

Fred Hutchinson Cancer Center 1100 Fairview Avenue N, M3-A410 PO Box 19024 Seattle, WA 98109

2021-2022

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EXTENSION STUDY

WHI MATTERS PUBLICATION OF THE WOMEN'S HEALTH INITIATIVE | 2021-2022

COSMOS Study Findings

We now have the results of the largest and longest randomized trial of daily cocoa extract supplementation, and the largest trial of multivitamin supplementation, for the prevention of cardiovascular disease and cancer! The results were published in *The American Journal of Clinical Nutrition* (AJCN). COSMOS includes 21,442 participants—12,666 women aged 65 or older and 8,776 men aged 60 or older—who were followed for an average of 3.6 years through the end of 2020. These are the summary of findings for the studied cocoa extract and multivitamin supplements:

Summary of Findings:

- COSMOS provides the first suggestive evidence that long-term cocoa extract supplementation may favorably impact clinical cardiovascular outcomes, including a significant 27% reduction in cardiovascular death. Although the results for the primary endpoint of total cardiovascular disease were not statistically significant, greater risk reductions were seen among those taking the study pills regularly.
- Additional research is needed to understand how cocoa extract supplementation may reduce cardiovascular events through continued follow-up of COSMOS participants and ongoing ancillary studies examining mechanisms of effect along with other aging-related outcomes.
- · COSMOS did not find that a daily multivitamin reduced the risk of total cancer or cardiovascular disease among generally healthy older men and women.
- Multivitamins are safe and remain the most frequently used dietary supplement, and future studies are needed to clarify its role on nutritional status and other aging-related outcomes.
- Preliminary promising results on multivitamins and cognition were previously reported to you, and the final reports on cognition for both COSMOS interventions should be published in several months.

Please visit cosmostrial.org to find more information about the COSMOS Trial.

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Long Life Study 2 (LLS2) Launching

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.

WESTERN REGIONAL CENTERS		NORTHEASTERN REGIONAL CENTERS		
Kaiser Permanente/Bay Area Clinic, Oakland, CA South Bay WHI Program, Torrance, CA 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 University of Hawaii, John A. Burns School of Medicine, Honolulu, HI	Stanford University (888) 729-8442	New Jersey Medical School, Newark, NJ 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 Brigham and Women's Hospital, Boston, MA Charlton Memorial Hospital, Fall River, MA	University at Buffalo (855) 944-2255 (716) 829-3128 Brigham and Women's Hospital	
University of Nevada, Reno, NV UC San Diego Clinical Center, Seattle, WA]	Memorial Hospital of Rhode Island, Pawtucket, RI UMASS/FALLON Women's Health, Worcester, MA	(800) 510-4858 (617) 278-0791	
Seattle Clinical Center, Seattle, WA University of Alabama, Birmingham, AL Emory University, Decatur, GA University of Florida Clinical Center, Gainesville, FL University of Florida Clinical Center, Jacksonville, FL University of Miami School of Medicine, Miami, FL	Fred Hutchinson Cancer Center (800) 514-0325	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	Ohio State	
SOUTHEASTERN REGIONAL CENTERS		Detroit Clinical Center, Detroit, MI	University	
UNC Women's Health Initiative, Chapel Hill and Durham, NC Women's Health Initiative of the Triad, Greensboro, NC Women's Health Initiative, Winston-Salem, NC University of Tennessee, Germantown, TN University of Tennessee – Medical Center, Memphis, TN Baylor College of Medicine, Houston, TX University of Texas Health Science Center, San Antonio, TX	Wake Forest University School of Medicine (877) 736-4962	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	(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



WHI Webinar Announcement

We are excited to announce the 2022 WHI webinar series which began in January 2022 on Zoom. The webinars will occur quarterly. The January 19 and April 20 webinars were recorded and available on our website. Additional webinars will be held on July 20, and October 19 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 http://www.whi.org/ **pptwebinar** for more details.

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FAQs about COSMOS Study

Should I start taking cocoa extract supplements and/or a multivitamin? 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. It remains very important to have a healthy, balanced diet rich in fruits, vegetables, and other foods. These final results, as well as the upcoming ancillary results from COSMOS, will create a more complete picture and help you and your doctor make a final decision. Our general guidance at this time is not to change whatever you are currently doing. For those taking either supplement, there were no safety concerns noted during the COSMOS trial.

Are the results tied to specific products? Should I expect the same effects with other similar products?

The multivitamin tested in COSMOS, Centrum Silver®, is very similar to the current Centrum Silver® Adults 50+ multivitamin, which contains a comprehensive array of essential vitamins and minerals to help meet recommended daily intakes. 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.

Can I consume cocoa flavanols from chocolate?

Though cocoa is a key ingredient in milk and dark but not 'white chocolate', variation in processing of the cocoa bean and its negative impact on flavanol content makes chocolate an unreliable source of flavanols. Chocolate products do not typically indicate their flavanol content, and darker or higher % cacao chocolate does not necessarily mean greater flavanol content. Importantly, it would be very difficult to consume the amount of cocoa flavanols studied in COSMOS from chocolate products without adding a large amount of fat, sugar and calories to your diet.

Focus on Findings

Here, we highlight a selection of the many research articles that have been published by the WHI investigators over the past year. As always, if you would like to read the full version of any of these papers, feel welcome to contact us and we will be happy to provide you with a copy. See the Correspondence box on page 7 for our contact information.

Disparities exist in how women recover from knee replacement

(Journal of the American Medical Association, May 2020)

Researchers looked at how well women recovered and got back to moving after knee replacement. They studied about 10,000 women who were part of the WHI.

About a million knee replacements are done in the United States each year, and about 60 percent of those surgeries are on women.

Using Medicare records from 1993 until 2014, lead author Dr. Alyson Cavanaugh, DPT, PhD, (from the University of California in San Diego), and her colleagues looked at how much function women had before and after the operation. They created a 36-point set of questions to try to measure this, such as how easily a person could walk a block among other items.

Different people approach getting a knee surgery differently. Some people may delay longer than others, due to worries about the procedure or paying for it. Others may come in sooner and have less worry about surgery. There are also differences in the way people

Puzzles & coloring

Coloring Pages

Coloring pages aren't just for kids! Coloring can help with reducing stress, anxiety, and bring more mindfulness.

Sudoku

Sudoku is easy to play and the rules are simple. Fill in the blanks so that each row, each column, and each of the nine 3x3 grids contain one instance of each of the numbers 1 through 9.

CORRESPONDENCE

Send your feedback on the newsletter and the new participant's webpage!

E-mail us at: whimatters@whi.org Or, send letters to: Fred Hutchinson Cancer Center 1100 Fairview Ave. N M3-A410 P.O. Box 19024 Seattle, WA 98109

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.



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Long Life Study 2 (LLS2) launching in summer of 2022

From 2012 to 2013, over 7,800 women in the 2nd WHI Extension Study participated in the Long Life Study (LLS1). They provided a blood sample, body measures, and performed physical and function tests at an in-home visit.

LLS1 was designed to collect data and fasting blood from a subset of WHI participants to establish a new baseline from which studies on aging and health/disease could be conducted. Long Life Study 2 (LLS2) is designed to repeat the protocol of the Long Life Study 1. Both LLS1 and LLS2 data are intended to support studies of aging and provide updated biospecimens. LLS2 will repeat the Long Life Study activities on all surviving members of the LLS1 group who consent to a second study in home visit.

LLS2 was originally planned to begin in 2021 however was delayed due to the COVID 19 pandemic. LLS2 visits will again involve an in home visits which will include a brief physical exam, including body measurements, blood pressure and pulse, and an assessment of functional status. A fasting blood sample will also be taken.

Recommendations from WHI participants for activities to stay engaged and combat loneliness

- "Check out "Make Room at the Table" on Facebook or elsewhere to help with loneliness."
- "Fact-checking research keeps me using my brain and my time!"
 - Outdoor walking group has been a major help for me. Others find tennis groups helpful."
 - "I've been really enjoying online courses with OLLI (Osher Livelong Learning Institute) and now have been accepted as a moderator to assist the instructor of a Broadway Musical course in a series which I really love. I am also participating in
 - OLLI and in my UU Fellowship workshops to increase my awareness of racial inequities and learn more to become an antiracist ally. (I am White and 82!) I've had to let go of Tai Chi in person, but I can participate in

a NIA (National Institute of Aging) dance class online and have been in a Course in Miracles study group now online for 10 years."

- "Love NIA (non-impact aerobics). Started during the pandemic and am continuing."
- "I lead an exercise group on Zoom 2x per week. Both exercise and socialization. Entering my 13th year of doing this and some of the group have been in class from the start."
- "Other ideas? Walking several times in the woodlands. I took many courses of Great Courses on sciences (bio, chem, physics), engineering, aeronautics, info sic tech., quantum physics + Coursera courses in Arctic Economy and Talmud! Fascinating and time consuming and fruit for thought! Never bored!"
- "I've been taking online classes at Masterclass. Everything from design, meditation, acting ... whatever interests you."
- For more information on classes and workshops that connect women please visit https://www.womens-exchange.org/

recover after coming home. Some may get better rehabilitation or physical therapy than others. Some people may have better family support for their post-surgery rehabilitation.

The study found that race made a difference in how well patients recovered.

Black women who had worse mobility before surgery also had worse function after surgery. The study also found that Black women had significantly poorer function than women of other races. Study authors speculated that Black women might delay getting surgery because of worries about post-surgery rehabilitation therapy mistrust of medicine in general, fewer financial resources for copayments, or how they will make up lost wages during recovery.

The study authors recommend offering Black women more help with arthritis in the years before surgery so they can maintain mobility and have better outcomes if surgery is required later.

This study found that race made a difference in how well patients recovered, with Black women having worse post-surgical function after surgery than women of other races.



Plant-based diets win gold star for lowering risks

(Journal of the American Heart Association, 2021)

All proteins are not equal. Researchers keep trying to figure out which ones are best for a long and healthy life.

In this large study, researchers used 18 years of follow-up information on about 100,000 WHI

participants to find whether diets high in meat protein pose different health risks than diets high in plant or dairy proteins.

Previous studies have tried to tease apart the difference in risk between different sources of protein in the diet but have had inconsistent results.

Lead author Dr. Wei Bao, MD, PhD, of University of lowa School of Public Health, and colleagues found

that WHI participants who ate more plant protein and those who substituted plant for animal protein had lower risk of death.

This lower risk includes less chance of suffering both heart disease and dementia.

This study was the first to show a connection between animal and plant proteins and dementia risk. The study also supports nuts as potentially healthier substitutes for red meat, eggs, and dairy products and legumes. Legumes include beans and peas.

The authors would like to see changes in the "dietary guidelines" that are recommended to people reflecting this discovery about plant proteins.

"Our findings highlight the need to consider healthier protein sources in future dietary guidelines," they wrote.



30 Year WHI Journey with Dr. Shumaker

Sally Shumaker, PhD, a long-time advocate for women's health research, shares her story.

I am excited to share my WHI journey with all of you—the incredibly amazing women who made this major study possible. My path goes back a bit before the launching of WHI, to the time when I was a Health Scientist Administrator at the National Heart, Lung & Blood Institute (NHLBI) at NHI. During that time there was a rapidly growing recognition throughout the United States that women had been excluded from most of the large studies on heart disease (the leading cause of death in women), as well as other important research areas. This led to pressure from congress (emanating in part from the women's caucus), health providers seeking more information on the health trajectory of their women patients, and research scientistsculminating in the requirement by congress that NIH include women in research studies. During that same period, I had the privilege of working with and becoming a friend and colleague of Dr. Bernadine Healy who was on the NHLBI Council—and a leading advocate for research on women's health. Dr. Healy became the first (and still the only—but hopefully not the last) woman Director of the NIH. Though Dr. Healy was NIH Director for a brief time, she garnered the support and resources to launch the

largest longitudinal study on post-menopausal women ever conducted—and the WHI was born. You may be surprised to learn, given the overwhelming success of WHI, that there was a fair amount of pushback in launching this pivotal study. Scientists and administrators raised concerns about the feasibility and costs of WHI. Nevertheless, and as we now know—they were wrong and a group of highly dedicated scientists, skilled staff on the front lines throughout the country, and public advocates, turned the impossible into reality. And most importantly, the strong commitment of women like yourselves, throughout the United States joined in this

"...through your participation [you continue to provide] the science-based information needed to better understand and address the leading causes of morbidity and mortality in women; serving not so much your own needs, but the needs of future generations."

landmark study and continue to provide, through your participation, the science-based information needed to better understand and address the leading causes of morbidity and mortality but the needs of future generations.

I have served on the WHI Steering Committee for most of WHI's existence, and recently as the in women; serving not so much your own needs, Steering Committee Chair, a role I transitioned out of on February 1 of this year. WHI has played What an exciting and fulfilling trip this has been a pivotal role in my life and being part of this for me. Over the years, I served in a number of study has been the most rewarding part of a roles within WHI. I was part of the first contract long and fortunate career. I look forward to with the Coordinating Center, as a co-investigator continuing to work with my colleagues in WHI on a subcontract at Wake Forest School of in further advancing the knowledge we gain on women's health. I appreciate the many scientists, Medicine. I later became the Principal Investigator on that contract and through this role visited administrators, and staff who continue to make several WHI clinical sites. During those visits I met WHI much more than simply "feasible"—but staff and spoke with many of the participants an unprecedented study that will contribute throughout the country; seeing firsthand the to our knowledge of women's health for many incredible dedication of the staff and investigators years to come. In addition, I am most grateful to at the sites who spent long hours including many all of the women who agreed to be part of this weekends to recruit and address the concerns complicated and demanding study. You are the of the participants, and together moving the ones who proved the skeptics wrong—by getting on board and giving of your time. I cannot begin "impossible" forward. I was also a co-investigator on the first round of clinical sites for WHI-referred to thank you enough for all you have done for to as the Vanguard Clinical Sites. My primary advancing our understanding of women's health interests are in women's health, aging, and the throughout the world. Your impact will be felt for more social and psychological domains that years to come.

include depression, anxiety, positivity, quality of life, and cognition and memory. I worked with the Behavioral Health Committee in WHI to identify important "psychosocial" issues to address in our various forms and questionnaires. When an opportunity arose to add cognition, memory and dementia to the WHI Hormone Trials, I brought together an outstanding group of scientists and led the Women's Health Initiative Memory Study (WHIMS), in which many of you participated. WHIMS went on to include several "ancillary" studies on cognition in younger women (WHIMS-Y), and two MRI studies. WHIMS continued until November 2021, becoming one

> of the largest longitudinal studies on cognition and memory in older women, significantly influencing treatment practices in post-menopausal women. In addition, we developed and validated a study methodology for measuring

memory by telephone and this method is in use in cognitive studies throughout the world.