Women’s Health Initiative Strong & Healthy Trial
A Pragmatic Trial of Physical Activity (PA) for CVD

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U01 HL122280-CCC

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U01 HL122273-DCC

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WHI Investigator Meeting (Bethesda, MD), May 2, 2019
Primary Hypothesis

A centralized, public health intervention based on DHHS-national recommendations designed to increase and/or maintain PA levels and reduce sedentary behavior will reduce incidence of major CVD clinical events (MI, stroke, CVD death) in older women.
Novelty and Significance of

1. Randomized Consent Design (49,333 eligible women)
   Pragmatic trial embedded in Women’s Health Initiative Extension Study (2010-2020): CVD outcomes, MRC + SRC-CMS

Figure 1: Schematic representation of the randomized consent design for WHISH physical activity trial of (based on Zelen. N Eng J Med 1979; 300: 1242-1245)

**Interactive Voice Response System
Novelty and Significance of WHISH

2. First-ever large, pragmatic trial testing whether a PA intervention can reduce hard CVD endpoints

3. Passive consent in the WHISH intervention group allows >96% of eligible women to be exposed to the intervention


5. Population-based, participant-engaged, adaptive, targeted PA intervention

6. Accelerometry (OPACH cohort) Substudy

7. “Informed” Power Calculations (for WHISH Renewal)
Centralized, Participant-Engaged, Dynamic, Adaptive Targeted Intervention

- **Quarterly** (Seasonal) *WHISH* ful Actions Mailings (Targeted inserts: Physical Function)
- **Monthly Motivational Telephone Messages** *(Outbound “Adriana” System; IVR tracking system)*
- **Monthly Emails** (~1/4 of Active Participants)
- **Website, upgraded** *(whish.org); tracking system*
- Telephone, Mail, Email contact with Staff
Intervention Participant Retention

23,940 Participants (Passively) Consented to Intervention

2576 (10.8%) Deceased
18,381 Receiving Intervention
86% among those Alive

as of March 31, 2019.
Intervention Group Engagement

Responded to **Survey 1**: 11,400 of 23,848 = 48%
Responded to **Survey 2**: 11,479 of 21,651 = 53%
Responded to **Survey 3**: 12,620 of 20,062 = 63%

Responded to Survey 2 or 3
15,414 of 21,657 = 70.0%

Responded to **Survey 4**
13,673 of 19,075 = 72%
New WHI Findings

Light Activity Matters!

The Women's Health Initiative (WHI) has published more exciting findings about physical activity in older women which is shaping national recommendations. Thank you, yet again, for "being part of the answer!"

About 2,000 of you (WHI participants) wore a special motion sensor that measured:

SEDENTARY ACTIVITY: sitting while watching TV, reading, doing a jigsaw puzzle.

LIGHT-TO-MODERATE ACTIVITY: washing & drying dishes, laundry, folding clothes, dusting, mopping, and walking (1-2 1/2 mph). Intensity may vary depending on fitness level and effort needed to do the task.

KEY FINDINGS:

Just 30 additional minutes of light-to-moderate physical activity per day lowered the risk of death by 12% to 39% compared with women who were sedentary. These findings were true regardless of age, weight, or chronic conditions. Light activity does count!

More information inside and on the WHISH website (whish.org).
WHISHful Actions
Every Minute Counts

Women’s Health Initiative Strong & Healthy (WHISH)
Summer 2018

How can you add small amounts of activity throughout your day?

- Get up and move for a minute each half hour to add 30 minutes of extra activity to your day.
- Make a “To-Do” list of chores or short activities that will add up to 30 minutes each day.

Even if you exercise for 1 hour a day (and sleep for 8 hrs), how do you spend the other 15 hours of your day?
**STEP 1:**
How much time are YOU inactive?

**Inactive time:** any time spent sitting or lying down while awake but not engaged in active movement.

Examples include:
- Reading or writing
- Watching TV
- Working at a computer
- Eating

In each box below, fill in the amount of inactive time (minutes or hours) that you spend.

**MORNING**

**AFTERNOON**

**EVENING**

**TOTAL INACTIVE TIME**

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**STEP 2:**
Find activities to replace your inactive time.

Even if you are meeting the physical activity guidelines, sitting for prolonged periods of time can compromise your health. Find ways to add regular activity into your day.

- Take a 2 min. stretch break
- Go for a walk
- Do errands
- Walk up and down the stairs
- Play with children or pets

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**STEP 3:**
Set a goal to add active movement.

Add 30 minutes of activity to your day in large or small increments.

You can make a list of “5-minute activities”, such as:
- walking to the end of the block and back whenever you pick up the mail
- dancing as you wait for your food in the microwave

Replace inactive sitting with light, moderate, or vigorous movement to gain health benefits. Start where you are and safely add effort. Do what you can. Take the Talk Test to find out if your activities are light, moderate, or vigorous.

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**The Talk Test:**
How much effort?

The Talk Test is a great guide for figuring out how hard you are pushing yourself. As you do an activity, take note of whether you can talk or sing. Keep track of the intensity of your activities. As you slowly add effort, notice the progress you are making over time. Challenge yourself each day to include all levels of activity in your routine.

**Inactive**
Awake and relaxed while seated or lying down

**Light**
Can sing and talk while moving

**Moderate**
Cannot sing, but can still talk

**Vigorous**
Can only speak a couple of words at a time
Self-reported Walking & Sitting Levels Reported by Quarter, 7/28/2015-6/29/2018

After 3 years, 9% difference in walking

and, significant difference in sitting

I-C difference increasing over time

I-C difference increasing over time
Walking (MET-hr/wk) by WHISH Intervention arm and Form 521 Collection Quarter, Weighted by WHISH Age Strata

Sitting (hours/day) by WHISH Intervention arm and Form 521 Collection Quarter, Weighted by WHISH Age Strata

Data as of 3/28/19
CHAMPS total exercise (hrs/wk) by WHISH Intervention arm and Form 521 Collection Quarter, Weighted by WHISH Age Strata

CHAMPS walking (hrs/wk) by WHISH Intervention arm and Form 521 Collection Quarter, Weighted by WHISH Age Strata

Data as of 3/28/19
CHAMPS aerobic exercise (hrs/wk) by **WHISH** Intervention arm and Form 521 Collection Quarter, Weighted by WHISH Age Strata

CHAMPS strength training (ses/wk) by **WHISH** Intervention arm and Form 521 Collection Quarter, Weighted by **WHISH** Age Strata Age Strata

Data as of 3/28/19
WHISHful Actions

Physical Activity: The Best Medicine

Women's Health Initiative Strong & Healthy (WHISH)
Fall 2018

Reduces pain and improves physical function in osteoarthritis of the knee and hip

Improves quality of life and sleep

Lowers risk of developing many cancers

Reduces fatigue during cancer treatment

Reduces risk of developing dementia and Alzheimer's disease. Improves cognitive function.

Research* shows that physical activity...

Reduced risk of developing heart disease and stroke and reduces blood pressure

Reduces risk of falling

Reduced risk of injury if a fall does occur

Reduces feelings of anxiety and depression

Lowers risk of death for many conditions such as cancer, heart disease, hip fracture and diabetes.

* Findings from the 2018 Physical Activity Guidelines Advisory Committee Scientific Report

2018 Physical Activity Guidelines Advisory Committee Scientific Report
Physical activity has a wide range of health benefits including...

**Cardiovascular Disease**
- The American Heart Association promotes physical activity to prevent heart disease and stroke, and to reduce blood pressure.
- Sitting less and activities that increase heart rate (such as walking or interval activity) are recommended to improve heart health.

**Cancer**
- The American Cancer Society recommends physical activity to reduce the risk of breast, colon, and other types of cancer.
- Both everyday activities and your exercise routine can be done as interval activities (below).

**Type 2 Diabetes**
- The American Diabetes Association recommends breaking up prolonged sitting every 30 min. with 3-4 min. of light activity, such as walking, to lower blood sugar.
- Regular activity reduces the risk of getting diabetes.

**Arthritis**
- The Arthritis Foundation indicates that exercise may be the single most effective non-drug treatment you can do for your body.
- Exercise eases the pain of arthritis and improves your energy level.

**Dementia**
- The Alzheimer’s Association promotes staying physically active for overall body wellness.
- Increasing blood flow to your brain is associated with lower risk of cognitive decline.

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**Interval Activity**

**What is It?**
Interval activity (also called High Intensity Interval Training or HIIT) is a routine that switches between short bursts of increased effort or going “all out,” and short periods of decreased effort, “easing up” or rest.

**How do I start?**
You can do intervals with any type of activity. Your workout can include one or more different activities. Use the Talk Test to measure how much effort you are using (see insert). When you go “all out” you should be at a moderate or vigorous level.

**Four Reasons To Try It**
1. Increases the health benefits of activities you are already doing.
2. Gives you a more beneficial workout - in less time.
3. Preserves muscle and increases your ability to take in oxygen and produce energy.
4. Helps manage chronic conditions such as diabetes and improves cardiovascular and respiratory health.

See the insert for examples of interval activities you can try!
**MET-hours per week (kcal/week per kg) from walking** (N=19,202)

Target Group Assignment and Randomization

**Targeted (Interval Activity) Inserts based on Physical Function* & MET hrs/wk**

* PF: Form 151 (annual WHI)
  Q 7-16 ask how health limits 10 specific activities, 3 choices:
  - no, not limited at all
  - yes, limited a little
  - yes, limited a lot

**MET hrs/wk: Form 521** (annual WHISH; incl. controls)
Q1 asks about walking outside home >10 min. w/o stopping:
- Frequency (X per week)
- Duration (minutes)
- Usual speed

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<th>Lower</th>
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<td>605</td>
<td>1234</td>
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<td>30%</td>
<td>568</td>
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<td>282</td>
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<tr>
<td>&gt;=90</td>
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<table>
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<tr>
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<th>Middle (± 5.8)</th>
<th>Higher (± 5.2)</th>
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<td>79.0 (± 5.8)</td>
<td>76.9 (± 5.2)</td>
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<tr>
<td>N=6122</td>
<td>40.7 (± 20.5)</td>
<td>70.4 (± 20.0)</td>
<td>91.7 (± 6.4)</td>
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* at randomization
Targeted (PF/PA) Intervention: Interval Activity (HIIT) Inserts

**Interval Activity**

**Latest Science to Improve Health**

**How?**
- Alternating short periods of increased effort with short periods of rest.
- What is increased effort? Your heart will beat a lot faster and you will breathe harder. Using the Talk Test, you can also be moderate to vigorous level of effort. Increase effort by walking more quickly, going uphill, adding resistance or going for a longer period of time.
- What is rest? Before your effort, stand up or rest.
- Include a warm-up and cool-down.

**How Long?**
- Push yourself a bit harder for 20 seconds, then ease up or rest for 40 seconds. Count out the seconds, 1-2-3-4-5, and say the Talk Test below.
- The new or more active activities using intervals for a total of 10-15 minutes.
- You can adjust the interval times and duration. Any active movement is better than doing nothing.
- The interval activities 3-5 times per week and some regular physical activity in the other days.

**The Talk Test: How much effort?**

- Inactive: Cannot sing or talk while walking.
- Light: Can sing and talk while walking.
- Vigorous: Can only speak a couple of words at a time.

**Do Interval Activity...**

**...During Everyday Activities**

**As you exercise:**
- Work as hard as you can for 20 seconds.
- Ease up or rest for 40 seconds.
- Repeat at least 4 times.

**As you walk:**
- Walk at a moderate to vigorous level of effort for 20 seconds.
- Ease up for 40 seconds.
- Repeat at least 4 times.

**For your favorite "at home" or gym exercises:**
- Go "all out" at a moderate to vigorous level of effort for 20 seconds.
- Ease up for 40 seconds.
- Repeat at least 4 times.

**...As Part of Your Exercise Routine**

**Think of your favorite "at home" or gym exercises:**
- Go "all out" at a moderate to vigorous level of effort for 20 seconds.
- Ease up for 40 seconds.
- Repeat at least 4 times.

**Go to whish.org for more activities**

**LOW**

**GENERIC**

**HIGH**

Go to whish.org for more activities
WHISHful Actions
You Are Making A Difference
Women’s Health Initiative Strong & Healthy (WHISH) Winter 2019

Thank you for your contributions to science and women’s health

Of the 40+ observational studies on the relationship of physical activity to heart disease, only 1/3 have included women, and WHI was the most important.

The WHISH trial will be the first to answer the question: If an older woman moves more and sits less, can she improve her heart health, and well-being?

You are part of that answer! And that answer will influence national guidelines for future generations of women, and men.

Your participation, at any level, benefits science. Even if you only read WHISH materials or send back a survey, you contribute! Of course, if you also move more or sit less, we will learn even more to benefit women’s health.

See page 2. WHISH contributes to 2018 Physical Activity Guidelines

WHISH STUDY NEWS
WHISH participants are a part of so many important research findings

You provided the first major evidence that physical activity may improve heart health in older women, and that moderate activity, such as walking, is nearly as good as more vigorous activity! This research shaped the 2008 national physical activity recommendations.

Half of you also provided the most valuable health data we have on physical functioning in women aged 80 and over. WHI findings featured in the March 2016 supplement of the Journals of Gerontology indicate that higher physical function is strongly associated with a more active lifestyle.

You also provided important evidence that light activity reduces risk of death and improves heart health in older women. This research influenced the new 2018 Physical Activity Guidelines — particularly those for older adults (Chapter 5).

You can read these, and other articles, on the WHISH website whish.org

Kudos to the WHISH website Treasure Hunt WINNERS!

Betty, 84, New Jersey
Dorothy, 78, Ohio
Betsy, 75, North Carolina
Brigitta, 81, Maryland

Log in to the WHISH website whish.org to read more about the winners

Reflecting on Your Participation

Reflective Writing
Research suggests that reflecting on your thoughts and writing them down benefits your emotional well-being as well as your physical health.

Aretha, 84, Washington, D.C. author, reflects:

Helping others gives me a sense of satisfaction. Community service is something I just naturally do! I believe that community service can also encourage women to stay active no matter what age. There is plenty to do even for those with limited mobility. I helped prepare for a “Feed the Community” church event. Reflecting on your service helps you stay aware of your connection to the community. I wrote my book to help with that.
WHISHful Actions
Activity, Strength and Balance
Women’s Health Initiative Strong & Healthy (WHISH)
Spring 2019

Physical activity can make your daily life better.

A Well-Rounded Routine

The new Physical Activity Guidelines promote Go4Life goals for:
• Aerobics (activities that get your heart rate up)
• Muscle-strengthening
• Balance & Flexibility

Start Where You Are

Find the level of effort that is right for you based on your current activity level. The type and amount of activity needed to get your heart rate up will be different for each of us.

Do What You Can

If you are not very active, start with an activity you enjoy and slowly work your way up. Big gains can be made even with 10 minutes of moderate activity each day. If you’re already active, adding 5 more minutes of activity throughout the day is beneficial. Any gain in strength is good, too. Keep up the good work!

WA #17 Postcard – Spring 2019
Website Promotion

Introducing TRUDI TRYGG, physical therapist
Go to the WHISH website: whish.org

We’d like to introduce Trudi Trygg, a licensed physical therapist who advises us on our WHISH materials.

Visit the WHISH website to try new exercises recommended by Trudi and demonstrated by WHISH participants!

Visit the HOME EXERCISES page on the WHISH website and win a prize!

To encourage you to view the activities and videos that we have created in response to your feedback, we’re giving prizes to lucky participants who visit the Home Exercises page. Enter a friend or family member to help you get onto the website. We hope they will enjoy it too!

How to Win:
To be entered into the raffle, go to whish.org, log in, and click on the Home Exercises page. You will automatically be entered into the raffle. The drawing will be held on June 1, 2019.

The Prizes:
Each winner will receive a $50 gift card.

NEW
WHISH Website
HOME EXERCISES

Videos produced by the WHISH staff using WHISH participants
**HOW MUCH ACTIVITY IS RECOMMENDED?**

**25-30 minutes per day**

**Moderate to Vigorous Aerobic Activity**
Anything that gets your heart beating faster

- 2 days per week

**Muscle-Strengthening**
Your muscles work harder than usual

See the INSERT for aerobic, strength and balance exercises

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**What is considered moderate or vigorous?**

The amount of work or effort needed to do a given activity differs for each of us. Your heart rate and breathing increase with greater effort. A given activity usually takes more effort for an inactive person than for a regularly active person.

When doing a moderate-intensity activity, you can talk, but not sing.

During vigorous activity, you can’t say more than a few words without pausing for a breath.

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**Chronic Conditions**

A chronic condition, such as high blood pressure, high blood sugar, or osteoarthritis, might affect your ability to do a given physical activity safely. Check with your doctor.

Evidence shows that staying active reduces pain and fatigue, and improves physical function, sleep, mood, and well-being.

Even if you're not able to do 25-30 minutes of moderate activity, stay as active as you can throughout each day.

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**Minute Activities**

Here are examples of activities that can be done in 2-5 minutes.

List a few activities that you can add to stay active throughout the day.

- March in place while on the phone
- Park further from your destination and walk the extra distance
- Do chair exercises while watching TV

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**A well-rounded daily routine**

A well-rounded routine each day includes getting your heart rate up for 30 minutes or more (aerobic activity), light activities for 8 hours, getting enough sleep, and avoiding long periods of inactive sitting or lying down.

To avoid sitting too long during the day, do some home exercises, household chores, 2-5 Minute Activities (as above), and activities that you enjoy such as shopping, gardening, volunteering, yoga, yard work, or outings with friends or family.

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**The 24-hour day**

Break-up long periods of sitting with light activity

- 1/2 hour Aerobic activity
- 8 hours Light activity
- 8 hours Inactive sitting or lying down
- 7 1/2 hours Sleep

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**NEWS & RESEARCH**

Recent research about physical activity

**BRAIN HEALTH**

Many benefits to brain health occur soon after a session of moderate-to-vigorous physical activity, including improved sleep and reduced anxiety. Longer-term benefits of regular physical activity include improvements in deep sleep and mental processes such as memory, attention, and problem-solving skills.

Exercising for 10-30 minutes has been shown to improve mood. Regular exercise reduces depressive symptoms and the risk of developing depression.

Physical activity also lowers your risk of developing cognitive impairment, such as dementia (including Alzheimer’s disease), and improves brain health after a stroke as well as for those with multiple sclerosis, or Parkinson’s disease.

*2018 Physical Activity Guidelines*

You can read more from the *2018 Physical Activity Guidelines on the WHISH website whish.org*
Power calculations

Using:
• Observed physical activity differences between arms
• Observed *combined arms* event rates
• Observed relation between physical activity and CVD from NHLBI-funded OPACH study (LaCroix, PI)

WHISH will have 4 years of follow-up as of January 1, 2020.
Need for **WHISH** Renewal

- Longer follow-up needed to definitely test the **WHISH** hypothesis
- Observed **WHISH** data provide the basis for better informed power calculations
- The **WHISH** Intervention may have beneficial effects on other aspects of CVD aging
Renewal Specific Aims

1° Continue **WHISH** Intervention and extend follow-up to a minimum of 8 years.

2° Examine **WHISH** intervention effects on key markers related to healthy CVD aging including physical function, sleep and depressive symptoms.

**Exploratory**: Conduct pilot studies examining **WHISH** intervention effects on novel biomarkers indicative healthy CVD aging (e.g., NT-proBNP, high sensitivity Troponin T)

Note: 2° and exploratory aims would leverage the LLS2 home visit, funded by **WHI** contract.
### Ancillary Studies

**WHISH to Prevent Heart Failure – 1R01HL130591-01 (PI: CB Eaton)**

**Primary Objective**: To evaluate the effect of the *WHISH* Physical Activity Intervention on incident and recurrent Heart Failure, HF with preserved Ejection Fraction (HFpEF) and HF with reduced EF (HFrEF)* and CVD mortality in women with antecedent HF, and perform dose-finding analyses in the *WHISH* PA trial of ~49,000 Women aged 65+ at baseline.

*all HF hospitalizations and CVD death in those with antecedent HF*

The imbedded *accelerometer study* allows for a dose-finding analysis regardless of the RCT results, using newly developed MET–equivalent indices for older women.

**WHISH - SilenT Atrial Fibrillation Recording Study (WHISH-STAR) – 1R01HL136390-01 (PI: MV Perez):**

**Primary Objective**: To measure the effect of the *WHISH* PA intervention on clinical and asymptomatic forms of *atrial fibrillation* using loop recorders