



2022-2023

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EXTENSION STUDY

WHI MATTERS

A PUBLICATION OF THE WOMEN'S HEALTH INITIATIVE | 2022-2023



30 Year Snapshot of WHI

In October of 1993, the first participant was enrolled in the WHI. Thirty years later, WHI continues on with over 50,000 women still active with WHI! This edition of the *WHI Matters* newsletter celebrates, you, the

participants, who have made WHI a success in so many ways. On pages 4 & 5, you will see exactly how you have contributed to advancing important science, the health of countless women, and the professional growth of numerous scientists and non-scientists alike. Your enduring commitment and enthusiasm for the essential work in WHI inspires future research. The work continues on through WHI and through new and ongoing ancillary studies. One new project is the WHI Long Life Study 2 (LLS2) which launched in late 2022. The National Institutes of Health (NIH) funded the WHI LLS2 to continue to learn about health and aging in women. The study will collect some of the same measurements that were taken for the Long Life Study 1, 10 years ago, in 2012 – 2013, such as, blood pressure, height, and weight. Only a sample of WHI participants were needed for the LLS2, so not all eligible WHI women will be invited to join. More information about the LLS2 can be found on our website, <https://www.whi.org/md/lls2>. We deeply appreciate your energy and loyalty to WHI, which is central to helping us understand more about how women age.

WHI Webinar Announcement

We are excited to announce continuation of the WHI Participant Webinar series in 2023. The webinars will occur quarterly. The January 18 and April 19 webinars were recorded and are available on our website. Additional webinars will be held on July 19 and October 18 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 <https://www.whi.org/ppt/pptwebinar> for more details.

Center Information

Stay in Touch } Please call your Regional Center if your address or phone number changes.

To locate your Regional Center, find the name of your WHI clinic center on the list below. The Regional Center and phone number for each center is shown in the right-hand column.

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Kaiser Permanente/Bay Area Clinic, Oakland, CA
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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
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University of Arizona, Tucson, AZ
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University of Nevada, Reno, NV

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Seattle Clinical Center, Seattle, WA
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WHI of the Nation's Capital – Medstar, Hyattsville, MD

University at Buffalo
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(716) 829-3128

Brigham and Women's Hospital, Boston, MA
Charlton Memorial Hospital, Fall River, MA
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Brigham and Women's Hospital
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Ohio State University
(800) 251-1175
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WHI COORDINATING CENTER Fred Hutchinson Cancer Center, Seattle, WA (message line): (800) 218-8415 | E-mail address: participant@whi.org

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Focus on Findings

If you would like to read the full version of any of the following papers, please contact us and we will be happy to provide you with a copy. See the Correspondence box on page 5 for our contact information.

Global Cognitive Function and Psychological Distress

The COVID-19 pandemic interrupted and postponed many aspects of our daily lives. Increasing evidence shows potentially harmful psychological effects from the disruptions of the pandemic. Psychological distress has been linked to risk of cognitive decline or impairment; therefore, psychological distress amid the pandemic has become a serious public health issue. The relationship between cognitive function and the adherence to COVID-19 health recommendations (e.g. wearing masks and practicing safe hygiene) is not well-understood; this relationship can amplify among older adults with lower cognitive function. WHI investigator Dr. Aladdin Shadyab and colleagues examined the relationship between pandemic-related stress and cognitive function using data from 3 WHI based studies: WHI Memory Study Epidemiology of Cognitive Health Outcomes (WHIMS-ECHO), WHI Sleep Hypoxia Effects of Resilience (WHISPER, and Cocoa Supplement and Multivitamin Outcomes Study for the Mind (COSMOS-Mind).

The authors reported that lower prepandemic global cognitive function was associated with higher perceived stress and depression symptoms during the pandemic.

These researchers found that higher depression symptoms during the pandemic were associated with cognitive decline during prepandemic and peripandemic timepoints. Women with lower cognitive function were less likely to practice safe hygiene in comparison to women with higher cognitive function. This study concludes that future studies on the long-term effects of the COVID-19 pandemic on cognitive and mental health as it relates to older women are a necessity.

Optimism, Lifestyle, and Longevity Among Various Racial Groups

Previous literature has reported that positive psychological factors reduce the risk of morbidity and mortality. Most studies look beyond the lack of depression and other negative psychological factors to evaluate positive psychological factors and various health outcomes. Optimism, described as the expectation of beneficial future outcomes, is associated with better health outcomes and longevity, which is surviving well beyond the average lifespan. Increasing evidence has suggested that optimism may provide benefits across racial and ethnic groups. The racial and ethnic groups included in the study consisted of non-Hispanic White, Black, Hispanic/Latina, and Asian post-menopausal women. Racially diverse participants from the observational and clinical trial arms of WHI were studied to determine the association of optimism with longer lifespan. In this study, Koga et. al. evaluated whether higher optimism was associated with longer and healthier lifespan and longevity and whether lifestyle factors could mediate this association within various racial and ethnic groups.

The researchers found that higher optimism levels were associated with longer lifespan and a greater likelihood of achieving longevity. They also reported no difference between racial and ethnic groups in the role optimism plays in longevity.

The factors evaluated in the study did not include depression which further suggests that optimism is beneficial for longevity beyond simply stating the absence of depression. The study concludes the effects of optimism may be proportionate to physical exercise.



Crossword Puzzle

- Across**
- 1. Movie mutt
 - 6. Virus prefix
 - 10. Imbibes slowly
 - 14. Use a blender, in a way
 - 15. Nail anagram
 - 16. College credit
 - 17. Surface extents
 - 18. It may get the brush-off
 - 19. Barker of filmdom
 - 20. Focal point of a weighty matter?
 - 23. It takes things to the extreme
 - 24. Preschooler
 - 25. Too much too much, briefly
 - 26. Bender
 - 27. "Casablanca" character
 - 29. Certain leather source
 - 32. Linebacker Junior
 - 35. ____ Reader (former magazine name)
 - 37. Boy toy
 - 39. Focal point of the politically moderate?
 - 42. Find diverting
 - 43. Natural table
 - 44. Some old laptops
 - 45. Job listing letters
 - 46. Tail end
 - 48. They're inhuman
 - 50. Gas or elec., e.g.
 - 52. Alphabetic run
 - 53. Fleur-de-____
 - 56. Focal point of a politician?
 - 61. Lovers' place
 - 62. Small and weak
 - 63. Played-out
 - 64. Slight interruption
 - 65. Emmy-winning Falco
 - 66. Available for occupation
 - 67. Turkeys
 - 68. Weightlifters' iterations
 - 69. Despots

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		50	51					52				53	54	55
56	57					58	59				60			
61					62					63				
64					65					66				
67					68					69				

- Down**
- 1. Maneuvering room
 - 2. Antidotes
 - 3. Word separating looks and everything
 - 4. Entree item, often
 - 5. It carries the words "Rey de Espana"
 - 6. Shell out
 - 7. Babe in the woods
 - 8. Soft bell sound
 - 9. Emcees' deliveries
 - 10. Charmingly sophisticated
 - 11. What employee theft is
 - 12. "Kalifornia" star
 - 13. Dog show command
 - 21. Noxious elephant, e.g.
 - 22. Poor Richard's forte
 - 26. One of the martial arts
 - 27. Extrapolate
 - 28. "I'm game!"
 - 30. The good earth
 - 31. Reebok competitor
 - 32. Hook hand
 - 33. One in Hanover
 - 34. More than recessed
 - 36. 1970s TV detective
 - 38. Bearded bloom
 - 40. Type of poetry
 - 41. The Santa Maria landed here
 - 47. One not getting any reception
 - 49. Expression of disapproval
 - 51. Is overrun
 - 52. They may appear on lids
 - 53. Bizet opera priestess
 - 54. ____ alia (among other things)
 - 55. Printer's retentions
 - 56. Iron follower
 - 57. Home of Iolani Palace
 - 58. In the altogether
 - 59. Quick cut
 - 60. Some still-life subjects



Most Common Questions from 2021-2022

WHI Matters Newsletter

What is your recommendation for plant-based items for older adults? Are legumes specifically a good source of plant-based protein?

You are spot-on in recognizing legumes as a source of protein. The authors of the Journal of the American Heart Association paper used a statistical analysis method to swap in (substitute) a 5% higher caloric proportion of plant-based proteins for an equal caloric portion of animal-based proteins. This technique allowed them to ask, what if the WHI participants consumed more plant-based proteins and less animal-based proteins. The result was that risk of death may be lower. Then, the authors went a step further by looking at specific types of protein foods. Here, as one example, they found that substituting a 2-ounce per day equivalent of eggs, dairy, or legumes with nuts may lower the risk of cardiovascular disease death. That's where the part about nuts for legumes comes in. Every WHI paper contributes to our understanding of health and disease risk among postmenopausal women.

You mention positive prognosis for those taking the cocoa extract (COSMOS). However, it might be advisable to enable those who are not part of the study to give us more details as to the quantity of cocoa taken and where the particular extract can be obtained.

This question is also a frequently asked question (FAQ) on the COSMOS website (<https://cosmostrial.org/results/>). "The cocoa extract supplement used in COSMOS is similar to CocoaVia™ Cardio Health as they both include 500 mg cocoa flavanols, including about 80 mg (-)-epicatechin. We do not know whether the COSMOS results would apply to other multivitamin and cocoa flavanol supplements with similar or different amounts of nutrients." In a separate FAQ the response stated "we recommend speaking with your healthcare provider if you have questions about whether or not to take a multivitamin and/or cocoa extract

supplement taking into consideration your individual health history and diet."

Newsletter correction from the article titled "Recommendations from WHI participants for activities to stay engaged and combat loneliness"

NIA means "neuromuscular integrative action", and not "non-impact aerobics".

Where can we find the full article for "Disparities exist in how women recover from knee replacement" on the web?

The actual paper is titled "Racial/Ethnic Disparities in Physical Function Before and After Total Knee Arthroplasty Among Women in the United States" and you can find a full link to the article on <https://pubmed.ncbi.nlm.nih.gov/32412635/>.

WHI Obituaries

It is with deep sadness that several pivotal WHI Investigators have passed away recently. To learn more about their career and impact on WHI please find their obituaries on the WHI website.

Dr. Gerardo Heiss, M.D., M.Sc., Ph.D., FAHA

- **Areas of Interest:** socioeconomic status over the life course, women's health, minority health, modifiable predictors of cardiovascular disease outcome
- **WHI Obituary Link:** <https://www.whi.org/md/news/gerardo-heiss>

Dr. Rebecca Jackson, M.D.

- **Areas of Interest:** endocrinology, diabetes, genomics, metabolism, and osteoporosis.
- **WHI Obituary Link:** <https://www.whi.org/md/news/remembering-dr-rebecca-jackson>

Dr. Lewis Kuller, M.D., Dr.P.H., M.P.H.

- **Areas of Interest:** internationally renowned physician-epidemiologist who conducted research in multiple areas of medicine and public health. We may know him best for his exceptional work in cardiovascular epidemiology.
- **WHI Obituary Link:** <https://www.whi.org/md/news/remembering-dr-lewis-kuller>

HRQoL, Sleep Disturbance, and CVD Risk in Breast Cancer Survivors

Breast cancer survivors have a higher likelihood of long-term cardiovascular disease (CVD) morbidity and mortality. Survivors experience symptoms (e.g., fatigue, depression, sleep disturbance, decreased physical function) that may contribute to a lower health-related quality of life (HRQoL). HRQoL is a person's subjective view of health, which includes assessments of physical and emotional well-being. Previous literature determined that various survivor symptoms associated with HRQoL may increase the odds of a CVD event. The associations have not been investigated in breast cancer survivors. Therefore, Alexi Vasbinder et. al evaluated post-cancer physical and mental HRQoL, sleep disturbance, and CVD events in postmenopausal women. Finding associations could aid in recommending guidance to nurses on strategies to reduce CVD in breast cancer survivors. The final sample size included 2,844 breast cancer survivors with and without CVD events. Data was included from The Life and Longevity After Cancer (LILAC) study — a cancer survivorship sub-cohort within WHI, and clinical trial and observational study WHI cohorts.

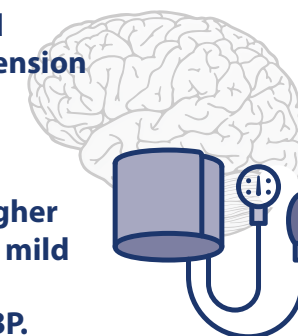
The researchers found that poorer physical HRQoL scores were associated with CVD in breast cancer survivors.

Physical function and perception of general health, two subcategories of HRQoL which have a significant impact on its overall score, appeared to drive this association. Researchers found no association of mental HRQoL or sleep disturbance with CVD risk. This was the first study to evaluate physical and mental HRQoL, sleep disturbance, and risk of CVD within a cohort of breast cancer survivors. Vasbinder et. al believe that future studies should include physical component scores from HRQoL in prediction models of CVD among breast cancer survivors and determine the effect of inflammation on physical HRQoL and CVD risk.

Blood Pressure Levels and Cognitive Impairment in Older Women

Current literature reports that hypertension is a major risk factor for cognitive impairment disorders, including dementia. To date, studies that iCurrent literature reports that hypertension is a major risk factor for cognitive impairment disorders, including dementia. To date, studies that include SBP (systolic blood pressure); PP (pulse pressure) and risk of cognitive impairment in older women have yielded inconsistent results. Therefore, Longjian Liu et. al evaluated the association of BP (blood pressure) and hypertension treatment status with mild cognitive impairment and dementia in postmenopausal women from the WHI Memory Study (WHIMS). Normal levels of BP are defined as less than 120/80 mm Hg. PP is the difference between SBP and DBP (diastolic blood pressure), and normal levels are less than 50 mm Hg. The outcome measures consisted of mild cognitive impairment, probable dementia, and cognitive loss. The study included 7,207 older women.

The researchers reported that women with hypertension and a SBP of 120 mm Hg or greater who took anti-hypertensive meds were at a significantly higher risk of cognitive loss and mild cognitive impairment than those with normal BP.

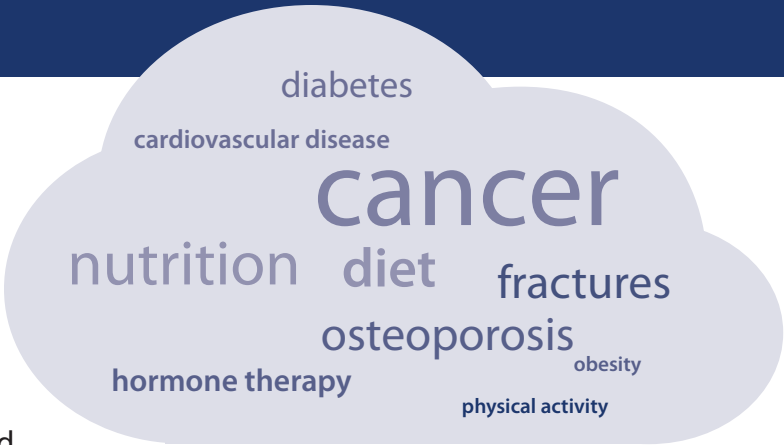


Women with hypertension and SBP lower than 120 mm Hg did not have a higher risk of cognitive loss or mild cognitive impairment. Next, women who did not take anti-hypertensive meds and who had a PP of 70 mm HG or higher or women who took anti-hypertensive meds and had a PP of 50 mm Hg or higher had an increased risk of cognitive loss and mild cognitive impairment compared to those with a PP less than 50 mm Hg. Lastly, hypertension, increased SBP, and increased PP were not associated with dementia risk. These results increase the growing evidence that normal SBP and PP levels are important in conserving cognitive health among older women.

You and the impact of your participation over the past 30 years

The Women’s Health Initiative remains one of the most important and influential studies in women’s health. This year we celebrate and thank the women who made it all possible and remind you that your decades of contributions have helped women around the world. WHI continues to play a crucial role in our understanding of women’s health issues, and will continue to do so for years to come.

Above is a word cloud showing some of the more common health topics that WHI covers. The larger the word, the more often the health topic has been covered using WHI data.



Demographics

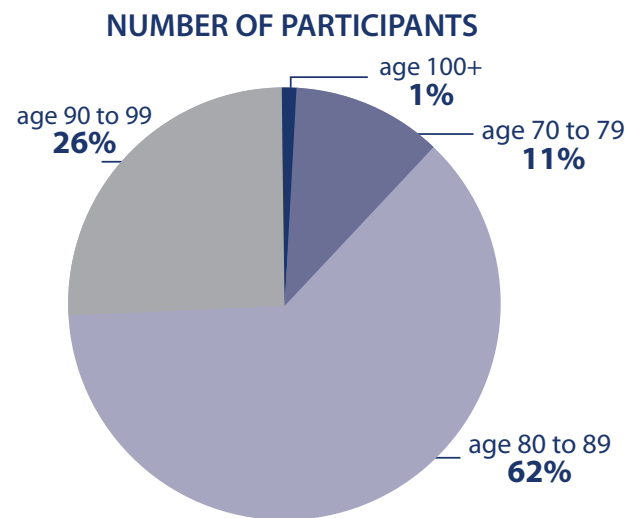
When recruitment ended in 1998, WHI had 161,808 participants enrolled and randomized in the study.

Here are some interesting WHI participant facts:

- ❖ Most of you are between 80-90 years old and 472 of you are over 100
- ❖ You have been participating in the study for an average of 26.4 years! The shortest time of participation has been 24.2 years, and the longest has been 29.4 years (practically 30 years!)
- ❖ You are from all 50 states plus Puerto Rico and the Virgin Islands
- ❖ 17% of participants were considered racial or ethnic minorities (the goal was 20%)
- ❖ Over 50,000 of you are still actively contributing data to WHI

Additional interesting facts about WHI:

- ❖ You have collectively completed a total of 3,237,092 Form 33s – the Medical History Updates forms
- ❖ Over 5 million blood samples and other products have been collected
- ❖ 2,264 publications have come out of WHI
- ❖ 313 studies have been funded using WHI data, and 28 studies are currently in submission
- ❖ Over 300 investigators are currently active with WHI with thousands of scientists and staff having been involved with WHI at some point in their careers.



Clinical Impact and Key Findings

- WHI estrogen plus progestin trial findings resulted in 4.3 million fewer combined hormone therapy users, 126,000 fewer breast cancer cases, 76,000 fewer cardiovascular disease cases, 263,000 more fractures, and 145,000 more quality-adjusted life-years over 10 years.

Reference: Roth, Joshua A. et al. Economic return from the Women's Health Initiative estrogen plus progestin clinical trial: a modeling study. *Ann Intern Med.* 160.9 (2014). 594-602.

Link: <https://pubmed.ncbi.nlm.nih.gov/24798522/>

- The US Preventative Services Task Force (USPSTF) found 20 randomized clinical trials that compared the effects of estrogen, either alone or in combination with progestin, versus placebo for the prevention of chronic conditions. Of these studies, the WHI trials were the only studies powered to assess the effectiveness of hormone therapy for the primary prevention of various chronic conditions.

Reference: Mangione, Carol M., et al. Hormone therapy for the primary prevention of chronic conditions in postmenopausal persons: US Preventive Services Task Force recommendation statement. *JAMA* 328.17 (2022). 1740-1746.

Available at: <https://pubmed.ncbi.nlm.nih.gov/36318127/>

- The WHI Calcium and Vitamin D trial, which studied daily supplementation with 1000mg of calcium and 400 IU of vitamin D3 (cholecalciferol), reported no significant reduction in any fracture outcome but a modest increase in bone density; thus, the US Preventative Services Task Force (USPSTF) concluded that supplementation with 1000mg or less of calcium and 400 IU or less of vitamin D does not prevent fractures.

Reference: Grossman, David C., et al. Vitamin D, calcium, or combined supplementation for the primary prevention of fractures in community-dwelling adults: US Preventive Services Task Force recommendation statement. *JAMA* 319.15 (2018). 1592-1599.

Available at: <https://pubmed.ncbi.nlm.nih.gov/29677309/>

- In a number of studies, including the WHI Low-fat dietary trial, dietary patterns that increased vegetables, fruits, and grains, and that were lower in animal products and refined carbohydrates, were associated with reduced risk of postmenopausal breast cancer and type-2 diabetes.

Reference: Dietary Guidelines Advisory Committee. 2020. Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

Available at: <https://doi.org/10.52570/DGAC202>

Economic Impact

- Congress originally approved \$625 million for WHI in 1992. An additional \$94 million was added before the study started enrolling participants in 1993.
- The WHI estrogen plus progestin trial resulted in a projected overall savings of \$35.2 billion in medical expenses. The corresponding net economic return of the trial was \$37.1 billion (\$140 per dollar invested in the trial) at a willingness-to-pay level of \$100,000 per quality-adjusted life-year.

Reference: Roth, Joshua A. et al. Economic return from the Women's Health Initiative estrogen plus progestin clinical trial: a modeling study. *Ann Intern Med.* 160.9 (2014). 594-602.

Available at: <https://pubmed.ncbi.nlm.nih.gov/24798522/>

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Send your feedback on the newsletter and participant’s webpage!

Due to the volume of correspondence we receive, we will not be able to respond to everyone individually. We also regret that we cannot answer questions about individual medical conditions.

Staff Information:

WHI Matters is produced by the WHI Coordinating Center at the Fred Hutchinson Cancer Center.