettinger, M.B., et al., 2002. Walking compared with vigorous exercise for the prevention of cardiovascular events in women. *N Engl J Med* 347:716-25.
- Mertz, K.J., Lee, D.C., Sui, X., Powell, K.E., Blair, S.N., 2010. Falls among adults: the association of cardiorespiratory fitness and physical activity with walking-related falls. *Am J Prev Med* 39:15-24.
- Meyer, A.M., Evenson, K.R., Morimoto, L., Siscovick, D., White, E., 2009. Test-retest reliability of the Women's Health Initiative physical activity questionnaire. *Med Sci Sports Exerc* 41:530-8.
- Morley, J.E., Baumgartner, R.N., Roubenoff, R., Mayer, J., Nair, K.S., 2001. Sarcopenia. *J Lab Clin Med* 137:231-43.
- Nguyen, H.Q., Herting, J.R., Kohen, R., Perry, C.K., LaCroix, A., Adams-Campbell, L.L., Beresford, S.A., Eaton, C.B., Tinker, L., 2013. Recreational physical activity in postmenopausal women is stable over 8 years of follow-up. *J Phys Act Health* 10:656-68.

- Nikander, R., Gagnon, C., Dunstan, D.W., Magliano, D.J., Ebeling, P.R., Lu, Z.X., Zimmet, P.Z., Shaw, J.E., Daly, R.M., 2011 [Feb 15 2011 Epub ahead of print]. Frequent walking, but not total physical activity, is associated with increased fracture incidence: A 5-year follow-up of an Australian population based prospective study (AusDiab). *J Bone Miner Res*.
- Owen, N., Healy, G.N., Matthews, C.E., Dunstan, D.W., 2010. Too much sitting: the population health science of sedentary behavior. *Exerc Sport Sci Rev* 38:105-13.
- Peeters, G.M., Verweij, L.M., van Schoor, N.M., Pijnappels, M., Pluijm, S.M., Visser, M., Lips, P., 2010. Which types of activities are associated with risk of recurrent falling in older persons? *J Gerontol A Biol Sci Med Sci* 65:743-50.
- Robbins, J., Aragaki, A.K., Kooperberg, C., Watts, N., Wactawski-Wende, J., Jackson, R.D., LeBoff, M.S., Lewis, C.E., Chen, Z., et al., 2007. Factors associated with 5-year risk of hip fracture in postmenopausal women. *Jama* 298:2389-98.
- Rubenstein, L.Z., 2006. Falls in older people: epidemiology, risk factors and strategies for prevention. *Age Ageing* 35 Suppl 2:ii37-ii41.
- Schwartz, A.V., Nevitt, M.C., Brown, B.W., Jr., Kelsey, J.L., 2005. Increased falling as a risk factor for fracture among older women: the study of osteoporotic fractures. *Am J Epidemiol* 161:180-5.
- Sims, S.T., Kubo, J., Desai, M., Bea, J., Beasley, J.M., Manson, J.E., Allison, M., Seguin, R.A., Chen, Z., et al., 2013. Changes in Physical Activity and Body Composition in Postmenopausal Women over Time. *Med Sci Sports Exerc*.
- Sims, S.T., Larson, J.C., Lamonte, M.J., Michael, Y.L., Martin, L.W., Johnson, K.C., Sarto, G.E., Stefanick, M.L., 2012. Physical activity and body mass: changes in younger versus older postmenopausal women. *Med Sci Sports Exerc* 44:89-97.
- Sorkin, D.H., Biegler, K.A., Billimek, J., 2015. Differences in Self-Reported Physical Activity and Body Mass Index Among Older Hispanic and Non-Hispanic White Men and Women: Findings from the 2009 California Health Interview Survey. *J Am Geriatr Soc* 63:2158-63.
- Stalenhoef, P.A., Diederiks, J.P., Knottnerus, J.A., Kester, A.D., Crebolder, H.F., 2002. A risk model for the prediction of recurrent falls in community-dwelling elderly: a prospective cohort study. *J Clin Epidemiol* 55:1088-94.
- Thibaud, M., Block, F., Tournoux-Facon, C., Breque, C., Rigaud, A.S., Dugue, B., Kemoun, G., 2012. Impact of physical activity and sedentary behaviour on fall risks in older people: a

- systematic review and meta-analysis of observational studies. *Eur Rev Aging Phys Act* 9:5-15.
- Thorngren, K.G., Norrman, P.O., Hommel, A., Cedervall, M., Thorngren, J., Wingstrand, H., 2005. Influence of age, sex, fracture type and pre-fracture living on rehabilitation pattern after hip fracture in the elderly. *Disabil Rehabil* 27:1091-7.
- Uusi-Rasi, K., Patil, R., Karinkanta, S., Kannus, P., Tokola, K., Lamberg-Allardt, C., Sievanen, H., 2015. Exercise and Vitamin D in Fall Prevention Among Older Women: A Randomized Clinical Trial. *JAMA Intern Med*.
- Voukelatos, A., Merom, D., Sherrington, C., Rissel, C., Cumming, R.G., Lord, S.R., 2015. The impact of a home-based walking programme on falls in older people: the Easy Steps randomised controlled trial. *Age Ageing* 44:377-83.
- Ware, J.E., Jr., Sherbourne, C.D., 1992. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 30:473-83.

Figure 1. Hypothesized mediation model among participants in the Women’s Health Initiative Observational Study recruited between 1993 and 1998 from 40 clinical centers across the United States ($n=93,676$)

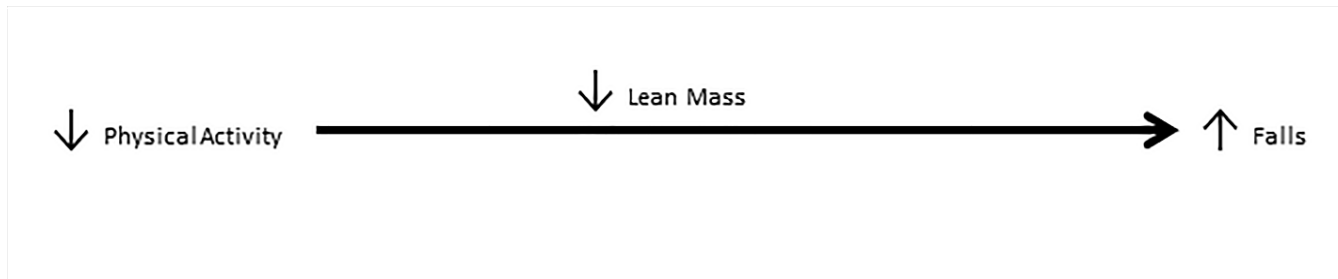


Table 1. Baseline demographic and medical history characteristics by physical activity group among participants in the Women's Health Initiative Observational Study recruited between 1993 and 1998 from 40 clinical centers across the United States (*n*=93,676)

		0METs (N=12,636)		>0-3METs (N=9,954)		3.1-8.9METs (N=21,192)		≥9METs (N=48,843)		p-value
		N	%	N	%	N	%	N	%	
Age group at screening	50-59	4215	33.36	3142	31.57	6610	31.19	15411	31.55	<0.001
	60-69	5341	42.27	4323	43.43	9147	43.16	21925	44.89	.
	70-79	3080	24.37	2489	25.01	5435	25.65	11507	23.56	.
Race/ ethnicity	White	9707	76.82	7823	78.59	17456	82.37	42223	86.45	<0.001
	Black	1612	12.76	1132	11.37	1874	8.84	2943	6.03	.
	Hispanic	692	5.48	492	4.94	868	4.10	1423	2.91	.
	American Indian	80	0.63	63	0.63	94	0.44	179	0.37	.
	Asian/Pacific									
	Islander	351	2.78	300	3.01	580	2.74	1422	2.91	.
	Unknown	194	1.54	144	1.45	320	1.51	653	1.34	.
Education	0-8 years	386	3.08	234	2.37	380	1.81	476	0.98	<0.001
	Some high school	766	6.11	519	5.26	836	3.98	1116	2.30	.
	High school diploma/GED	2841	22.67	1993	20.18	3745	17.82	6370	13.15	.
	School after high school	4817	38.44	3875	39.24	7875	37.46	16999	35.09	.
	College degree or higher	3722	29.70	3255	32.96	8184	38.93	23484	48.48	.
Years menopausal	< 10 yrs	3539	29.46	2712	28.72	6086	29.90	14849	31.39	<0.001
	≥10 yrs	8472	70.54	6730	71.28	14266	70.10	32453	68.61	.
Smoking status	Never	6332	50.68	5198	52.96	11077	52.84	24026	49.76	<0.001
	Past	4878	39.04	3769	38.40	8422	40.17	22134	45.84	.
	Current	1284	10.28	848	8.64	1466	6.99	2128	4.41	.
Alcohol intake	Non Drinker	7028	55.71	5111	51.42	9327	44.06	17292	35.45	<0.001
	≤ 1 drink/day	4437	35.17	3913	39.37	9522	44.98	24292	49.80	.
	> 1 drink/day	1150	9.12	915	9.21	2319	10.96	7200	14.76	.
Treated diabetes (pills or shots)	No	11797	93.50	9285	93.43	20191	95.40	47383	97.12	<0.001
	Yes	820	6.50	653	6.57	973	4.60	1403	2.88	.
History of hypertension	Never hypertensive	7454	59.71	5937	60.31	13410	63.95	34250	70.68	<0.001

	Untreated hypertensive	1123	9.00	826	8.39	1742	8.31	3613	7.46	.
	Treated hypertensive	3906	31.29	3081	31.30	5816	27.74	10595	21.86	.
Hormone Therapy use	Never used	5635	44.63	4502	45.26	8875	41.91	18527	37.97	<0.001
	Past user	1924	15.24	1497	15.05	3190	15.06	7147	14.65	.
	Current user	5067	40.13	3948	39.69	9110	43.02	23122	47.39	.
Beta blockers use	No	11399	90.21	9025	90.67	19174	90.48	45422	93.00	<0.001
	Yes	1237	9.79	929	9.33	2017	9.52	3421	7.00	.
Antianxiety agents use	No	12035	95.24	9531	95.75	20387	96.21	47423	97.09	<0.001
	Yes	601	4.76	423	4.25	804	3.79	1420	2.91	.
Hypnotics use	No	12197	96.53	9652	96.97	20578	97.11	47612	97.48	<0.001
	Yes	439	3.47	302	3.03	613	2.89	1231	2.52	.
Narcotics use	No	12167	96.29	9651	96.96	20732	97.83	48115	98.51	<0.001
	Yes	469	3.71	303	3.04	459	2.17	728	1.49	.
Sedative use	No	12501	98.93	9854	99.00	21015	99.17	48458	99.21	0.007
	Yes	135	1.07	100	1.00	176	0.83	385	0.79	.
Fainted, last 12 months	No	12157	97.05	9599	97.28	20507	97.44	47406	97.64	0.001
	Yes	369	2.95	268	2.72	539	2.56	1144	2.36	.
Prior falls, last 12 months	None	8390	66.87	6585	66.50	14184	67.35	33297	68.51	<0.001
	1 time	2498	19.91	1988	20.08	4253	20.19	9524	19.60	.
	2 times	1023	8.15	858	8.66	1787	8.48	3851	7.92	.
	3 or more times	635	5.06	471	4.76	837	3.97	1930	3.97	.
Physical function > 90	No	9585	77.64	7463	76.60	14252	68.40	25128	52.28	<0.001
	Yes	2760	22.36	2280	23.40	6584	31.60	22935	47.72	.
Body Mass Index (kg/m ²), baseline	<25	3376	27.12	2881	29.24	7744	36.95	23408	48.48	<0.001
	25 - <30	3988	32.03	3268	33.17	7461	35.60	16408	33.99	.
	>=30	5085	40.85	3704	37.59	5755	27.46	8464	17.53	.
Body composition		Mean	SD	Mean	SD	Mean	SD	Mean	SD	p-value
Whole body lean mass (%)		54.60	7.42	54.06	6.88	56.25	7.29	58.70	7.34	<0.001

Appendicular lean mass (kg)	15.05	2.98	14.83	3.12	14.47	2.85	14.26	2.46	<0.001
Activity									
Total Physical activity, (MET-hrs/wk)	0.00	0.00	1.62	0.69	5.72	1.74	23.15	13.94	<0.001
Time spent sitting (hrs/d)	7.94	3.72	7.57	3.43	7.40	3.36	6.87	3.19	<0.001
Time spent sleeping (hrs/d)	7.76	2.60	7.79	2.47	7.83	2.33	7.92	2.18	<0.001

Table 2. Change in lean body mass, energy expenditure and physical activity from baseline to years three and six of follow-up by physical activity group among participants in the Women’s Health Initiative Observational Study recruited between 1993 and 1998 from 40 clinical centers across the United States (*n*=93,676)

	Inactive 0 METs		(>0-3) METs		(3.1- 8.9) METs		≥ 9 METS		p-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Change from Baseline to Year 3									
Whole body lean mass (%)	-0.46	3.19	-0.37	3.31	-0.60	3.18	-0.87	3.17	<0.001
Appendicular lean mass (kg)	-0.60	3.19	-0.41	3.21	-0.74	3.26	-1.17	3.47	<0.001
Physical activity, (MET-hrs/wk)	3.54	7.13	3.56	7.51	2.56	8.61	-3.29	14.58	<0.001
Time spent sitting (hrs/d)	-0.49	3.41	-0.48	3.25	-0.45	3.17	-0.37	3.01	<0.001
Time spent sleeping (hrs/d)	0.19	2.62	0.13	2.56	0.05	2.39	-0.04	2.23	<0.001
Change from Baseline to Year 6									
Whole body lean mass (%)	-0.23	4.43	-0.06	3.89	-0.55	3.87	-1.02	3.85	<0.001
Appendicular lean mass (kg)	-1.13	4.16	-1.02	3.31	-1.27	3.67	-2.23	3.78	<0.001
Physical activity, (MET-hrs/wk)	4.27	7.84	4.25	8.49	2.84	9.62	-4.71	15.32	<0.001
Time spent sitting (hrs/d)	-0.53	3.68	-0.57	3.46	-0.53	3.35	-0.42	3.20	<0.001
Time spent sleeping (hrs/d)	0.25	2.69	0.22	2.54	0.13	2.45	0.03	2.27	<0.001

Table 3. Baseline physical activity and falling at years three and six among participants in the Women's Health InitiativeObservational Study recruited between 1993 and 1998 from 40 clinical centers across the United States (*n*=93,676)

		Non-Fallers	Fallers*	Odds Ratio	95% CI		p value
Three Years Follow-up							
All	0METs	8871	1034
	>0-3METs	7041	860	0.95	(0.86,	1.05)	0.02
	3.1- 8.9METs	15689	1757	0.95	(0.87,	1.03)	.
	≥9METS	37886	3460	1.04	(0.96,	1.12)	.
BMI≥30	0METs	3482	458
	>0-3METs	2510	383	0.85	(0.73,	0.99)	0.10
	3.1- 8.9METs	4048	568	0.86	(0.75,	0.99)	.
	≥9METS	6143	751	0.93	(0.81,	1.06)	.
BMI<30	0METs	5389	576
	>0-3METs	4531	477	1.04	(0.91,	1.18)	0.04
	3.1- 8.9METs	11641	1189	1.02	(0.91,	1.14)	.
	≥9METS	31743	2709	1.12	(1.01,	1.24)	.
Six Years Follow-up							
All	0METs	8556	1085
	>0-3METs	6843	859	1.01	(0.92,	1.12)	<0.001
	3.1- 8.9METs	15389	1735	1.04	(0.95,	1.13)	.
	≥9METS	37579	3382	1.18	(1.09,	1.27)	.
BMI≥30	0METs	3332	510
	>0-3METs	2470	347	1.11	(0.95,	1.29)	0.12
	3.1- 8.9METs	3995	523	1.10	(0.96,	1.26)	.
	≥9METS	6126	712	1.17	(1.03,	1.34)	.
BMI<30	0METs	5224	575
	>0-3METs	4373	512	0.95	(0.84,	1.09)	<0.001
	3.1- 8.9METs	11394	1212	1.00	(0.90,	1.12)	.
	≥9METS	31453	2670	1.16	(1.05,	1.28)	.

^aFaller≥2falls per year. All models were adjusted for age, BMI (Body Mass Index), ethnicity, education, years since menopause, smoking, alcohol, number of falls at baseline, diabetes, hypertension, fainted, general health, hormone status, Beta blocker, Antianxiety agents, Hypnotics, narcotics, sedatives, physical function >= 90.

Table 4. Odds falling based on change in physical activity (METs/wk) categories among participants in the Women's Health Initiative Observational Study recruited between 1993 and 1998 from 40 clinical centers across the United States (*n*=93,676)

		Base Model					Change in % Lean Body Mass Adjusted				
		Non-Fallers	Fallers*	OR	95% CI	p value	Non-Fallers	Fallers*	OR	95% CI	p value
Baseline to Year 3											
All	No change/ Inactive	22466	2721	.	.	.	1528	185	.	.	.
	Increase	7711	774	1.12	(1.02, 1.22)	<0.001	481	41	1.35	(0.93, 1.97)	0.010
	Active maintainer	28003	2281	1.21	(1.13, 1.29)	.	1362	120	1.16	(0.88, 1.52)	.
	Decrease	8929	1066	0.95	(0.88, 1.03)	.	538	82	0.73	(0.54, 0.98)	.
BMI≥30	No change/ Inactive	7560	1100	.	.	.	500	78	.	.	.
	Increase	1878	237	1.13	(0.96, 1.32)	0.03	126	13	1.44	(0.74, 2.81)	0.60
	Active maintainer	3777	415	1.15	(1.01, 1.30)	.	192	28	0.93	(0.56, 1.54)	.
	Decrease	2126	313	0.92	(0.80, 1.07)	.	126	19	0.84	(0.47, 1.52)	.
BMI<30	No change/ Inactive	14906	1621	.	.	.	1020	106	.	.	.
	Increase	5833	537	1.12	(1.00, 1.24)	<0.001	351	28	1.33	(0.83, 2.12)	0.006
	Active maintainer	24226	1866	1.23	(1.14, 1.33)	.	1160	90	1.23	(0.88, 1.71)	.
	Decrease	6803	753	0.96	(0.87, 1.06)	.	408	62	0.66	(0.46, 0.95)	.
Baseline to Year 6											
All	No change/Inactive	20943	2588	.	.	.	1312	157	.	.	.
	Increase	8278	841	1.11	(1.02, 1.21)	<0.001	434	44	1.04	(0.72, 1.51)	0.72
	Active maintainer	25906	2007	1.30	(1.22, 1.39)	.	1136	92	1.19	(0.88, 1.60)	.
	Decrease	10543	1218	1.03	(0.95, 1.11)	.	567	68	1.03	(0.74, 1.42)	.
BMI≥30	No change/Inactive	6979	1006	.	.	.	424	62	.	.	.
	Increase	2127	273	1.04	(0.90, 1.21)	0.30	125	11	1.51	(0.74, 3.08)	0.65
	Active maintainer	3361	369	1.12	(0.98, 1.28)	.	146	16	1.18	(0.63, 2.22)	.
	Decrease	2472	309	1.11	(0.96, 1.28)	.	148	22	0.94	(0.53, 1.67)	.
BMI<30	No change/ Inactive	13964	1582	.	.	.	876	94	.	.	.
	Increase	6151	568	1.15	(1.03, 1.27)	<0.001	308	33	0.91	(0.58, 1.41)	0.72
	Active maintainer	22545	1638	1.36	(1.26, 1.47)	.	980	75	1.16	(0.82, 1.66)	.
	Decrease	8071	909	1.01	(0.92, 1.11)	.	414	46	1.05	(0.70, 1.57)	.

^aFaller \geq 2falls per year. All models were adjusted for age, BMI (Body Mass Index), ethnicity, education, years since menopause, smoking, alcohol, number of falls at baseline, diabetes, hypertension, fainted, general health, hormone status, Beta blocker, Antianxiety agents, Hypnotics, narcotics, sedatives, physical function \geq 90.