WOMEN'S HEALTH INITIATIVE
2023-2024

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- Stanford University/San Jose Clinical Center, Palo Alto, CA
- UCLA David Geffen School of Medicine, Los Angeles, CA
- University of California, Davis, CA
- WHI-UC Irvine Clinical Center, Orange, CA
- Center for Health Research, Portland, OR
- University of Arizona, Phoenix, AZ
- University of Arizona, Tucson, AZ
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- University of Nevada, Reno, NV

Stanford University
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- UC San Diego Clinical Center, Seattle, WA
- Seattle Clinical Center, Seattle, WA
- University of Alabama, Birmingham, AL
- Emory University, Decatur, GA
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- University of Florida Clinical Center, Jacksonville, FL
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(800) 514-0325

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- UNC Women's Health Initiative, Chapel Hill and Durham, NC
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- Women's Health Initiative, Winston-Salem, NC
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- UMDMJ – Robert Wood Johnson Medical School, New Brunswick, NJ
- Albert Einstein College of Medicine, Bronx, NY
- School of Medicine, SUNY, Stony Brook, NY
- University at Buffalo, Buffalo, NY
- George Washington University, Washington, DC
- WHI of the Nation's Capital – Medstar, Hyattsville, MD

University at Buffalo
(855) 944-2255
(716) 829-3128

- Brigham and Women's Hospital, Boston, MA
- Charlton Memorial Hospital, Fall River, MA
- Memorial Hospital of Rhode Island, Pawtucket, RI
- UMASS/FALLON Women's Health, Worcester, MA

Brigham and Women's Hospital
(800) 510-4858
(617) 278-0791

MIDWESTERN REGIONAL CENTERS

- Evanston Hospital (Northwestern University), Evanston, IL
- Northwestern University, Chicago, IL
- Medical College of Wisconsin, Milwaukee, WI
- Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL
- Ohio State University, Columbus, OH
- University of Cincinnati College of Medicine, Cincinnati, OH
- Detroit Clinical Center, Detroit, MI
- University of Pittsburgh, Pittsburgh, PA
- Berman Center for Outcomes and Clinical Research, Minneapolis, MN
- University of Iowa, Davenport, IA
- University of Iowa, Des Moines, IA
- University of Iowa, Iowa City, IA
- University of Wisconsin, Madison, WI

Ohio State University
(800) 251-1175
(614) 688-3563

WHI COORDINATING CENTER Fred Hutchinson Cancer Center, Seattle, WA (message line): **(800) 218-8415** | E-mail address: **participant@whi.org**

Word Scramble Answer Key:

1. prevention, 2. webinar, 3. health, 4. research, 5. women, 6. menopause, 7. trial, 8. initiative, 9. study, 10. participants, Secret Message: We appreciate you!

WOMEN'S HEALTH INITIATIVE

EXTENSION STUDY

WHI MATTERS

A PUBLICATION OF THE WOMEN'S HEALTH INITIATIVE | 2023-2024

WHI Clinical Trial Findings

The Women's Health Initiative (WHI) has changed the landscape of post-menopausal women's health in the US and abroad. WHI advanced our knowledge of chronic disease prevention, has changed clinical practice, saved thousands of lives and reduced estimated medical expenditures within 10 years of the trial's results, an amount that surpassed the trial costs many times over. Post-menopausal women now have reliable data to inform their choices regarding use of menopausal hormone therapy, calcium and vitamin D supplements, and a diet that is lower in fat and higher in fruits, vegetables and grain on chronic disease risk. These population-based trials, each involving tens of thousands of women like you, provide the highest quality evidence available on the major causes of morbidity and mortality in older women, including cardiovascular disease, cancer and fractures.

The WHI has also had a significant impact on the research enterprise itself. The disparities between the prior observational studies and these clinical trials led to a better understanding of the limitations of observational studies and in some cases, the complementarity of the two types of studies. Insights from these comparisons have drove efforts to increase the dependability of observational studies.

WHI findings have not been without controversy. Some of this arose from a misunderstanding of the context and goals of the menopausal hormone trials. But admittedly, there has been resistance to trial results, mostly from a small yet vocal component of the medical community who were adversely affected by the results. As Dr. Elias Zerhouni, the Director of the National Institutes of Health in 2002, noted in his closing remarks of a special NIH symposium on menopausal hormone therapy,

> ***"As you look through the history of science, the reaction to a new scientific finding, whatever that finding is, is really proportional to the strength of the dogma it overturns."***

WHI results continue to be discussed in the popular press and medical literature. So that you have an accurate picture of the latest results, here we provide a high-level summary of each WHI trial. WHI Clinical Trials Summary: **jamanetwork.com/journals/jama/article-abstract/2818206.** *Continue article on page 4.*

WHI Webinar Announcement

Thank you to those who have watched the live or recorded Participant Webinars in 2024. The remaining webinar in the 2024 series will occur on October 16th, 2024 at 11am PT/1pm CT/2pm ET. Tune in and learn more about WHI research, hear from experts, and ask questions! You can join via the Zoom link or by calling a toll-free number to listen. All webinars will be recorded and available to view on our website.

Visit **whi.org/ppt/pptwebinar** for more details.

Global Quality of Life Among WHI Women Aged 80 Years and Older

How does quality of life change among the oldest? A study published in a special issue of the Journal of Gerontology found that most women in the study rated their quality of life highly. Researchers also found that women with the highest ratings were more likely to also report good general health and fewer symptoms of depression. The analysis showed that current health and social and mental health status had a stronger association with women's self-reported quality of life than their historical health conditions. To improve or maintain quality of life in women over 80, the researchers suggest regular depression screening and treatment, as well as continuing efforts to maintain or improve physical health.

pubmed.ncbi.nlm.nih.gov/26858327/

Sugar-Sweetened and Artificially Sweetened Beverages and Risk of Liver Cancer and Chronic Liver Disease Mortality

In the U.S., liver cancer rates have more than tripled since 1985. Certain conditions including hepatitis B infection, type 2 diabetes and excess alcohol consumption all raise the risk of liver cancer, but 40% of liver cancer cases occur in patients without known risk factors. Previous research has linked regular consumption of sugar-sweetened beverages to increased liver cancer risk, but these studies did not assess that risk, specifically in women. WHI researchers found that women who consumed one or more sugar-sweetened beverages daily had a higher likelihood of developing liver cancer and death from chronic liver disease compared to those who drank three or fewer servings per month. There was no observed link between consumption of artificially sweetened beverages and liver cancer or death from chronic liver disease.

These findings point to a link between sugar-sweetened beverage consumption and liver cancer and death from chronic liver disease, a leading cause of death in women in the U.S.

Further research is needed to understand the biology that may drive these increased risks.

pubmed.ncbi.nlm.nih.gov/37552302/

Association of Physical Activity and Fracture Risk Among Postmenopausal Women

Previous research has established that physical activity reduces the risk of hip fractures in older women, but its effect on other types of fractures has remained unclear. WHI investigators examined the relationship between various physical activities and fractures at multiple body sites, making this study the most comprehensive study at this time.

Using data from 77,206 WHI participants, these investigators found that higher overall physical activity was associated with a lower risk of total and hip fractures but a higher risk of knee fractures.

Women who walked or did mild physical activity for more than 3.5 hours per week were at reduced risk of hip and total fractures compared to women reporting no mild physical activity. However, increased moderate to vigorous physical activity was associated with a higher risk of knee fractures and, to a lesser extent, wrist, or forearm fracture. Greater sedentary time was also related to an increased risk of total fractures. Mild activity and walking were associated with a lower risk of fractures, which has significant public health implications. These activities are easily attainable and particularly popular among older adults, making them effective strategies for reducing total fracture risk in postmenopausal women.

pubmed.ncbi.nlm.nih.gov/31651972/

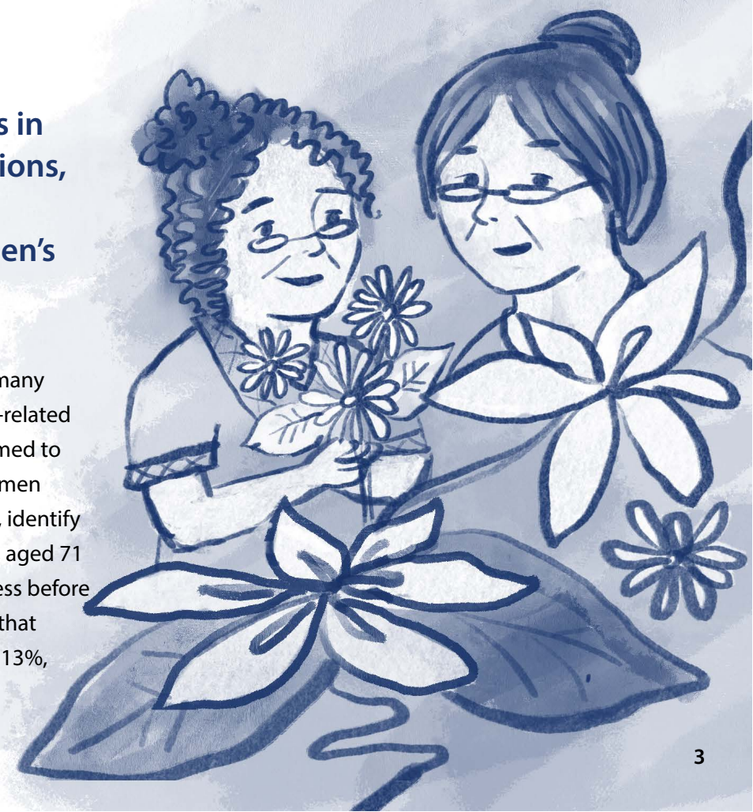
Associations Between Changes in Loneliness and Social Connections, and Mental Health During the COVID-19 Pandemic: The Women's Health Initiative

The COVID-19 pandemic significantly strained mental health and increased isolation across many demographics. Previous studies on pandemic-related loneliness yielded mixed results. This study aimed to determine if loneliness increased for older women during the first year of the pandemic and if so, identify contributing factors. A total of 27,479 women, aged 71 to 104, participated in two surveys on loneliness before and during the pandemic. Researchers found that loneliness increased overall by approximately 13%, with a near doubling of those who reported the most severe loneliness. Decreased loneliness was associated with identifying as Black or Asian/Pacific Islander, engaging in more physical activity, being optimistic, and having a higher purpose in life. Conversely, increased loneliness was linked to older age, stressful life events, bereavement, vascular disease and depression, and disruptions in social connections.

Loneliness is a gateway symptom to depression, which itself is associated with poorer health outcomes.

Older women, particularly those experiencing significant life stressors and health issues, may benefit from interventions aimed at reducing loneliness.

pubmed.ncbi.nlm.nih.gov/34915558/



WHI Clinical Trial Findings

Hormone Trials

WHI studied the two most commonly used forms of menopausal hormone therapy in full-scale, randomized, placebo-controlled clinical trials:

- Estrogen alone, in women with prior hysterectomy (brand name Premarin)
- Estrogen plus progestin (brand name PremPro) in women with an intact uterus

These hormones were known to be highly effective for treating menopausal symptoms. At study initiation, observational studies had strongly suggested that they would be helpful for preventing heart disease, the major cause of death for older women then and now.

The primary motivation for the trial was to establish definitively whether women could use hormone therapy to prevent heart disease. Since hormones were known to affect many aspects of women's health, including breast cancer, the WHI was designed to assess hormone effects on multiple critical health outcomes so that their overall impact could be evaluated.

RESULTS:

Estrogen plus progestin used for about 5 years

- Increased the risk of blood clots, stroke, breast cancer, and heart disease.
- Reduced the risk of fractures, endometrial cancer and colorectal cancer.
- Did not show differences in effects by age.
- Among 10,000 women treated with combined hormones, 20 additional women would experience one of these life altering events.
- 10 years after the trial was stopped, all hormone effects went away except for the breast cancer increase which has stayed remarkably stable.

Estrogen alone used for nearly 7 years in women with prior hysterectomy

- Reduced risk of fractures and surprisingly reduced breast cancer rates.
- Increased risk of stroke and blood clots.
- Showed that adverse effects were generally concentrated in older women, suggesting that younger women (in their 50s) could use them with much less concern.
- Estrogen effects mostly went away within 9 years after the trial stopped. Only the breast cancer reduction persisted.

Many other conditions have been examined in both hormone therapy trials. The one additional area where trial participants experienced some benefit was a reduction in incident diabetes. No benefits were seen for hypertension, incontinence, gall bladder disease, cognitive function or dementia.

CONCLUSIONS:

Menopausal hormone therapy does not reduce the risk of cardiovascular disease and carries more risks than benefits for chronic disease prevention. Menopausal hormone therapy should not, in general, be used for chronic disease prevention.

These diseases are age-related and uncommon in younger postmenopausal women. For early postmenopausal women suffering from moderate to severe menopausal symptoms, these hormone-associated risks are very small, particularly for estrogen alone. It seems reasonable for these women and their doctors to consider hormone therapy at the lowest dose and shortest time needed to alleviate bothersome symptoms.

These recommendations do not necessarily apply to women with premature or early-onset menopause, as this age group was not included in the current study.`

IMPACT:

Upon publication of these results, women throughout the world re-examined their use of hormone therapies, resulting in a considerable drop in usage. This was followed shortly thereafter by a reduction in breast cancer incidence rates which has been credited to these findings. An economic analysis over the 10 years following the release of the combined hormone trial result estimated $35.2 billion in medical savings associated with changing hormone use patterns in the US alone.

Calcium and Vitamin D Trial

Calcium is an important nutrient for maintaining strong bones. WHI tested whether taking calcium (1000 mg/d) and vitamin D (400 IU/d) supplements would reduce hip fractures rates in average risk post-menopausal women. The effects of these supplements on colorectal cancer were also of interest in this randomized, double-blind, placebo-controlled trial.

RESULTS:

With over 7 years of calcium and vitamin D supplements, WHI found

- A modest improvement in hip bone density
- A small reduction in hip fracture rates that did not reach statistical significance
- No significant effect on other fracture rates
- No effect on colorectal cancer or other cancer rates
- A small increase in risk of kidney stones
- Somewhat stronger fracture benefits among women who consistently took their supplements

CONCLUSIONS:

WHI results do not support use of calcium and vitamin D supplements to prevent fractures.

WHI recommends that women seek to obtain the recommended levels of these nutrients through dietary sources as much as possible.

Dietary Modification Trial

A variety of observational studies suggested that consuming a diet lower in fat and higher in fruit, vegetables and grains would reduce the risk of several health concerns, including breast and colorectal cancer. The strongest evidence came from international and migration studies. The WHI randomized trial of dietary

modification compared two groups. The intervention group was taught how to significantly reduce their dietary fat intake and increase their consumption of fruits, vegetables and grains. Women randomized to the control were given standard nutritional information.

RESULTS:

Over approximately 8 years of participation in the DM trial, WHI found that compared to the control group, women in the intervention group:

- Made substantial changes to their diets.
- Reduced fat intake by about 11%
- Increased fruit and vegetable intake by 1 serving/day
- Increased grain intake by ½ serving/day.
- Had a slight weight reduction.
- Had similar rates of breast cancer, colorectal cancer, and coronary heart disease.
- Had a lower rate of breast cancer mortality.

CONCLUSIONS:

This low-fat eating pattern was not effective in changing a woman's risk of getting cancer or heart disease.

Further research is needed to confirm the benefits of this diet for breast cancer mortality.

WHI Matters 2024
Most Common Questions

DIABETES

Is it possible to reverse a diabetic diagnosis? If so, how?

Type 2 diabetes can be considered in remission after three or more months of sustained normal blood glucose levels, which can sometimes be achieved through lifestyle changes (eating choices, physical activity, weight management), medications, or surgery that addresses obesity. However, the diagnosis of type 2 diabetes is not usually reversed, nor is the diabetes considered cured, because the physiology leading to type 2 diabetes rarely changes. Please consult your health care team for additional information about type 2 diabetes remission and management options that can be tailored for you.

For more information, see:
pubmed.ncbi.nlm.nih.gov/34462270/

RADON EXPOSURE AND TESTING

What is the WHI Radon Risk Investigation (WHI Risk It)?

The Centers for Disease Control, Surgeon General, American Lung Association, and American Medical Association recommend testing homes for radon gas and recommend taking action to reduce radon levels in homes with levels at or above 4 picoCuries per liter (pCi/L). Radon is the second leading cause of lung cancer, after smoking, and one in 15 U.S. homes has elevated levels. Radon is radioactive, but we cannot see, smell, or taste it. You may be breathing radon gas and not know it. Radon also is a suspected cause of other diseases of the brain, heart, lungs, and blood. WHI Risk It? is a study to help understand these possible relationships.

For more information, see:

- EPA's Radon Frequently Asked Questions: **rb.gy/01v0i1**
- EPA's A Citizen's Guide to Radon: **rb.gy/n7yofm**
- WHI Participant Webinar on WHI Risk It?: **rb.gy/o17lwg**

WEIGHT

How can I overcome obstacles to exercise, such as osteoporosis and sleep related issues?

Choose activities you enjoy and can do safely. If you're managing osteoporosis, care guidelines suggest consulting with your care team or specialists before undertaking exercise - which can be an effective way to prevent and manage further bone loss. If sleep issues are an obstacle, consider scheduling your activity at times when you tend to feel energetic.

SLEEP

How can I achieve good sleep quality?

To achieve good sleep quality, maintain a consistent sleep schedule by going to bed and waking up at the same time every day. Create a relaxing bedtime routine, keep your bedroom cool, quiet, and dark, and use comfortable bedding. Additionally, finish eating 2-3 hours before bedtime, exercise regularly, and limit caffeine, alcohol, and nicotine, especially in the evening.

For more information, see: **thensf.org/sleep-tips/**

WHI 2024 Online Resources

About WHI: Learn more about the Women's Health Initiative (WHI), one of the largest women's health research projects ever undertaken in the United States. Discover its mission, objectives, and the groundbreaking studies conducted to improve women's health. Please visit **whi.org/about-whi** to learn more about WHI.

WHI News Archive: Stay up to date with the latest news and posts from the Women's Health Initiative. From research breakthroughs to upcoming events, this section keeps participants informed about the study's progress and its impact on women's health. Please visit **whi.org/news/archive/fp** to learn more about WHI News Archive.

WHI Matters Newsletters (2011-2023): Delve into the annual WHI Matters Newsletters spanning from 2011 to 2023. These newsletters offer study updates, participant profiles, and health and other information of interest to women. WHI Matters is provided in both English and Spanish (estos boletines también están disponibles en español).

Please visit **whi.org/whimatters** to read the WHI Matters Newsletters.

Participant Webinar Series: Explore our archive of recorded webinars designed specifically for WHI participants. These informative sessions feature expert speakers discussing various aspects of WHI research, sharing valuable insights, and addressing participant questions. Tune in to deepen your understanding of women's health and the ongoing efforts of the WHI study. Please visit **whi.org/ppt/pptwebinar** to find the latest link to the upcoming webinar and to watch previously recorded webinars.

Word Scramble

Unscramble the words, then use the highlighted letters to figure out the secret message.
Hint: The secret message is in scrambled form.

1. RTEVNOEPIN
2. EBAWRIN
3. HAHETL
4. ESCRRAHE
5. MNWEO
6. ENSMUPEOA
7. ILTAR
8. NTVIIAEITI
9. UYSDT
10. ATNPAISRPICT

SECRET MESSAGE: _____ _____ _____ !