Research Article

Women’s Health Initiative Strong and Healthy Pragmatic Physical Activity Intervention Trial for Cardiovascular Disease Prevention: Design and Baseline Characteristics

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Abstract

Background: National guidelines promote physical activity to prevent cardiovascular disease (CVD), yet no randomized controlled trial has tested whether physical activity reduces CVD.

Methods: The Women’s Health Initiative (WHI) Strong and Healthy (WHISH) pragmatic trial used a randomized consent design to assign women for whom cardiovascular outcomes were available through WHI data collection (N = 18 985) or linkage to the Centers for Medicare and Medicaid Services (N = 30 346), to a physical activity intervention or “usual activity” comparison, stratified by ages 68–99 years (in tertiles), U.S. geographic region, and outcomes data source. Women assigned to the intervention could “opt out” after receiving initial physical activity materials. Intervention materials applied evidence-based behavioral science principles to promote current national recommendations for older Americans. The intervention was adapted to participant input regarding preferences, resources, barriers, and motivational drivers and was targeted for 3 categories of women at lower, middle, or higher levels of self-reported physical functioning and physical activity. Physical activity was assessed in both arms through annual questionnaires. The primary outcome is major cardiovascular events, specifically myocardial infarction, stroke, or CVD death; primary safety outcomes are hip fracture and non-CVD death. The trial is monitored annually by an independent Data Safety and Monitoring Board. Final analyses will be based on intention to treat in all randomized participants, regardless of intervention engagement.

Results: The 49 331 randomized participants had a mean baseline age of 79.7 years; 84.3% were White, 9.2% Black, 3.3% Hispanic, 1.9% Asian/Pacific Islander, 0.3% Native American, and 1% were of unknown race/ethnicity. The mean baseline RAND-36 physical function score was 71.6 (± 25.2 SD). There were no differences between Intervention (N = 24 657) and Control (N = 24 674) at baseline for age, race/ethnicity, current smoking (2.5%), use of blood pressure or lipid-lowering medications, body mass index, physical function, physical activity, or prior CVD (10.1%).

Conclusion: The WHISH trial is rigorously testing whether a physical activity intervention reduces major CV events in a large, diverse cohort of older women.
National guidelines promote physical activity and limiting sedentary behavior to prevent cardiovascular disease (CVD) and other chronic diseases in older adults (1,2). The U.S. population aged 65 years and older is projected to reach 95 million (23% of the population) by the year 2060, with persons aged 85 years and older reaching 19 million, the majority of whom will be women (3). Decades of evidence-based interventions have shown that increasing physical activity can improve levels of physical function and cardiovascular (CV) risk factors (4-7), but these trials have mostly enrolled subjects less than 75 years old, and have mostly tested supervised, clinic-based exercise programs. There have been no randomized controlled trials with physical activity as the sole intervention that tested the hypothesis that increasing physical activity and/or reducing sedentary time reduces the incidence of major CV events. While the LIFE Trial showed that a physical activity intervention modestly preserved mobility in older adults with low physical function (8), a pragmatic centralized physical activity intervention delivered to aging adults across the functional continuum has not yet been tested. We designed the WHISH Strong & Healthy (WHISH) trial as a large-scale, randomized, controlled, pragmatic trial to fill this critical evidence gap. The WHISH trial is rigorously testing whether a physical activity intervention increases coronary artery revascularization (coronary artery bypass graft surgery or percutaneous coronary intervention) and reduces major CV events in a large, geographically diverse, multiethnic cohort of older women.

**Method**

**Objectives and Outcomes**

The primary hypothesis being tested is that a centralized, public health behavioral intervention designed to increase or maintain physical activity levels and reduce sedentary behavior will reduce the incidence of major CV clinical events, specifically myocardial infarction (MI), stroke, or CVD death, in older women. Secondary hypotheses are that the WHISH physical activity intervention will lower rates of venous thromboembolism, peripheral artery disease, and reduced physical functioning.

The primary safety aims are to evaluate whether the WHISH intervention increases risks of total clinical fracture, hip fracture, falls, or non-CVD mortality over ~8 years, compared with the usual follow-up (control). A secondary safety aim is to evaluate whether the physical activity intervention increases coronary artery revascularization (coronary artery bypass graft surgery or percutaneous coronary intervention).

The ultimate goal of the WHISH trial is to provide definitive evidence on the benefits and risks of this pragmatic physical activity intervention and, if efficacious, to disseminate an easily scalable intervention to improve the CV health of aging Americans.

**Randomized Consent Design**

The WHISH trial uses the randomized consent design proposed by Zelen (9) (Figure 1), in which eligible participants are randomized before being contacted and before informed consent is obtained. The design is based on the intention-to-treat principle; outcomes are assessed on the entire randomized population, regardless of their subsequent level of participation. This design is appropriate when the goal is to test the impact of a public health intervention on the population at large, not just within the subgroup of the population that is willing to participate, and tests the most critical research question: “Can a centrally delivered public health physical activity intervention reduce CVD events in a large population of older women?”

**Study Population and Eligibility Criteria**

The WHISH trial is embedded in the WHI Extension Study (WHI-ES), which is continuing to collect health outcomes and related data on women who were originally enrolled in the WHI Clinical Trial Program or the Observational Study at 40 U.S. clinical sites from 1993 to 2005, and which is expected to continue through at least 2027. Women in the WHI-ES consented to continued participation and extended follow-up in 2004–2005 and again in 2010. Earlier phases of the WHI program have been described in detail previously (10-18).

Participants in the WHI-ES were eligible for WHISH if they were alive in 2015, and free of conditions that would limit their full participation, specifically known dementia, living in a nursing home, inability to walk, inability to read English, or unavailability of follow-up CVD outcomes data.

The WHISH Data Coordinating Center (DCC) used the WHI database to screen women for eligibility based on previously collected WHI data. Of the original 93,567 women who consented to ongoing follow-up in the WHI Extension Study in 2010, 10,252 were known to have died before the date of randomization into WHISH, and 8533 were excluded due to known dementia (n = 6043), living in a nursing home (n = 2650), self-reported inability to walk (n = 934), or Spanish language preference (n = 269). An additional 3311 participants had been lost to follow-up due to inadequate contact information such as invalid addresses (Figure 2).

Availability of adjudicated CVD outcomes differed for 2 categories of WHI-ES participants. The “Medical Records Cohort (MRC)” is a subcohort in which CVD outcomes continued to be verified by review of medical records and physician-adjudication. The MRC cohort includes women who had participated in the WHI Hormone Trials, or were an African American or Hispanic participant in the Diet Modification Trial.

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**Figure 1.** Randomized consent study design (based on Zelen, N Engl J Med 1979) (9). Full color version is available within the online issue.
Before Randomization and Initial Contact

κ = 0.74) (19), stroke κ showed that CMS diagnosis codes had good agreement with Medicaid Services (CMS) database. Previous validation studies available through linkage to the Centers for Medicare and the criteria above and their follow-up hospitalization data were Outcomes Cohort (SRC)” and eligible for WHISH if they met other eligibility criteria as detailed above. The remaining WHI-ES women are part of the “Self-reported Outcomes Cohort (SRC)” and eligible for WHISH if they met the criteria above and their follow-up hospitalization data were available through linkage to the Centers for Medicare and Medicaid Services (CMS) database. Previous validation studies showed that CMS diagnosis codes had good agreement with WHI MRC adjudicated outcomes for MI (κ = 0.74) (19), stroke (κ = 0.84) (20), and other CVD outcomes (21,22). Unavailability of CMS follow-up for major CVD events excluded 21 871 SRC participants, leaving a total of 49 331 participants eligible for randomization (Figure 2).

The WHISH protocol is registered on clinical trials.gov (23) and was approved by Human Subjects Review committees at the Fred Hutchinson Cancer Research Center, Stanford University, and the University of California, San Diego.

Randomization and Initial Contact

Before WHISH randomization, all WHI-ES participants were mailed a newsletter describing new studies underway for eligible WHI participants. WHISH was described as a study testing whether increasing physical activity would lower the risk of heart disease and help maintain independent living. Eligible WHI-ES participants were randomized using the Zelen design in equal numbers either to the WHISH physical activity intervention or to continue usual follow-up. For practical reasons, participants were randomized in 3 waves about 1 month apart. Randomization was carried out in 24 strata formed by baseline age in tertiles (<77, 77–82, and ≥83 years), 4 WHI regions, and the method of outcomes collection (MRC or CMS Medicare hospitalization data). Among WHI-ES participants who met other eligibility criteria, 16 251 were in the MRC and 30 346 had sufficient Medicare data to be included in WHISH. An additional 2734 SRC women had outcomes adjudicated by the WHI for other reasons, yielding a total of 49 331 women randomized into the WHISH Trial.

Figure 2. WHISH Trial Consort Diagram. Full color version is available within the online issue.

or Observational Study. All MRC cohort women were eligible for WHISH if they met other eligibility criteria as detailed above. The remaining WHI-ES women are part of the “Self-reported Outcomes Cohort (SRC)” and eligible for WHISH if they met the criteria above and their follow-up hospitalization data were available through linkage to the Centers for Medicare and Medicaid Services (CMS) database. Previous validation studies showed that CMS diagnosis codes had good agreement with WHI MRC adjudicated outcomes for MI (κ = 0.74) (19), stroke (κ = 0.84) (20), and other CVD outcomes (21,22). Unavailability of CMS follow-up for major CVD events excluded 21 871 SRC participants, leaving a total of 49 331 participants eligible for randomization (Figure 2).

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Figure 2. WHISH Trial Consort Diagram. Full color version is available within the online issue.

Consent

Participants in the WHI-ES had all previously consented to follow up and collection of outcomes data. Women randomized in WHISH to usual follow-up received no further information about the trial. Women randomized to the physical activity intervention were sent an initial mailing from the WHISH DCC that included intervention materials, a Go4Life Workout to Go: Mini Exercise Guide (24), and a telephone number to call if they preferred to opt out of receiving additional physical activity materials. After removing 870 (3.5%) women who “opted out,” 53 who had undeliverable addresses and 81 who had died after randomization but before the intervention began, Stanford received names and contact information for 23 653 participants for the WHISH physical activity intervention.

Intervention participants received written information meeting HIPAA requirements in the fourth Stanford mailing (November 2015), and were provided a Stanford telephone number, postal address, and e-mail addresses to use if the participant did not consent to the use of data collected from surveys and postcards, data entered by participants into a WHISH website tracking tool, recorded through the WHISH automated telephone-based interactive voice response system, or returned as handwritten entries on annual WHISH calendars, or input received by telephone, e-mail, or other means. Intervention participants were reminded that they could request no further contact at any time in the future, thereby withdrawing passive consent, or request discontinuation of any specific component of the intervention, including but not limited to quarterly mailings, outbound monthly telephone messages, or emails.

WHISH Physical Activity Intervention

The WHISH physical activity intervention goals are based on the U.S. Department of Health and Human Services 2008 Physical Activity Guidelines for older Americans (1), as presented in the National Institute on Aging (NIA) Go4Life health education campaign (25), and the updated 2018 Physical Activity Guidelines for older Americans (2). These federal initiatives emphasize increasing or maintaining aerobic physical activity (primarily walking) and decreasing sedentary behavior (especially sitting), as well as multicomponent physical activity recommendations regarding muscle-strengthening, balance, and flexibility. Based on state-of-the-science behavioral theories, including Social Cognitive Theory (26), the Transtheoretical Model of behavior change (27), and Stages of (Readiness of) Change (28), the intervention is delivered through multiple channels including quarterly (seasonal) WHIshful Actions newsletters, with inserts targeted at 3 participant groups based on lower, middle and higher levels of self-reported physical functioning and physical activity levels; monthly outbound telephone calls with short (~1 minute) motivational messages; monthly motivational e-mails, for the approximately one-fourth of participants who provided email addresses; access to the WHISH website which includes videos of participants demonstrating exercises as well as many additional resources; and occasional personal contact with intervention staff by phone, e-mail, or regular mail as required or requested. The physical activity intervention adapts to participant input received from annual surveys or other inbound communication channels, regarding physical activity preferences, resources, barriers, and motivational drivers (29–31).

In the first year of the intervention, all physical activity participants received the Go4Life Exercise & Physical Activity: Your Everyday Guide (32), pedometers and calendars with instructions on how to track their physical activity, and resistance bands with...
examples of exercises using the bands for muscle-strengthening. In subsequent years, participants have received annual calendars, new pedometers and resistance bands, targeted inserts demonstrating various strength, balance, flexibility and endurance exercises, a WHISH sun visor, and chances to win gift cards by participating in special WHISH challenges, and they may request replacements of these materials as needed. Further specific details of the intervention program will be presented in a subsequent manuscript.

Outcomes Ascertainment

The primary outcome of the WHISH trial is major CV events, defined as the first event since randomization in WHISH of either MI, stroke, or CV Death. The primary safety outcomes include non-CV death, hip fracture, other clinical (non-hip) fractures, and falls. Secondary outcomes are venous thromboembolism, peripheral artery disease, physical functioning as determined by the Rand-36 10-item score (33), and coronary revascularization (coronary artery bypass graft or percutaneous coronary intervention) as the secondary safety outcome. Additional outcomes, including cancer, heart failure, and a wide array of clinical diagnoses, are ascertained on all participants through CMS linkage and annual WHI surveillance (34). Two ancillary studies to the WHISH Trial have been funded specifically to adjudicate heart failure and atrial fibrillation endpoints (R01HL130591, CB Eaton, Principal Investigator, and R01HL136390, MV Perez, Principal Investigator).

Details of the WHI outcomes ascertainment and adjudication procedures have been published (34,35) with modifications presented in the WHI-ES Protocol (36). Briefly, WHI-ES participants are followed annually, primarily by mailed questionnaires, to collect data on self-reported health events and related conditions. Mailings include a Form 33 - Medical History Update (Supplementary Appendix A) and additional questionnaires (see below), which most participants (or their proxies) return by mail. WHI staff may collect Form 33 by phone for women who have not returned it after repeat mailings.

Outcomes ascertainment procedures for WHISH depend on the outcome and whether the participant is in the MRC or in Medicare. These procedures use a combination of self-report and adjudicated events, as well as National Death Index and CMS linkages to identify outcome events (Table 1).

An overlap of 8431 participants in the MRC with CMS linkage allows a comparison of outcomes from the 2 sources. Highly concordant results reported from these sources in WHI for MI (19), stroke (20), peripheral vascular events (22), and venous thromboembolism (21) suggest that it is possible to combine adjudicated and CMS data to monitor outcomes in the WHISH trial.

Physical Functioning Assessment

Physical functioning (PF) is based on participant responses to questions in an annual WHI form (Form 151 Activities of Daily Living, Supplementary Appendix B), which is mailed with Form 33, that ask about limitations (no, not limited at all; yes, limited a little; yes, limited a lot) regarding 10 specific activities (Q 7–16) from RAND-36 (33). The PF score ranges from 0 to 100 (in 5-point increments), with 100 meaning no limitations on any activities.

Physical Activity Assessment

Physical Activity assessment is based on both a self-reported physical activity questionnaire (Form 521 Physical Activity Questionnaire, Supplementary Appendix C), which is mailed annually to all

| Table 1. Methods Used to Ascertian Outcomes in the WHISH Trial |
|---------------------------------------------------------------|
| **Outcome** | **MRC Participants** | **Participants With Medicare Part A+B or A Only** |
| Numbers at time of randomization | N = 18 985 | N = 30 346 |
| Health | Outcomes ascertainment procedures | From CMS codes using established algorithms |
| Coronary heart disease, revascularization, heart valve problem/repair, aortic aneurysm, stroke, carotid artery disease, heart failure, atrial fibrillation, venous thromboembolism, peripheral artery disease, hip fracture | Full review | National Death Index, medical records, and adjudication |
| Death | National Death Index | Full review |
| Cancer (all sites except nonmelanoma skin cancer), Angina, transient ischemic attack, other fractures and several other age-related diseases, including chronic obstructive pulmonary disease, diabetes mellitus requiring therapy, hypertension requiring therapy, intestinal or colon polyps or adenomas, macular degeneration, osteoarthritis or arthritis with aging, Parkinson’s disease, systemic lupus erythematosus, moderate/severe memory problems (dementia/Alzheimer’s), falls, hysterectomy | Self-report | Self-report |

| **Physical functioning (10-item Rand-36 scale)** |
|------------------------------------------------|
| **Self-report** | **Self-report** |

Note: CMS = Centers for Medicare and Medicaid Services; MRC = Medical records cohort.

A previous WHI ancillary study, the Objective Physical Activity and Cardiovascular Health (OPACH) Study (R01 HL105065, AZ
LaCroix, PI) provided an opportunity to conduct a substudy of accelerometry within a subset of 4730 WHISH participants who had successfully worn and returned Actigraph GT3X+ accelerometers in 2012–2014, thereby providing pre-WHISH Trial data for comparison between randomized groups (39). Surviving WHISH-OPACH participants who had returned usable accelerometer data were invited to join and actively consent to participation in the “WHI Physical Activity Follow-up Study” with no reference to the WHISH trial. To achieve balanced groups of at least 1000 women in both the WHISH arms throughout the planned follow-up period, the recruitment target was set at 2300; 2349 women consented. Of these, 85.4% (n = 2007) returned accelerometers in Year 1 of WHISH. Among those who were still alive, 75.1% (n = 1731) returned accelerometers in Year 2, and 63.7% (n = 1394) returned them at Year 4. Details of Accelerometer Substudy are provided in Supplementary Appendix D.

Trial Monitoring

An NHLBI-appointed Data Safety and Monitoring Board (DSMB) meets annually and receives updates on the physical activity intervention, including measurements of participant engagement, and monitors self-reported and accelerometer-measured physical activity and clinical outcomes data.

In early discussions, the DSMB determined that the trial would not have formal monitoring boundaries for stopping early for futility with respect to the CVD outcomes in recognition of the potential value of increasing or maintaining physical activity on multiple health conditions. The DSMB also suggested that the trial not have monitoring boundaries for stopping early for CVD efficacy because the benefit of getting a definitive answer will likely outweigh any benefit of making a less clear result public. This decision was justified based on several considerations: (i) the need for a broader assessment of the benefits and risks of increasing physical activity in older women; (ii) a strong anticipation of CVD benefits from prior studies of physical activity (4,5); and (iii) the availability to the general public including the WHISH usual follow-up comparison group of the NIA Go4Life materials (24,25,32) which were provided to the physical activity intervention group. Thus, trial monitoring for WHISH focuses on 2 main purposes: assuring the safety of participants; and testing the primary and secondary hypotheses adequately. WHISH could be stopped if the intervention group does not appear to be more physically active or less sedentary than the comparison group, which could result in a noninformative test. In addition, the NHLBI has requested an interim monitoring for benefit and futility with respect to the CVD outcomes and together with non-CV death and hip fracture is no effect, is approximately 5%, assuming that these 3 outcomes will exceed 2.42 at any meeting, if in truth there is no effect, is approximately 5%, assuming that these 3 outcomes are independent. The primary safety aims, total clinical fracture, hip fracture, and falls are also monitored, whereas less severe outcomes, including coronary revascularization, falls, and other clinical fractures, are provided regularly but not formally monitored because the clinical implications for these outcomes may or may not be apparent at the time they are observed. For example, increased physical activity in the intervention group may uncover symptoms of angina or claudication, which could lead to revascularization procedures which are intended to reduce the rate of subsequent, more serious events such as MI, and hence do not carry the same adverse safety signal as other events being monitored.

Duration of Follow-up and Statistical Considerations

The WHISH trial was funded for an initial 5 years (2015–2020). Renewal funding will extend the follow-up to approximately 9 years (to September 2024). Power calculations for the renewal of the WHISH trial were based on the observed effects of the WHISH physical activity intervention, the observed event rates for the intervention and comparison arms combined, and the observed relation between physical activity and CVD from the OPACH study. The OPACH study was also carried out in WHI participants and should, thus, give us the best possible effect estimates. As of February 1, 2020, WHISH had 4 years of follow-up, the renewal would extend that follow-up to 8 years. The current difference in MET-hours/week walking, as reported by the complete cohort, is over 8.5%, and has been increasing during the study. The currently observed event rates as a function of age for the primary WHISH outcome (CHD, stroke, CVD death), and the “censoring outcome” (death from other causes) is estimated from the observed data, combining both arms. The observational OPACH study obtained a hazard ratio of 0.79 for the WHISH CVD outcome, for a 1-hour increment of light physical activity which is comparable to nonpurposeful (daily life) walking in the age range of women studied in WHISH. In OPACH, the average light physical activity was 4.76 hours/day, so an 8.5% intervention group difference is equivalent to 0.4 hours/day, corresponding to a 9% decreased rate of the primary CVD outcome. Using the age distribution of WHISH participants and the observed event and censoring rates, we obtain the power estimates shown in Figure 3. We note that with an intervention effect of 9% we have over 90% power, and with an effect of 8% we have close to 85% power after 8 years.

For each of the primary, safety, and secondary outcomes, intervention effect sizes, confidence intervals, and Z-statistics are based on the observed effect size of physical activity. Full color version is available within the online issue.
Table 2. Descriptive Statistics of WHISH Participants—by Trial Arm

| Category                        | All (n = 49331) | Intervention (n = 24657) | Control (n = 24674) | p Value |
|---------------------------------|-----------------|--------------------------|---------------------|---------|
| **Outcome Coverage**            |                 |                          |                     |         |
| WHI-adjudicated only            | 10,554 (21.4)   | 5,306 (21.5)             | 5,248 (21.3)        | .76     |
| CMS only                        | 30,346 (61.5)   | 15,156 (61.5)            | 15,190 (61.6)       |         |
| WHI + CMS                       | 8,431 (17.1)    | 4,195 (17.0)             | 4,236 (17.2)        |         |
| **Age, mean (SD)**              |                 |                          |                     |         |
| <77                             | 16,878 (34.2)   | 8,421 (34.2)             | 8,457 (34.3)        | .45     |
| 77–82                           | 16,220 (32.9)   | 8,122 (32.9)             | 8,098 (32.8)        |         |
| ≥83                             | 16,233 (32.9)   | 8,114 (32.9)             | 8,119 (32.9)        |         |
| **Ethnicity**                   |                 |                          |                     | .93     |
| Non-Hispanic White              | 41,606 (84.3)   | 20,771 (84.2)            | 20,835 (84.4)       |         |
| Non-Hispanic Black/African      | 4,514 (9.2)     | 2,276 (9.2)              | 2,238 (9.1)         |         |
| Hispanic/Latina                 | 1,628 (3.3)     | 819 (3.3)                | 809 (3.3)           |         |
| American Indian/Alaskan          | 151 (0.3)       | 71 (0.3)                 | 80 (0.3)            |         |
| **Current smoker**              |                 |                          |                     | >.99    |
| Yes                             | 12,16 (2.5)     | 607 (2.5)                | 609 (2.5)           |         |
| No                              | 48,103 (97.5)   | 24,044 (97.5)            | 24,059 (97.5)       |         |
| **Use of BP Meds**              |                 |                          |                     | .41     |
| Yes                             | 30,136 (61.1)   | 15,018 (60.9)            | 15,118 (61.3)       |         |
| No                              | 19,195 (38.9)   | 9,639 (39.1)             | 9,556 (38.7)        |         |
| **Use of Lipids Meds**          |                 |                          |                     | .64     |
| Yes                             | 21,801 (44.2)   | 10,871 (44.1)            | 10,930 (44.3)       |         |
| No                              | 27,530 (55.8)   | 13,786 (55.9)            | 13,744 (55.7)       |         |
| **BMI, mean (SD)**              |                 |                          |                     | .67     |
| >30                             | 28,0 (5.8)      | 14,921 (30.2)            | 7,489 (30.4)        |         |
| ≤30                             | 34,383 (69.7)   | 17,210 (69.8)            | 17,173 (69.6)       |         |
| **Physical Functioning Score, mean (SD)** | 71.6 (25.2) | 71.5 (25.2) | 71.6 (25.2) | .76 |
| <65                             | 15,152 (30.7)   | 7,601 (30.8)             | 7,531 (30.6)        |         |
| 65–75                           | 8,283 (16.8)    | 4,119 (16.7)             | 4,164 (16.9)        |         |
| 76–89                           | 8,312 (16.8)    | 4,163 (16.9)             | 4,149 (16.8)        |         |
| ≥90                             | 17,525 (35.5)   | 8,742 (35.5)             | 8,783 (35.6)        |         |
| **Limited ability to go up one flight of stairs** | 35,051 (71.1) | 17,539 (71.1) | 17,512 (71.0) | .83 |
| No, not limited                 | 10,777 (21.8)   | 5,378 (21.8)             | 5,399 (21.9)        |         |
| Yes, limited a little           | 3,497 (7.1)     | 1,736 (7.0)              | 1,761 (7.1)         |         |
| **Limited ability to walk one block** | 38,899 (78.9) | 19,380 (78.6) | 19,519 (79.1) | .58 |
| No, not limited                 | 7,294 (14.8)    | 3,714 (15.1)             | 3,580 (14.5)        |         |
| Yes, limited a little           | 3,130 (6.3)     | 1,559 (6.3)              | 1,571 (6.4)         |         |
| **Episodes of exercise, mean (SD)** | 4.7 (3.9) | 4.7 (3.9) | 4.7 (3.9) | .86 |
| 0–2                             | 15,377 (30.7)   | 7,527 (30.5)             | 7,610 (30.8)        |         |
| ≥2–6                            | 18,920 (38.4)   | 9,511 (38.6)             | 9,409 (38.1)        |         |
| >6                              | 15,274 (31.0)   | 7,619 (30.9)             | 7,655 (31.0)        |         |
| **Self-report treated diabetes ever** | 8,446 (17.1) | 4,205 (17.1) | 4,241 (17.2) | .69 |
| **WHI outcomes**                |                 |                          |                     |         |
| CVD                             | 5,041 (10.2)    | 2,542 (10.3)             | 2,499 (10.1)        | .51     |
| MI                              | 1,799 (3.6)     | 927 (3.8)                | 872 (3.5)           | .18     |
| CABG/PCI                        | 3,030 (6.1)     | 1,537 (6.2)              | 1,493 (6.1)         | .40     |
| Stroke                          | 1,632 (3.3)     | 811 (3.3)                | 821 (3.3)           | .81     |
| **WHI HT Trial Arm**            |                 |                          |                     | .88     |
| Active                          | 573 (11.6)      | 2,868 (11.6)             | 2,868 (11.6)        |         |
| Placebo                         | 5,645 (11.4)    | 2,804 (11.4)             | 2,841 (11.5)        |         |
| **WHI DM Trial Arm**            |                 |                          |                     | .66     |
| Intervention                    | 6,402 (13.0)    | 3,203 (13.0)             | 3,199 (13.0)        |         |
on Cox-proportional hazards models, with the exceptions of falls, which are compared using Poisson regression, and physical function, for which the mean difference between the groups is compared using linear regression. All analyses are stratified by categories applied to the randomization of participants, including age on April 1, 2015 (in tertiles), WHI region, and outcomes data source (MRC vs CMS fee-for-service). Using standard risk sets in survival analysis, participants who change from fee-for-service to managed care will have their self-reports adjudicated after the switch and are moved to the MRC stratum at the time of the switch in insurance coverage. Similarly, outcomes for participants who have 2 types of data, but do not return their self-report Form 33, will be assessed using CMS data after their last returned Form 33.

All analyses will be carried out using an intention-to-treat analysis. Participants randomized to the intervention who “opted out” or requested that the intervention be stopped as the trial progressed will be included in all analyses, as assigned, for monitoring and primary reporting purposes. Deaths that occurred between randomization and the start of intervention are also included in the analyses.

Discussion

The WHISH trial is the first randomized, controlled trial to test whether an intervention designed specifically to increase physical activity and reduce sedentary behavior, independent of diet, weight loss, or other interventions, will reduce major CVD outcomes. As it is specifically testing this hypothesis in older women, additional aims focus on determining whether the intervention benefits physical function and other issues of particular importance to older adults, including maintaining independence and mobility, and its safety with respect to non-CVD mortality and falls and fractures. By recognizing the opportunity to utilize a randomized consent design (9) in the large multiethnic and well-characterized WHI cohort of older women, the WHISH trial meets the challenge posed by NHLBI leadership to design highly efficient pragmatic clinical trials, embedded within ongoing epidemiologic cohort studies, to test hypotheses of major public health significance (40,41). Utilization of materials available through the National Institute of Aging Go4Life program and website (24,25,32) to deliver an intervention based on accepted physical activity recommendations for all older Americans (1,2,42) adds to the efficiency and potential scalability of the WHISH trial program being tested.

The consistent evidence to date that physical activity reduces CVD mortality and incidence, including coronary heart disease and stroke, is based on a large body of observational data studying these endpoints, as well as randomized controlled trials focusing on CV risk factors rather than clinical outcomes (4,5). It is, of course, recognized that physical activity has many health benefits, with sufficient rigorous evidence irrespective of CVD reduction to recommend physical activity as part of a broader public health framework (1,2). However, because CVD deaths in women aged 80 years and older account for two thirds of all CVD deaths in U.S. women, experimental evidence that physical activity reduces CVD in this population would have extraordinary public health significance.

The randomized consent design (9) in the WHISH trial removes a serious bias of the majority of previous physical activity trials which attract and recruit individuals whose willingness to increase activity may be directly related to an inherent physiology that yields greater benefit than what the general population is likely to experience. Many such trials have excluded individuals who are already active but might benefit from even further physical activity change.

Table 2. Continued

| Category | All (n = 49 331) | Intervention (n = 24 657) | Control (n = 24 674) |
|----------|-----------------|--------------------------|---------------------|
|          | n               | %                        | n                   | %                   | n                   | %                   | p Value |
| Comparison |                 |                          |                     |                     |                     |                     | .35     |
| Not randomized | 32 997          | 66.9                     | 16 451              | 66.7                | 16 546              | 67.1                | .09     |
| WHI CaD Trial Arm |                 |                          |                     |                     |                     |                     | .35     |
| Active | 7369            | 14.9                     | 3656                | 14.8                | 3713                | 15.0                |         |
| Placebo | 7079            | 14.4                     | 3623                | 14.7                | 3456                | 14.0                |         |
| Not randomized | 34 883          | 70.7                     | 17 378              | 70.5                | 17 505              | 70.9                |         |
| WHI study component |             |                          |                     |                     |                     |                     |         |
| Clinical Trial | 24 186          | 49.0                     | 12 141              | 49.2                | 12 045              | 48.8                |         |
| Observational study | 25 145          | 51.0                     | 12 516              | 50.8                | 12 629              | 51.2                |         |

Note: BMI = Body mass index; BP = Blood pressure; CABG = Coronary artery bypass graft; CaD = Calcium/Vitamin D Supplementation; CMS = Centers for Medicare and Medicaid Services; CVD = Cardiovascular disease; DM = Dietary modification; HT = Hormone Trial; MRC = Medical records cohort; PCI = Percutaneous coronary intervention; SD = Standard deviation.

‘BMI is based on the most recent WHI clinic visit weight and height, none of which were after 2005.

WHISH Trial Baseline characteristics for women assigned to the Intervention (N = 24 657) versus Control (N = 24 674) were well balanced by randomized intervention group (Table 2). The average age of women was 80 years with 9% Black or African American (n = 4514), 3.3% Hispanic/Latina (n = 1628), 2% Asian (n = 923), and 84% non-Hispanic White. Average body mass index based on the most recent WHI clinic visit (no later than 2005) was 28 kg/m2, with 30% of all WHISH participants in the obese range, ≥30 kg/m2. Use of blood pressure medications at WHI baseline was common (61%), 44% were taking lipid medication, 17% self-reported a history of having diabetes requiring treatment, and 10.2% had history of CVD. At WHISH baseline (2015), about 20% of women reported being limited in walking one block a little or a lot and 10% had a previous history of CVD defined as MI, coronary artery bypass graft/percutaneous coronary intervention, or stroke. Baseline characteristics varied by baseline age tertiles for most variables including race/ethnic distribution (Table 3).
Table 3. Descriptive Statistics of WHISH Participants—by Baseline Age Tertiles

| Category                                      | <77 (n = 16 878) |         | 77–82 (n = 16 220) |         | ≥83 (n = 16 233) |         |
|-----------------------------------------------|------------------|---------|-------------------|---------|-----------------|---------|
| **Outcome coverage**                          |                  |         |                   |         |                 |         |
| WHI-adjudicated only                          | 3849             | 22.8    | 3493              | 21.5    | 3212            | 19.8    |
| CMS only                                      | 10 094           | 59.8    | 9980              | 61.5    | 10 272          | 63.3    |
| WHI + CMS                                     | 2935             | 17.4    | 2747              | 16.9    | 2749            | 16.9    |
| Age, mean (SD)                                | 73.1 (2.2)       |         | 79.4 (1.7)        |         | 87.0 (3.2)      |         |
| **Ethnicity**                                 |                  |         |                   |         |                 |         |
| Non-Hispanic White                            | 13 544           | 80.2    | 13 735            | 84.7    | 14 327          | 88.3    |
| Non-Hispanic Black/African American           | 1946             | 11.5    | 1493              | 9.2     | 1075            | 6.6     |
| Hispanic/Latina                               | 771              | 4.6     | 502               | 3.1     | 355             | 2.2     |
| American Indian/Alaskan Native                | 73               | 0.4     | 45                | 0.3     | 33              | 0.2     |
| Asian/Pacific Islander                        | 375              | 2.2     | 277               | 1.7     | 271             | 1.7     |
| **Current smoker**                            |                  |         |                   |         |                 |         |
| Yes                                           | 603              | 3.6     | 385               | 2.4     | 228             | 1.4     |
| No                                            | 16 268           | 96.4    | 15 831            | 97.6    | 16 004          | 98.6    |
| **Use of BP Meds**                            |                  |         |                   |         |                 |         |
| Yes                                           | 8770             | 52.0    | 9989              | 61.6    | 11 377          | 70.1    |
| No                                            | 8108             | 48.0    | 6231              | 38.4    | 4856            | 29.9    |
| **Use of Lipids Meds**                        |                  |         |                   |         |                 |         |
| Yes                                           | 6841             | 40.5    | 7464              | 46.0    | 7496            | 46.2    |
| No                                            | 10 037           | 59.5    | 8756              | 54.0    | 8737            | 53.8    |
| BMI, mean (SD)†                                | 28.4             | (6.3)   | 28.2              | (5.8)   | 27.4            | (5.2)   |
| >30                                           | 5561             | 32.9    | 5077              | 31.3    | 4283            | 26.4    |
| ≤30                                           | 11 305           | 67.0    | 11 135            | 68.6    | 11 943          | 73.6    |
| **Physical Functioning Score, mean (SD)**     | 79.3             | (21.8)  | 72.3              | (24.1)  | 62.7            | (26.6)  |
| <65                                           | 3241             | 19.2    | 4720              | 29.1    | 7191            | 44.3    |
| 65–75                                         | 2382             | 14.1    | 2894              | 17.8    | 3007            | 18.5    |
| 76–89                                         | 2921             | 17.3    | 2929              | 18.1    | 2462            | 15.2    |
| ≥90                                           | 8328             | 49.3    | 5657              | 34.9    | 3540            | 21.8    |
| **Limited ability to go up one flight of stairs** |              |         |                   |         |                 |         |
| No, not limited                               | 13 609           | 80.6    | 11 762            | 72.5    | 9680            | 59.6    |
| Yes, limited a little                         | 2650             | 15.7    | 3507              | 21.6    | 4620            | 28.5    |
| Yes, limited a lot                            | 619              | 3.7     | 948               | 5.8     | 1930            | 11.9    |
| **Limited ability to walk one block**         |                  |         |                   |         |                 |         |
| No, not limited                               | 14 854           | 88.0    | 12 991            | 80.1    | 11 054          | 68.1    |
| Yes, limited a little                         | 1482             | 8.8     | 2330              | 14.4    | 3482            | 21.5    |
| Yes, limited a lot                            | 542              | 3.2     | 897               | 5.5     | 1691            | 10.4    |
| **Episodes of exercise, mean (SD)**           |                  |         |                   |         |                 |         |
| 0–2                                          | 4381             | 26.0    | 4809              | 29.6    | 5947            | 36.6    |
| >2–6                                         | 6419             | 38.0    | 6331              | 39.0    | 6170            | 38.0    |
| >6                                           | 6078             | 36.0    | 5080              | 31.3    | 4116            | 25.4    |
| **Self-report treated diabetes ever**         |                  |         |                   |         |                 |         |
| WHI outcomes                                  |                  |         |                   |         |                 |         |
| CVD                                           | 1005             | 6.0     | 1638              | 10.1    | 2398            | 14.8    |
| MI                                            | 341              | 2.0     | 578               | 3.6     | 880             | 5.4     |
| CABG/PCI                                      | 620              | 3.7     | 1001              | 6.2     | 1409            | 8.7     |
| Stroke                                        | 301              | 1.8     | 518               | 3.2     | 813             | 5.0     |
| WHI HT Trial Arm                              |                  |         |                   |         |                 |         |
| Active                                        | 1841             | 10.9    | 1881              | 11.6    | 2014            | 12.4    |
| Placebo                                       | 1743             | 10.3    | 1863              | 11.5    | 2039            | 12.6    |
| Not randomized                                | 13 294           | 78.8    | 12 476            | 76.9    | 12 180          | 75.0    |
| WHI DM Trial Arm                              |                  |         |                   |         |                 |         |
| Intervention                                  | 2221             | 13.2    | 2252              | 13.9    | 1929            | 11.9    |
| Comparison                                    | 3507             | 20.8    | 3508              | 21.6    | 2917            | 18.0    |
| Not randomized                                | 11 150           | 66.1    | 10 460            | 64.5    | 11 387          | 70.1    |
| WHI CaD Trial Arm                             |                  |         |                   |         |                 |         |
| Active                                        | 2572             | 15.2    | 2514              | 15.5    | 2283            | 14.1    |
| Placebo                                       | 2439             | 14.5    | 2436              | 15.0    | 2204            | 13.6    |
| Not randomized                                | 11 867           | 70.3    | 11 270            | 69.5    | 11 746          | 72.4    |
Table 3. Continued

| Category                  | <77 (n = 16878) | 77–82 (n = 16220) | ≥83 (n = 16233) |
|---------------------------|-----------------|-------------------|-----------------|
| WHI study component       |                 |                   |                 |
| Clinical trial            | 8096            | 48.0              | 8297            | 51.2           | 7793          | 48.0           |
| Observational study       | 8782            | 52.0              | 7923            | 48.8           | 8440          | 52.0           |

Note: BMI = Body mass index; BP = Blood pressure; CABG = Coronary artery bypass graft; CaD = Calcium/Vitamin D Supplementation; CMS = Centers for Medicare and Medicaid Services; CVD = Cardiovascular disease; DM = Dietary modification; HT = Hormone trial; MRC = Medical records cohort; PCI = Percutaneous coronary intervention; SD = Standard deviation.

*BMI is based on the most recent WHI clinic visit weight and height, none of which were after 2005.

or reduction in time spent sedentary. While some portion of WHI-ES participants were initially attracted to the WHI hormone therapy or diet modification trials, and were likely more health-oriented than the general population of women their ages, use of the randomized consent design basically ensures that none of the WHISH participants joined because of their physical activity habits. Another novel design element that increased the efficiency of this pragmatic trial was the “opt out,” passive consent process which resulted in >96% of women randomly assigned to the intervention receiving the intervention.

The WHISH Trial accelerometry substudy took advantage of the fact that a large number of WHISH participants had participated in the OPACH study and had a first accelerometer wear in 2012–2014 before WHISH randomization. This is another example of a highly efficient study design leading to a truly rare sequence of 4 longitudinal accelerometer measures to evaluate trajectories of physical activity over time by WHISH randomization group.

In conclusion, the pragmatic WHISH trial is an innovative physical activity trial with the potential to provide strong evidence of the power of physical activity as a sole modality to reduce CVD in older adults. If this easily scalable intervention proves to be safe and effective in improving cardiovascular health and other outcomes of importance to older women, the WHISH physical activity intervention can be widely disseminated, as well as adapted to meet the needs of many additional segments of the U.S. population.

Supplementary Material
Supplementary data are available at The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences online.

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Conflict of Interest
None declared.

References
1. U.S. Department of Health and Human Services. 2008 Physical Activity Guidelines for Americans. Washington, DC: U.S. Department of Health and Human Services; 2008.
2. U.S. Department of Health and Human Services. 2018 Physical Activity Guidelines for Americans, 2nd ed. Washington, DC: U.S. Department of Health and Human Services; 2018.
3. Vespa J, Armstrong DM, Medina L. Demographic Turning Points for the United States: Population Projections for 2020 to 2060. Current Population Reports. Washington, DC: U.S. Census Bureau; 2018.
4. Physical Activity Guidelines Advisory Committee. Physical Activity Guidelines Advisory Committee Report, 2008. Washington, DC: U.S. Department of Health and Human Services; 2008.
5. Physical Activity Guidelines Advisory Committee. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. Washington, DC: U.S. Department of Health and Human Services; 2018.
6. King AC. Interventions to promote physical activity by older adults. J Gerontol A Biol Sci Med Sci. 2001;56 Spec No 2:36–46. doi:10.1093/gerona/56.suppl_2.36
7. King AC, Rejeski WJ, Buchner DM. Physical activity interventions targeting older adults. A critical review and recommendations. Am J Prev Med. 1998;15:316–333. doi:10.1016/s0749-3797(98)00085-3
8. Pahor M, Guralnik JM, Ambrosius WT, et al. Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial. JAMA. 2014;311:2387–2396. doi:10.1001/jama.2014.5616
9. Zelen M. A new design for randomized clinical trials. N Engl J Med. 1979;300:1242–5. doi:10.1056/NEJM197905313002203
10. Design of the Women’s Health Initiative clinical trial and observational study. The Women’s Health Initiative Study Group. Control Clin Trials. 1998;19:61–109. doi:10.1016/s0197-2456(97)00078-0
11. Anderson GL, Limacher M, Assaf AR, et al. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: The Women’s Health Initiative randomized controlled trial. JAMA. 2004;291:1701–1712. doi:10.1001/jama.291.14.1701
12. Beresford SA, Johnson KC, Ritenbaugh C, et al. Low-fat dietary pattern and risk of colorectal cancer: the women’s health initiative randomized controlled dietary modification trial. JAMA. 2006;295:643–654. doi:10.1001/jama.295.6.643
13. Chlebowski RT, Aragaki AK, Anderson GL, et al. Low-fat dietary pattern and breast cancer mortality in the women’s health initiative randomized controlled trial. J Clin Oncol. 2017;35:2919–2926. doi:10.1200/JCO.2016.72.0326
14. Jackson RD, LaCroix AZ, Gass M, et al. Calcium plus vitamin D supplementation and the risk of fractures. N Engl J Med. 2006;354:669–683. doi:10.1056/NEJMoa055218
15. Manson JE, Aragaki AK, Rossouw JE, et al. Menopausal hormone therapy and long-term all-cause and cause-specific mortality: the women’s health initiative randomized trials. JAMA. 2017;318:927–938. doi:10.1001/jama.2017.11217
16. Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal hormone therapy and health outcomes during the intervention and extended...
poststopping phases of the Women's Health Initiative randomized trials. JAMA. 2013;310:1353–1368. doi:10.1001/jama.2013.278040
17. Prentice RL, Caan B, Chlebowski RT, et al. Low-fat dietary pattern and risk of invasive breast cancer: the women's health initiative randomized controlled dietary modification trial. JAMA. 2006;295:629–642. doi:10.1001/jama.295.6.629
18. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women’s Health Initiative randomized controlled trial. JAMA. 2002;288:321–333. doi:10.1001/jama.288.3.321
19. Hlatky MA, Ray RM, Burwen DR, et al. Use of Medicare data to identify coronary heart disease outcomes in the Women’s Health Initiative. Circ Cardiovasc Qual Outcomes 2014;7:157–62. doi:10.1161/CIRCOUTCOMES.113.00373
20. Lakshminarayanan K, Larson JC, Virnig B, et al. Comparison of Medicare claims versus physician adjudication for identifying stroke outcomes in the Women’s Health Initiative. Stroke 2014;45:815–21. doi:10.1161/STROKEAHA.113.003408
21. Burwen DR, Wu C, Cirillo D, et al. Venous thromboembolism incidence, recurrence, and mortality based on Women’s Health Initiative data and Medicare claims. Thromb Res. 2017;150:78–85. doi:10.1016/j.thromres.2016.11.015
22. Mell MW, Pettinger M, Proulx-Burns L, et al. Evaluation of Medicare claims data to ascertain peripheral vascular events in the Women’s Health Initiative. J Vasc Surg 2014;60:98–105. doi:10.1016/j.jvs.2014.01.056
23. ClinicalTrials.gov. Women’s Health Initiative Strong and Healthy Study (WHISH). Identifier: NCT02425345. https://clinicaltrials.gov/ct2/show/NCT02425345.
24. NIA. Go4Life® Exercise & Physical Activity: Your Everyday Guide. https://order.nia.nih.gov/sites/default/files/2018-04/nia-exercise-guide.pdf.
25. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-item health survey 1.0. Health Econ. 1993;2:217–227. doi:10.1002/hec.4730020305
26. Bandura A. Social cognitive theory: an agentic perspective. *Annu Rev Psychol*. 2001;52:1–26. doi:10.1146/annurev.psych.52.1.1
27. Marshall SJ, Biddle SJ. The transtheoretical model of behavior change: a meta-analysis of applications to physical activity and exercise. *Ann Behav Med*. 2001;23:229–246. doi:10.1207/s15324796abm2304_2
28. Prochaska JO, Velicer WF, Rossi JS, et al. Stages of change and decisional balance for 12 problem behaviors. *Health Psychol* 1994;13:39–46. doi:10.1037/0278-6133.13.1.39
29. King AC, Hekler EB, Greco LA, et al. Harnessing different motivational frames via mobile phones to promote daily physical activity and reduce sedentary behavior in aging adults. *PLoS One*. 2013;8:e62613. doi:10.1371/journal.pone.0062613
30. King AC, Hekler EB, Greco LA, et al. Effects of three motivationally targeted mobile device applications on initial physical activity and sedentary behavior change in midlife and older adults: a randomized trial. *PLoS One*. 2016;11:e0156370. doi:10.1371/journal.pone.0156370
31. Ryan RM, Deci EL. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. *Am Psychol*. 2000;55:68–78. doi:10.1037/0003-066x.55.1.68
32. NIA. Go4Life® Exercise & Physical Activity: Your Everyday Guide. https://order.nia.nih.gov/sites/default/files/2018-04/nia-exercise-guide.pdf.
33. Stewart AL, Mills KM, King AC, Haskell WL, Gillis D, Ritter PL. CHAMPS physical activity questionnaire for older adults: outcomes for interventions. *Med Sci Sports Exerc*. 2004;36:1152–1158. doi:10.1093/mss/ehn114
34. Lauer MS, Gordon D, Wei G, Pearson G. Efficient design of clinical trials and epidemiological research: is it possible? *Nat Rev Cardiol*. 2017;14:493–501. doi:10.1038/nrcardio.2017.60
35. Heckbert SR, Kooperberg C, Safford MM, et al. Comparison of self-report, hospital discharge codes, and adjudication of cardiovascular events in the Women’s Health Initiative. *Am J Epidemiol*. 2004;160:1152–1158. doi:10.1093/aje/kwh314
36. Rossouw JE, Anderson GL, Prentice RL, et al. Low-fat dietary pattern and risk of invasive breast cancer: principal results from the Women’s Health Initiative randomized controlled trial. JAMA. 2006;295:629–642. doi:10.1001/jama.295.6.629
37. LaCroix AZ, Rillamas-Sun E, Buchner D, et al. The Objective go4life.nia.nih.gov/. 2021, Vol. 76, No. 4
38. Stewart AL, Mills KM, King AC, Haskell WL, Gillis D, Ritter PL. CHAMPS physical activity questionnaire for older adults: outcomes for interventions. *Med Sci Sports Exerc*. 2004;36:1152–1158. doi:10.1093/mss/ehn114
39. Ryan RM, Deci EL. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. *Am Psychol*. 2000;55:68–78. doi:10.1037/0003-066x.55.1.68
40. Goff DC, Buxton DB, Pearson GD, et al. Implementing the national heart, lung, and blood institute’s strategic vision in the division of cardiovascular sciences. *Circulation Research*. 2019;124:491–497. doi:10.1161/CIRCRESAHA.118.314338
41. King AC, Whitt-Glover MC, Marquez DX, et al. Physical activity promotion: highlights from the 2018 physical activity guidelines advisory committee systematic review. *Med Sci Sports Exerc*. 2019;51:1340–1353. doi:10.1249/MSS.0000000000001945
42. LaCroix AZ, Rillamas-Sun E, Buchner D, et al. The Objective go4life.nia.nih.gov/.
Form 33 - Medical History Update

Please use a pencil or black pen only to complete this form.

This form asks about any health problems and health care since: ___ / ___ / _____

Do not report events that happened before the date above. However, if you are not sure of a date and don’t think that you have reported it to us before, please answer the questions.

1. What is today’s date? Write date here: ___ / ___ / ___
   Month    Day    Year

Mark the month, day and year below. Mark only one bubble per line.

Month
1 2 3 4 5 6 7 8 9 10 11 12
Day
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
Year
20 21 22 23 24 25

2. Who is completing this form?
   ○ Self (WHI Study participant)
   ○ Other, on behalf of the WHI participant
   Name and relationship to participant: ________________________________

3. Best phone number to reach the person completing this form: (____) _______ _______
4. Since the date on the front of this form, have you had any of the following exams, tests, or procedures done by a doctor or other health care provider? Mark all that apply.

- [ ] Breast exam
- [ ] Mammogram
- [ ] Test of breast tissue or fluid for disease (breast biopsy or aspiration)
- [ ] Other breast examination tests such as MRI or ultrasound
- [ ] Test for the presence of blood in your stool or bowel movement (Hemoccult®, guaiac, Cologuard®)
- [ ] Tube inserted into your bowel to check for bowel problems (sigmoidoscopy or colonoscopy)
- [ ] Hysterectomy (surgery to remove the uterus or womb)
- [ ] Biopsy of the endometrium (lining of the uterus or womb)
- [ ] None of the above apply

5. Since the date on the front of this form, has a doctor or other health care provider told you that you have any of the following conditions? Mark all that apply.

- [ ] Chronic obstructive pulmonary disease (COPD), emphysema, or chronic bronchitis
- [ ] Angina or chest pain from a heart condition for which you were hospitalized for one night or more (not a heart attack)
- [ ] Transient ischemic attack (not a stroke)
- [ ] Osteoarthritis or arthritis associated with aging
- [ ] Macular degeneration associated with aging
- [ ] Moderate or severe memory problems
- [ ] Dementia or Alzheimer’s
- [ ] Parkinson’s disease
- [ ] Intestine or colon polyps or adenomas
- [ ] None of the above apply

6. Since the date on the front of this form, has a doctor or other health care provider prescribed any of the following treatments for diabetes? Mark all that apply.

- [ ] Insulin
- [ ] Pills or medications other than insulin
- [ ] Diet and/or physical activity
- [ ] None of the above apply (I do not have or no longer have diabetes.)
7. **Since the date on the front of this form**, has a doctor or other health care provider prescribed for the first time pills for high blood pressure or hypertension?
   - [ ] Yes
   - [ ] No

8. **Since the date on the front of this form**, how many times did you fall and land on the floor or ground? Do not include falls due to sports. **Mark only one.**
   - [ ] None
   - [ ] One time
   - [ ] Two times
   - [ ] Three or more times

   **8.1 Were you injured as a result of any falls?**
   - [ ] Yes
   - [ ] No

Since the date on the front of this form, have you been diagnosed or treated for any of the following conditions or procedures? **Mark Yes or No for each item.**

|   | Yes | No |
|---|-----|----|
| 9. Stroke | [ ] | [ ] |
| 10. MI, heart attack (coronary, myocardial infarction) | [ ] | [ ] |
| 11. Heart failure (congestive heart failure, CHF or HF) | [ ] | [ ] |
| 12. Heart bypass operation (coronary bypass surgery or CABG) | [ ] | [ ] |
| 13. Heart valve problem or surgery to repair or replace a heart valve | [ ] | [ ] |
| 14. Abdominal aortic aneurysm (AAA) requiring surgery or stent | [ ] | [ ] |
| 15. Procedure or surgery to unblock narrowed blood vessels in your neck (carotid endarterectomy, carotid angioplasty, or carotid stent) | [ ] | [ ] |
| 16. Poor blood circulation or any procedure to unblock narrowed arteries to your legs or feet (claudication, peripheral arterial disease, PAD, or gangrene). Do not include varicose veins. | [ ] | [ ] |
| 17. Blood clots in your lungs (pulmonary embolism or PE) | [ ] | [ ] |
| 18. Blood clots in the veins of your legs (deep vein thrombosis or DVT) | [ ] | [ ] |
| 19. Atrial fibrillation, atrial flutter, or irregular heartbeat, requiring medications OR a procedure (such as electrical shock, cardioversion, ablation, or surgery) | [ ] | [ ] |
| 20. Procedure to unblock narrowed blood vessels to your heart (opening the arteries of the heart with a stent, balloon, laser, or other device). Also called PTCA, angioplasty, or percutaneous coronary intervention (PCI). | [ ] | [ ] |
| 21. Other heart or circulation conditions. Specify: __________________________ | [ ] | [ ] |
If you marked Yes to any of the heart or circulation items in questions 9-21, complete the health care provider information below. If not, go to Question 28 on the next page.

22. **1st hospital or doctor’s office** where you were diagnosed, treated, or admitted.
   Facility name: ____________________________________________
   _________________________________________________________
   Street                                           City                                           State

23. Date you were diagnosed, treated, or admitted to a hospital: ___ ___-___ ___-___ ___
    (Estimate if unsure.)
    Month       Day       Year

   23.1 For what condition: ____________________________________________

24. Were you hospitalized?   ○ Yes    ○ No   → **Go to Question 25.**

   24.1 How many nights?    ___ ___ Nights (write “0” if no nights)

25. **2nd hospital or doctor’s office** where you were diagnosed, treated, or admitted.
   Facility name: ____________________________________________
   _________________________________________________________
   Street                                           City                                           State

26. Date you were diagnosed, treated, or admitted to a hospital: ___ ___-___ ___-___ ___
    (Estimate if unsure.)
    Month       Day       Year

   26.1 For what condition: ____________________________________________

27. Were you hospitalized?   ○ Yes    ○ No   → **Go to Question 28 on next page.**

   27.1 How many nights?    ___ ___ Nights (write “0” if no nights)

Record any additional provider information in the Comments section at the end of this form, then continue to the next page.
28. Since the date on the front of this form, has a doctor or other health care provider told you that you have a new cancer, malignant growth, or tumor? Do not include benign tumors.

☐Yes ☐No → Go to Question 29 on page 7.

28.1 What type of new cancer? Mark all that apply.

☐Breast ☐Ovary ☐Kidney

☐Endometrium (lining of the uterus or womb) ☐Liver ☐Leukemia

☐Cervix ☐Lung ☐Melanoma

☐Other female genital organs (not ovary, endometrium, or cervix) ☐Multiple myeloma ☐Pancreas

☐Colon or rectum ☐Skin cancer (not melanoma) ☐Stomach

☐Bladder or urinary tract ☐Thyroid ☐Other or unknown cancer

Specify: __________________________

_______________________________

Complete the diagnosis information for the first new cancer.

28.2 When was this cancer diagnosed (estimate if unsure)? _________-_______-_______

Month Day Year

28.3 Who was the doctor or other health care provider who diagnosed this cancer and at what facility was this cancer first diagnosed?

Doctor or provider name: ______________________________________________________

Facility name: ________________________________________________________________

________________________________________

Street City State

28.4 What is the name of your oncologist? ________________________________________
28.5 Was an outpatient X-ray or imaging scan (CT, MRI, mammogram, bone or PET scan) taken to diagnose the cancer?

- Yes  - No → Go to Question 28.8.

28.6 Facility name:

| Street | City | State |
|--------|------|-------|

28.7 Date of X-ray or scan (estimate if unsure):

- Month  - Day  - Year

---

Cancer-related surgeries for the first new cancer:

28.8 Since the date on the front of this form, have you had any cancer-related surgeries following the diagnosis of the first cancer?

- Yes  - No → 28.9 If No, are any planned?

- Yes  → Go to Question 29 on the next page.

- No

---

Since the date on the front of this form:

28.10 Number of cancer-related surgeries you had:  ____  

28.11 At what facility was this first cancer-related surgery done?

Facility name:

| Street | City | State |
|--------|------|-------|

28.12 Date of first cancer-related surgery (estimate if unsure):

- Month  - Day  - Year

---

Record any additional provider information in the Comments section at the end of this form, then continue to the next page.
29. Since the date on the front of this form, has a doctor or other health care provider told you that you have a new broken, fractured, or crushed hip or upper leg bone?
   ○ 1 Yes  ○ 0 No —> Go to Question 30 on the next page.

29.1 Which bone(s) did you break, fracture, or crush? Mark all that apply.
   ○ 1 Hip
   ○ 2 Upper leg (not hip)

29.2 Was this broken, fractured, or crushed hip or upper leg bone first diagnosed or treated during a hospital stay?
   ○ 1 Yes  ○ 0 No —> Go to Question 29.6.

29.3 In what hospital or medical facility were you diagnosed or treated for the broken, fractured, or crushed hip or upper leg bone?

   Facility name: ________________________________

   Street
   City
   State

29.4 Date you entered the hospital (estimate if unsure): __ __ - __ __ - __ __

29.5 Did you stay overnight? ○ 1 Yes  ○ 0 No

29.6 Was an outpatient X-ray or imaging scan (CT or MRI) taken to diagnose the broken, fractured, or crushed hip or upper leg bone at a facility not reported above?
   ○ 1 Yes  ○ 0 No —> Go to Question 30 on the next page.

29.7 In what hospital or medical facility were you diagnosed or treated for the broken, fractured, or crushed hip or upper leg bone?

   Facility name: ________________________________

   Street
   City
   State

29.8 Date of X-ray or other imaging scan (CT or MRI) (estimate if unsure): __ __ - __ __ - __ __
30. Since the date on the front of this form, has a doctor or other health care provider told you that you have a **new** broken, fractured, or crushed bone **other than** hip or upper leg?  
1. Yes  
2. No  

30.1 Which bone(s) did you break, fracture, or crush? **Mark all that apply.**  
1. Pelvis  
2. Knee (patella)  
3. Lower leg or ankle  
4. Foot (not toe)  
5. Tailbone (coccyx)  
6. Spine or back (vertebra)  
7. Upper arm or shoulder  
8. Elbow  
9. Lower arm or wrist  
10. Hand (not finger)  
11. Finger or toe  
12. Jaw, nose, face, and/or skull  
13. Ribs and/or chest or breast bone  
88. Another fracture not listed  
Specify: ____________________________  

---

**Final Instructions**  
Please take a moment to review any questions you may have missed. Feel free to write any comments in the Comments section below.  
You may receive a follow-up call to clarify your answers on this form.  
Please sign the enclosed Medical Record Release form and return both forms in the postage paid envelope.  

---

**Comments**  
Please report comments/additional provider information below. Provider information includes: Hospital/physician name, city and state, date of admission, length of stay, and reason for stay.  

__________________________________________________________________________  
__________________________________________________________________________  
__________________________________________________________________________  
__________________________________________________________________________  
__________________________________________________________________________  
__________________________________________________________________________  

---

**Thank you for completing this form!**  
PLEASE DO NOT WRITE IN THIS AREA
Form 151– Activities of Daily Life

This form has questions about your current experiences. Please answer the questions as honestly as you can, using your first thoughts about each question. You should not go back later to “figure out” answers. Please answer the questions on both sides. Your answers will be kept confidential and will never be put with your name in a published report, but they will help us to understand the health of women like you. Thank you for your help.

1. In general, would you say your health is: (Mark one circle only.)

   Excellent  Very good  Good  Fair  Poor
   1          2          3          4          5

2. Overall, how would you rate your quality of life? (Mark one circle below.)

   0  1  2  3  4  5  6  7  8  9  10
   Worst  Halfway  Best
   As bad or worse than being dead  Best quality of life

3. Does the place (home, apartment, assisted living facility) where you live have special services for older people (such as help with transportation, meals, medicines, or bathing)?

   O  No  O  Yes

   3.1. Are you currently receiving any of these services?

   O  No  O  Yes

4. In the past year, have you stayed in a nursing home?

   O  No  O  Yes

5. What aid, if any, do you usually use to walk on a level surface? (Mark one.)

   I do not use any aid  I use a cane  I use crutches  I use a walker  I use a wheelchair
   1          2          3          4          5

---

Public reporting burden for this collection of information is estimated to average 6 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to: NIH, Project Clearance Branch, 6705 Rockledge Drive, MSC 7974, Bethesda, MD 20892-7974, ATTN: PRA (0925-0414). Do not return the completed form to this address.
6. Are you taking a calcium supplement such as Oscal, Viactiv, or Tums?
   - [ ] No
   - [ ] Yes

The following are questions about a typical (or usual) day’s activities. Does your health now limit you in these activities and, if so, how much? (Mark one circle for each question.)

|   | No, not limited at all | Yes, limited a little | Yes, limited a lot |
|---|------------------------|-----------------------|-------------------|
| 7. Vigorous activities, such as running, lifting heavy objects, or strenuous sports | [ ] 3 | [ ] 2 | [ ] 1 |
| 8. Moderate activities, such as moving a table, vacuuming, bowling, or golfing | [ ] 3 | [ ] 2 | [ ] 1 |
| 9. Lifting or carrying groceries | [ ] 3 | [ ] 2 | [ ] 1 |
| 10. Climbing several flights of stairs | [ ] 3 | [ ] 2 | [ ] 1 |
| 11. Climbing one flight of stairs | [ ] 3 | [ ] 2 | [ ] 1 |
| 12. Bending, kneeling, stooping | [ ] 3 | [ ] 2 | [ ] 1 |
| 13. Walking more than a mile | [ ] 3 | [ ] 2 | [ ] 1 |
| 14. Walking several blocks | [ ] 3 | [ ] 2 | [ ] 1 |
| 15. Walking one block | [ ] 3 | [ ] 2 | [ ] 1 |
| 16. Bathing or dressing yourself | [ ] 3 | [ ] 2 | [ ] 1 |

These next questions ask about how much help (if any) you need to do routine activities for yourself. Help can be defined as getting assistance from another person or using a device. (Mark one circle for each question.)

|   | I can do this activity: By myself without help | With some help | Completely unable to do this by myself |
|---|-----------------------------------------------|----------------|-------------------------------------|
| 17. Can you feed yourself? | [ ] 1 | [ ] 2 | [ ] 3 |
| 18. Can you dress and undress yourself? | [ ] 1 | [ ] 2 | [ ] 3 |
| 19. Can you get in and out of bed yourself? | [ ] 1 | [ ] 2 | [ ] 3 |
| 20. Can you take a bath or shower? | [ ] 1 | [ ] 2 | [ ] 3 |
| 21. Can you do your own grocery shopping? | [ ] 1 | [ ] 2 | [ ] 3 |
| 22. Can you keep track of and take your medicines? | [ ] 1 | [ ] 2 | [ ] 3 |
These questions ask about physical activity and other habits that may affect your health. Please answer each question as accurately as possible. There are no right or wrong answers.

The first question is about your walking.

1. Think about the walking you do outside the home. How often do you walk outside the home for more than 10 minutes without stopping? Mark only one.

[Options: Rarely or never, 1 to 3 times each month, 1 time each week, 2 to 3 times each week, 4 to 6 times each week, 7 or more times each week]

Go to the next page.

When you walk outside the home for more than 10 minutes without stopping,

1.1 For how many minutes do you usually walk?

[Options: Less than 20 minutes, 20 to 39 minutes, 40 to 59 minutes, 1 hour or more]

1.2 What is your usual speed?

[Options: Casual strolling or walking (less than 2 miles an hour), Average or normal (2-3 miles an hour), Fairly fast (3-4 miles an hour), Very fast (more than 4 miles an hour), Don't know]
2. When you exercise or walk in your usual fashion how would you rate your level of exertion (degree of effort)? **Mark only one.**

| Nothing at all | Very, very weak (just noticeable) | Very weak | Weak | Moderate | Somewhat strong | Strong | Very strong | Very, very strong (almost maximal) | Maximal |
|----------------|----------------------------------|-----------|------|----------|----------------|--------|-------------|----------------------------------|---------|
| O 0            | O 1                              | O 2       | O 3  | O 4      | O 5            | O 6    | O 7         | O 8                              | O 9     |

3. Are you able to walk at a normal pace for a half hour (30 minutes) or more?

O 0 No  O 1 Yes

4. Are you able to walk slowly for a half hour (30 minutes) or more?

O 0 No  O 1 Yes

5. During a usual **day and night**, about how many hours do you spend sitting? Be sure to include the time you spend sitting at work, sitting at the table eating, driving or riding in a car or bus, and sitting up watching TV or talking.

| Less than 4 hours | 4-5 hours | 6-7 hours | 8-9 hours | 10-11 hours | 12-13 hours | 14-15 hours | 16 or more hours |
|-------------------|-----------|-----------|-----------|-------------|-------------|-------------|-----------------|
| O 1               | O 2       | O 3       | O 4       | O 5         | O 6         | O 7         | O 8             |

6. During a usual **day and night**, about how many hours do you spend sleeping or lying down with your feet up? Be sure to include the time you spend sleeping or trying to sleep at night, resting or napping, and lying down watching TV.

| Less than 4 hours | 4-5 hours | 6-7 hours | 8-9 hours | 10-11 hours | 12-13 hours | 14-15 hours | 16 or more hours |
|-------------------|-----------|-----------|-----------|-------------|-------------|-------------|-----------------|
| O 1               | O 2       | O 3       | O 4       | O 5         | O 6         | O 7         | O 8             |
7. On a typical **DAY**, how much time do you spend (from when you wake up until you go to bed) doing the following? **Mark only one answer per question.**

|   | None | 15 min. or less | 30 min. | 1 hour | 2 hours | 3 hours | 4 hours | 5 hours | 6 hours or more |
|---|------|----------------|---------|--------|---------|---------|---------|---------|----------------|
| 7.1 Sitting while watching television (including videos on VCR/DVD). | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 10 | 11 |
| 7.2 Sitting while using the computer for non-work activities or playing video games. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 10 | 11 |
| 7.3 Sitting while doing non-computer office work or paperwork not related to your job (paying bills, etc.). | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 10 | 11 |
| 7.4 Sitting listening to music, reading a book or magazine, or doing arts and crafts. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 10 | 11 |
| 7.5 Sitting and talking on the phone or texting. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 10 | 11 |
| 7.6 Sitting in a car, bus, train, or other mode of transportation. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 10 | 11 |
8. If you fell when you are away from your home, how confident are you that someone would be able to quickly help you?

- 1 Not at all confident
- 2 Somewhat confident
- 3 Very confident
- 0 Don’t know/not sure

9. Have you had a fall in the past 12 months? By a "fall", we mean
   • Fell all the way to the floor or the ground, or
   • Fell and hit an object like a chair or stair

- 0 No — Go to page 6.
- 1 Yes

10. How many times have you fallen in the past 12 months? (If you are unsure, make your best guess.)

- 1 One time
- 2 Two or three times
- 3 Four or five times
- 4 Six or more times
11. At the time of your most recent fall, were you:

| Question                                                                 | No | Yes |
|--------------------------------------------------------------------------|----|-----|
| 11.1 Walking outside the home?                                           |    |     |
| 11.2 Doing strenuous exercise (but not walking outside the home)?        |    |     |
| Strenuous means you work up a sweat and would be exhausted by prolonged participation. For example, aerobics, aerobic dancing, jogging, tennis, swimming laps. |    |     |
| 11.3 Doing moderate exercise (but not walking outside the home)?         |    |     |
| Moderate means exercise that is not exhausting. For example, biking outdoors, using an exercise machine (like a stationary bike or treadmill), calisthenics, easy swimming, popular and folk dancing. |    |     |
| 11.4 Doing mild exercise? For example, slow dancing, bowling, or golf.   |    |     |
| 11.5 Doing other exercise (not previously listed)?                       |    |     |
| 11.6 Doing strenuous indoor household chores (such as scrubbing floors, sweeping, or vacuuming)? |    |     |
| 11.7 Working in the yard (such as mowing, raking, gardening, or shoveling snow)? |    |     |

12. Were you injured as a result of any fall in the past 12 months?

- **0** No
- **1** Yes

12.1 Please indicate what types of injuries. Mark all that apply.

| Injury Type                                                                 |   |
|---------------------------------------------------------------------------|---|
| Fracture                                                                  | 1 |
| Laceration/cut                                                            | 2 |
| Bruising                                                                  | 3 |
| Sprained or strained joint (wrist, knee, ankle, etc.)                     | 4 |
| Other injury (Please specify:___________________________________________)| 5 |

12.2 Did you injure your head?

- **0** No
- **1** Yes

Go to the next page.
Form 521 - Physical Activity Questionnaire

This set of questions is to help us understand the full range of activities you are doing. These questions are about activities that you may have done in the past 4 weeks. The questions on the following pages are similar to the example shown below.

If you DID NOT do the activity:
- Mark NO and move to the next question.

If you DID the activity in the past 4 weeks:
   Step #1   Mark YES.
   Step #2   Think about how many TIMES a week you usually did it and mark one answer.
   Step #3   Mark one answer to show the TOTAL HOURS in a typical week you did the activity.

Here is an example of how Mrs. Jones would answer the first question: Mrs. Jones usually visits her friends Maria and Olga twice a week. She usually spends one hour on Monday with Maria and two hours on Wednesday with Olga. Therefore, the total hours a week that she visits with friends is 3 hours a week.

**EXAMPLE**

| In a typical week during the past 4 weeks, did you... | How many TIMES a week? Think in terms of days | How many TOTAL hours a week did you usually do it? |
|-----------------------------------------------------|-----------------------------------------------|--------------------------------------------------|
| 0                                                  | 1 2 3-4 5 or more                           | Less than 1 hour 1-2.5 hours 3-4.5 hours 5-6.5 hours 7-8.5 hours 9 or more hours |

Visit with friends or family (other than those you live with)?

| 0 | 1 |
|---|---|

13. In a typical week during the past 4 weeks, did you...

13.1 Jog or run (including use of treadmill)?

| 0 | 1 |
|---|---|

Go to the next page. ——
| In a typical week during the past 4 weeks, did you... | How many TIMES a week? Think in terms of days | How many TOTAL hours a week did you usually do it? |
|------------------------------------------------------|-----------------------------------------------|-----------------------------------------------|
|                                                     | No | Yes | 1 | 2 | 3-4 | more | Less than 1 hour | 1-2.5 hours | 3-4.5 hours | 5-6.5 hours | 7-8.5 hours | 9 or more hours |
| 13.2 Walk uphill or hike uphill (count only uphill part; include use of treadmill)? | 0  | 1   | 1  | 2 | 3   | 4    | 1   | 2   | 3   | 4   | 5   | 6    |
| 13.3 Walk fast or briskly for exercise (do not count walking leisurely or uphill; include use of treadmill)? | 0  | 1   | 1  | 2 | 3   | 4    | 1   | 2   | 3   | 4   | 5   | 6    |
| 13.4 Walk to do errands (such as to/from a store or to take children to school (count walk time only))? | 0  | 1   | 1  | 2 | 3   | 4    | 1   | 2   | 3   | 4   | 5   | 6    |
| 13.5 Walk leisurely for exercise or pleasure? | 0  | 1   | 1  | 2 | 3   | 4    | 1   | 2   | 3   | 4   | 5   | 6    |
| 13.6 Ride a bicycle or stationary cycle? | 0  | 1   | 1  | 2 | 3   | 4    | 1   | 2   | 3   | 4   | 5   | 6    |
| 13.7 Do other aerobic machines such as rowing, or step machines (do not count treadmill or stationary cycle)? | 0  | 1   | 1  | 2 | 3   | 4    | 1   | 2   | 3   | 4   | 5   | 6    |
| 13.8 Do water exercises (do not count other swimming)? | 0  | 1   | 1  | 2 | 3   | 4    | 1   | 2   | 3   | 4   | 5   | 6    |
### In a typical week during the past 4 weeks, did you...

| Question                                                                 | No | Yes | 1 | 2 | 3-4 | 5 or more | Less than 1 hour | 1-2.5 hours | 3-4.5 hours | 5-6.5 hours | 7-8.5 hours | 9 or more hours |
|-------------------------------------------------------------------------|----|-----|---|---|-----|------------|------------------|-------------|-------------|-------------|-------------|-----------------|
| 13.9 Swim moderately or fast?                                           |    |     |   |   |     |            |                  |             |             |             |             |                 |
| 13.10 Swim gently?                                                     |    |     |   |   |     |            |                  |             |             |             |             |                 |
| 13.11 Do stretching or flexibility exercises (do not count yoga or Tai-chi)? |    |     |   |   |     |            |                  |             |             |             |             |                 |
| 13.12 Do yoga or Tai-chi?                                               |    |     |   |   |     |            |                  |             |             |             |             |                 |
| 13.13 Do aerobics or aerobic dancing?                                   |    |     |   |   |     |            |                  |             |             |             |             |                 |
| 13.14 Do moderate to heavy strength training (such as hand-held weights of more than 5 lbs., weight machines, or push-ups)? |    |     |   |   |     |            |                  |             |             |             |             |                 |
| 13.15 Do light strength training (such as hand-held weights of 5 lbs., or less or elastic bands)? |    |     |   |   |     |            |                  |             |             |             |             |                 |
| 13.16 Do general conditioning exercises, such as light calisthenics or chair exercises (do not count strength training)? |    |     |   |   |     |            |                  |             |             |             |             |                 |

Thank you for completing this questionnaire. Please take a moment to review any questions you may have missed.
Appendix D: WHISH Accelerometry Substudy

Sample selection

A subcohort of WHISH participants were invited to join the “WHI Physical Activity Follow-up Study” to provide objective data on changes in physical activity and time spent sedentary (measured by accelerometers). These women were part of a previous WHI ancillary study of 6,489 participants who in 2012-2014 participated in the Objective Physical Activity and Cardiovascular Health (OPACH) Study (R01 HL105065, AZ LaCroix, PI). Details on the design and implementation of the OPACH Study have been published previously.¹ Briefly, all women were ambulatory, community-living, and without major cognitive decline at OPACH baseline. African American and Hispanic women were oversampled and comprised 50% of OPACH participants—the average age was 79±7 years. Surviving members of the OPACH cohort who had successfully worn and returned accelerometers were mailed invitations and consent forms beginning in February 2015. This subcohort was targeted for device-monitored changes in physical activity because of they had previous experience using accelerometers and because the OPACH measurement provided a pre-WHISH Trial measurement for comparison. To achieve balanced groups of at least 1,000 women in both of the WHISH study groups throughout the planned follow-up period, the recruitment target was set at 2,300 and 2,349 women consented.

Accelerometer deployment and wear protocol

Accelerometer data collection was conducted by the Exercise and Physical Activity Resource Center at UC San Diego http://ucsdparc.ucsd.edu. Participants who consented were mailed a package containing an Actigraph GT3X+ accelerometer, an elastic waist band, a sleep journal to track in-bed and out-of-bed times, and instructions for wearing and returning the accelerometer
in an addressed express mail return envelope. Women were instructed to wear the accelerometer over the right hip, 24-hours per day for 7 days, and to remove them only for bathing and other water-based activities. If women were unwilling to wear the accelerometer at night, they were instructed to remove it when they got into bed, and to replace it upon getting out of bed. Participants were given a phone number to call for assistance during the accelerometer wear period, and at least 1 phone call was made to each participant during accelerometer wear to facilitate accurate placement and adherence. Participants were sent a thank-you letter and a $10 gift card upon receipt of their accelerometer and sleep logs. Accelerometers were deployed at three separate time points—6, 18, and at 36 months, so that along with the OPACH baseline, up to four separate weeks of accelerometer-measured physical activity is available on this subcohort of WHISH participants. Of the 2,349 women who consented to the WHISH Accelerometry Substudy, 85.4% returned an accelerometer in Year 1 of WHISH. Of the women who were still alive, 75.1% returned accelerometers in Year 2, and 67.3% returned accelerometers in Year 4.

**Data processing (including variables)**

As accelerometers were returned by mail, raw data were stored on a secure server and ActiLife v6 was used to integrate data to 15-second epochs using the normal filter and the low-frequency filter. Raw data were also converted to 41 descriptive features for each 1-minute epoch—the resulting features were input to a random forest machine learning (ML) classifier that was developed and validated specifically for older women in a separate study\(^2\) to measure sitting, standing without ambulation, standing with ambulation (i.e., puttering), and walking/running. In-bed time was identified in the 15-second epoch files and the 1-minute ML classified files using data from sleep journals, with missing data imputed using person-specific times if available, and
the overall sample in-bed and out-of-bed times if person-specific times were not available. Non-wear time was identified using the commonly used\textsuperscript{3} Choi algorithm\textsuperscript{4,5} applied to the vector magnitude of counts-per-minute that identified 90 minute intervals with 0 counts per minute as non-wear time, requiring a 30-minute stream frame and allowing for one 2-minute tolerance. Each 15-second epoch of awake wear time was classified as either sedentary, light physical activity (PA), or moderate-to-vigorous PA (MVPA) using vector magnitude cutpoints determined in the OPACH laboratory-based calibration study of 200 older women using the respective counts per 15-second cutpoints of $\leq 18$, 19 through 518, and $\geq 519$.\textsuperscript{6} Days with 10 or more hours of awake wear time were considered adherent,\textsuperscript{3} and sedentary time, light PA, MVPA, sitting time, standing without ambulation, standing with ambulation, and walking/running were computed by averaging the respective minutes spent in each activity over all adherent days for each participant.
REFERENCES

1. LaCroix AZ, Rillamas-Sun E, Buchner D, et al. The Objective Physical Activity and Cardiovascular Disease Health in Older Women (OPACH) Study. *BMC Public Health*. 2017;17(192). doi:10.1186/s12889-017-4065-6

2. Rosenberg D, Godbole S, Ellis K, et al. Classifiers for Accelerometer-Measured Behaviors in Older Women. *Med Sci Sports Exerc*. 2017;49(3):610-616. doi:10.1249/MSS.0000000000001121

3. Migueles JH, Cadenas-Sanchez C, Ekelund U, et al. Accelerometer Data Collection and Processing Criteria to Assess Physical Activity and Other Outcomes: A Systematic Review and Practical Considerations. *Sport Med*. 2017;47(9):1821-1845. doi:10.1007/s40279-017-0716-0

4. Choi L, Liu Z, Matthews CE, Buchowski MS. Validation of accelerometer wear and nonwear time classification algorithm. *Med Sci Sports Exerc*. 2011;43(2):357-364. doi:10.1249/MSS.0b013e3181ed61a3. Validation

5. Choi L, Ward SC, Schnelle JF, Buchowski MS. Assessment of wear/nonwear time classification algorithms for triaxial accelerometer. *Med Sci Sports Exerc*. 2012;44(10):2009-2016. doi:10.1249/MSS.0b013e318258cb36

6. Evenson KR, Wen F, Herring AH. Associations of Accelerometry-Assessed and Self-Reported Physical Activity and Sedentary Behavior with All-Cause and Cardiovascular Mortality among US Adults. *Am J Epidemiol*. 2016;184(9):621-632. doi:10.1093/aje/kww070