INFORMED CONSENT FORM

Official Title of Study:
Resveratrol for the Prevention of Bone Loss in Postmenopausal Women

ClinicalTrials.gov Identifier (NCT Number):
NCT06250283

Document Date:
March 31, 2025

This document is being submitted to ClinicalTrials.gov in accordance with applicable requirements. This informed consent form does not contain any personally identifiable information of research participants.

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Title of Study: Resveratrol for the prevention of bone loss in postmenopausal women

Principal Investigator(s): Sheau Ching Chai, PhD, RD, Xin L. Lu, PhD

This study is funded by the National Institutes of Health

KEY INFORMATION

Important aspects of the study you should know about first:

- **Purpose:** The purpose of this study is to examine whether daily supplementation of resveratrol would improve bone health in postmenopausal women.
- **Procedures**: If you choose to participate, you will be asked to either take a capsule of resveratrol (500 mg) or placebo daily for 24 weeks. In addition, you will also be asked to take 500 mg calcium plus 400 IU vitamin D3 daily for 24 weeks. Bone markers will be assessed before and after 12 weeks and 24 weeks intervention. Bone density will be assessed before and after 24 weeks intervention using dual-energy X-ray absorptiometry (DXA).
- **Duration:** In addition to the screening session, there will be 3 sessions over a 24-week period. Each session will take about 1.5 to 2 hours. You will be asked to collect a stool sample and a 24-hour urine and record a 3-day diet prior to sessions 2, 3 and 4. Supplements will be picked up monthly and unused supplements will be returned.
- **Risks**: The risk or discomfort from this research is that the stool and urine collection may disrupt normal daily living. You may experience a little discomfort with the blood draw. You will be exposed to minimal radiation during DXA scans. You may experience gastrointestinal discomfort with taking new supplements.
- **Benefits:** There are no direct benefits to participation. However, you will receive DXA reports.
- **Alternatives:** There are no known alternatives available to you other than not taking part in this study.
- **Costs and Compensation:** If you decide to participate, there will be no additional cost to you, and you will be compensated up to $200 for the full completion of the study.
- **Participation:** Taking part or not in this research study is your decision. You can decide to participate and then change your mind at any point.

Please carefully read the entire document. You can ask any questions you may have before deciding if you want to participate.

You are being invited to participate in a research study. This consent form tells you about the study including its purpose, what you will be asked to do if you decide to take part, and the risks and benefits of being in the study. Please read the information below and ask us any questions you may have before you decide whether or not you want to participate.

PURPOSE OF THE STUDY

Menopause increases the risk of osteoporosis. On average, women lose up to 10% of their bone mass in the first five years after menopause. Resveratrol is a natural antioxidant present in the human diet in foods such as blueberries, red grapes, and peanuts. The purpose of this study is to examine whether daily supplementation of resveratrol would improve bone health in postmenopausal women. This study will also be used for the development of a student's thesis.

WHO IS BEING ASKED TO PARTICIPATE?

You will be one of approximately 68 participants.

You are being asked to participate because you are a postmenopausal woman (1 to 10 years after natural menopause), whose lumbar spine, hip, or forearm bone mineral density (BMD) t-score is between 1 and 2.5 SD below the mean (indicating low bone mass).

There are several factors that may result in your exclusion from the study. These include the use of blood thinners (e.g., heparin, warfarin, aspirin, clopidogrel), endocrine (e.g., prednisone, other glucocorticoids) or neuroactive (e.g., Dilantin, phenobarbital) drugs, hormone therapy or any drugs known to influence bone and calcium metabolism or having a diagnosed or history of metabolic bone disease, renal disease, a history of kidney stones, cancer, cardiovascular disease, diabetes mellitus, respiratory disease, gastrointestinal disease (i.e. irritable bowel syndrome, inflammatory bowel disease, chronic constipation, and functional dyspepsia), and liver disease. Women with severe menopausal symptoms, serious mood alterations, sleep disturbances, abnormal uterine bleeding, endometriosis, pelvic inflammatory disease, endometrial polyps, and significant uterine fibroids will also be excluded. Additionally, women with bone mineral density (BMD) t-score at any site that falls below 2.5 SD (osteoporosis) or between 1 and -1 SD of the mean, smokers (≥ 20 cigarettes per day), those with a BMI <20 and > 30 kg/m^2 or those who have a history of resveratrol/microcrystalline cellulose intolerance, or an allergic reaction to resveratrol, microcrystalline cellulose, grapes, red wine, or blueberries will be excluded from the study. Participants will be requested to take a daily dose of 500 mg calcium plus 400 IU vitamin D3. Those who wish to take more than the recommended protocol doses will be excluded from the study.

PROCEDURES: WHAT WILL YOU BE ASKED TO DO?

As part of this study, you will be asked to come to the STAR Tower and Health Sciences Complex at the STAR campus of the University of Delaware for a total of 6-8 times (including pick-up monthly supplements). The following description is a breakdown of what will happen at each session:

Session 1 (screening, approximately 1.5-2 hours): A researcher will explain the complete study to you and answer any questions that you might have. If you agree to participate, you will be asked to sign the consent form. Next, you will be asked to complete a DXA scan, various questionnaires including medical history, demographic, food frequency questionnaire, physical activity questionnaire, Greene Climacteric Scale, Hospital Anxiety and Depression Scale, and Women's Health Questionnaire. You will be weighed, and your height, hip & waist circumference, and

resting blood pressure will be measured. Based on the results of this session, we will let you know if you are eligible to participate in this 24-week intervention study.

24-week intervention study: You will be randomly assigned to either take a capsule of resveratrol (500 mg) or placebo daily for 24 weeks. You will also be asked to take a 500 mg calcium plus 400 IU vitamin D3 daily for 24 weeks. Neither you nor the researcher will know whether you are receiving resveratrol or the placebo capsules until the study is over.

Supplements: A commercially available resveratrol (Mega Resveratrol), microcrystalline cellulose (Mega Resveratrol), calcium with vitamin D3 (Nature Made) will be used in this study. Placebo capsules that contain inactive ingredients (microcrystalline cellulose within vegetarian capsule). Microcrystalline cellulose is a common food and pharmaceutical additive that adds texture to food and delivers active ingredients in medication. Microcrystalline cellulose is also known as cellulose (fiber).

Study Procedure/Assessment	Session 1 (screening)	Session 2 (baseline)	Session 3 (12-week)	Session 4 (24-week)
Eligibility Criteria and Informed Consent	X			
Medical History and Demographic	X			
Food Frequency Questionnaire	X			
Greene Climacteric Scale (menopausal symptoms), Hospital Anxiety and Depression Scale, and Women's Health Questionnaire	X	X	X	X
Anthropometrics, Blood Pressure, and Physical Activity	X	X	X	X
3-day Diet Record		X	X	X
DXA scan	X			X
Fasting Blood Draw, Urine and Fecal		X	X	X

You will come to the STAR campus between sessions 1 and 2 to pick up a urine and stool container. Prior to returning to the study site for your session 2 and 3, you will be instructed to collect a stool sample and a 24-hour urine sample. You will be asked to record a 3-day diet record.

Sessions 2 and 3 (approximately 1.5 hours each): A physical activity questionnaire, Greene Climacteric Scale, Hospital Anxiety and Depression Scale, and Women's Health Questionnaire will be administered. Fasting blood (2 oz) will be collected. You will be weighed, and your hip & waist circumference, and resting blood pressure will be measured. You will be asked to submit a 3-day diet record.

For the next 24 weeks, you will be asked to consume the provided supplements in the morning after breakfast. You will be instructed to continue your typical physical activity and diet routines for 24 weeks.

Prior to returning to the study site for your session 4, you will be instructed to collect a stool sample and 24-hour urine sample. You will be asked to record a 3-day diet record.

Session 4 (approximately 2 hours): A physical activity questionnaire, Greene Climacteric Scale, Hospital Anxiety and Depression Scale, and Women's Health Questionnaire will be administered. Fasting blood (2 oz) will be collected. You will be weighed, and your hip & waist circumference, and resting blood pressure will be measured. You will be asked to submit a 3-day diet record and complete a DXA scan.

Here is a specific explanation of each procedure you will be asked to do:

DXA scan: You will be asked to have DXA scans for bone mineral density at sessions 1 and 4. This scan tells us your body mass and bone mineral density. The scan is done fully clothed. We ask that you refrain from wearing metal that day (i.e. do not wear an underwire bra, jewelry, watches or belts). During this test, you will lie flat on a table and a machine will take x-ray pictures of different areas of the body. As an option, if you had a DXA scan performed within the three months prior to joining the study, you may share your report with the research team for screening purposes.

Stool and 24-hour urine collection: You will be asked to collect a 24-hour urine and a small stool sample into a plastic container at home and return it during an in-person visit. Your name will not appear on the stored stool samples, rather, the sample will be coded with a number. To determine how supplementation of resveratrol influences bone health, stool samples will be analyzed for gut bacteria and plant-based substances metabolism. The urine samples will be analyzed for markers of bone formation and bone resorption, and plant-based metabolism. The samples will be stored for up to 20 years, then will be destroyed.

Blood draw: Fasting blood is drawn at sessions 2-4 during the in-person visits. Venous blood samples will be drawn by a nurse from the Nurse Managed Primary Care Center or by Dr. Sheau Ching Chai. Your name will not appear on the stored samples, rather, the sample will be coded with a number. The samples will be analyzed for markers of bone formation and bone resorption. The samples will be stored for up to 20 years, then will be destroyed.

WHAT ARE POSSIBLE RISKS AND DISCOMFORTS?

DXA scan: This research study involves exposure to radiation from a DXA scan. The total effective radiation dose from DXA scan is about 1.87 mrem. For comparison, the average person in the United States receives a radiation exposure of .82 mrem per day from natural background sources. The total amount of radiation dose that you will receive during this study is approximately equal to an exposure of 2.5 days of natural background radiation. It does not include any exposure you may have received or will receive from other tests outside of this study that are a part of your medical care.

Blood draw, urine, and stool collection: You may experience local discomfort with the blood draw, but the discomfort is temporary. As with any break in the skin, there is a light risk of infection. Stool and urine collection may disrupt normal daily living. There are no known risks to providing a stool and urine sample.

Study regimen: Resveratrol, a dietary supplement, is commercially available but not regulated by the FDA. Like all dietary supplements, this makes it difficult to know the correct dose for safety and effectiveness. Resveratrol appears to have beneficial properties as well as potential risks. Risks and benefits may vary depending on the dose

given as well as other factors such other medications someone is taking. It is possible to develop an allergy/intolerance to resveratrol/microcrystalline cellulose. Researchers will follow-up with you after a couple of days of your first consumption. Additional follow-up will be made every two weeks until the study is completed. You should stop taking the supplement if there is any suspicion of allergic/intolerance reactions (nausea, vomiting, diarrhea, itchy rash, bloating) and report problems to the researcher and your primary physician. You should seek immediate medical care if a severe allergic (anaphylaxis) reaction occurs (dial 911). Anaphylaxis symptoms include: 1) skin reactions such as hives along with itching and flushed or pale skin (almost always present with anaphylaxis), 2) swelling of the lips, 3) difficulty breathing, 4) nausea, vomiting or diarrhea, and 5) dizziness or fainting. Although we do not anticipate that you will gain or lose weight as a result of participating in this study, there is a chance that your weight can change.

WHAT ARE POTENTIAL BENEFITS FROM THE STUDY?

You will not benefit directly from taking part in this research. However, you will receive a DXA reports. The results will not be interpreted but are provided for information. We encourage you to discuss your DXA reports with your Primary Care Practitioner.

Research is designed to benefit society by gaining new knowledge. Overall, the findings of this research may help us to learn more about how resveratrol influences bone health.

NEW FINDINGS THAT COULD AFFECT YOUR PARTICIPATION

During the course of this study, we may learn new important information. This may include information that could cause you to change your mind about participating in the study. If any new important

CONFIDENTIALITY: WHO MAY KNOW THAT YOU PARTICIPATED IN THIS RESEARCH?

Your study data will be handled as confidentially as possible. If the results of this study are published or presented, individual names and other personally identifiable information will not be used.
To minimize the risks to confidentiality, you will be assigned a participant number and will only be identified by the number on all questionnaires, biospecimens (blood, urine, and fecal), and in all databases. A list of names with corresponding numbers will be maintained only as a cross-reference for consent forms. The list and the consent forms will be in a locked cabinet located in a locked file room to which only the research team will have access. The linkage file will be destroyed at the time of study closure. Data may be used for retrospective analysis (for example, uses existing data to examine the association between an exposure and outcome). The electronic data will be stored in password protected files. Sensitive electronic data will be encrypted. The research team will make every effort to keep all research records that identify you confidential. All data stored as paper files or on a computer disk may be kept indefinitely. The biospecimen will be coded with a number and stored in a -80 freezer in a locked freezer room to which only the research team will have access. The collected biospecimen will be kept for up to 20 years, then will be destroyed.

We will keep your study data as confidential as possible, with the exception of certain information that we must report for legal or ethical reasons, such as intent to hurt yourself or others. If required, your records may be inspected by authorized personnel in the following groups and agencies: the University of Delaware Institutional Review Board.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

USE OF DATA COLLECTED FROM YOU IN FUTURE RESEARCH:

Identifiers about you will be removed from the identifiable private information and identifiable biospecimens and after such removal, the information and blood samples could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative. The researcher will investigate how resveratrol affects cardiovascular health and the way your genes work. Understanding that relationship could help identify how resveratrol and diet change modify/improve health outcomes.

COSTS AND COMPENSATION

There are no costs associated with participating in the study. You will be paid up to $200 to reimburse you for your time for the screening visit and the full completion of the 24-week trial. You will be paid in the form of cash or gift card at each session. The compensation will vary depending on the session. For instance, $20 for session 1, $30 for session 2, $30 for session 3, and $120 for the final session. If you decide to withdraw from the study, you will be compensated on a prorated basis for each session that you have completed.

WHAT IF YOU ARE INJURED DURING PARTICIPATION IN THE STUDY?

If you are injured during research procedures, you will be offered first aid at no cost to you. If you need additional medical treatment, the cost of this treatment will be your responsibility or that of your third-party payer (for example, your health insurance). By signing this document, you are not waiving any rights that you may have if injury was the result of negligence of the university or its investigators.

DO YOU HAVE TO TAKE PART IN THIS STUDY?

Taking part in this research study is your decision. You do not have to participate in this research. If you choose to take part, you have the right to stop at any time. If you decide later not to participate, or if you decide to stop taking part in the research, there will be no penalty or loss of benefits to which you are otherwise entitled. Your decision to stop participation, or not to participate, will not influence current or future relationships with the University of Delaware. As a student, if you decide not to take part in this research, your choice will have no effect on your academic status or your grade in the class.

If, at any time, you decide to end your participation in this research study, please inform our research team (Chai Nutrition & Health Laboratory) by calling (302) 831-7218 or emailing ChaiResearchLab@udel.edu. If you, or the

investigators, stop your participation in the study, we will keep any data collected of you until that point. If you do not complete all procedures listed in this form, you will only receive compensation for the tasks you finish.

INSTITUTIONAL REVIEW BOARD

This research study has been reviewed and approved by the University of Delaware Institutional Review Board (UD IRB), which is a committee formally designated to approve, monitor, and review biomedical and behavioral research involving humans. This study has also been registered on clinicaltrials.gov with the ID NCT06250283. If you have any questions or concerns about your rights as a research participant, you may contact the UD IRB at hsrb-research@udel.edu or (302) 831-2137.

CONTACT INFORMATION

If you have any questions about the purpose, procedures, or any other issues related to this research study, you may contact the Principal Investigator, Sheau Ching Chai, PhD, RD at (302) 831-7345 or scchai@udel.edu.

CONSENT TO PARTICIPATE IN THE RESEARCH STUDY:

I have read and understood the information in this form and I agree to participate in the study. I am 18 years of age or older. I have been given the opportunity to ask any questions I had and those questions have been answered to my satisfaction. I understand that I will be given a copy of this form for my records.

_____	_____	_____
Printed Name of Participant (PRINTED NAME)	Signature of Participant (SIGNATURE)	Date
_____	_____	_____
Person Obtaining Consent (PRINTED NAME)	Person Obtaining Consent (SIGNATURE)	Date

---

<u>OPTIONAL</u> CONSENT TO BE CONTACTED FOR FUTURE STUDIES:

Do we have your permission to contact you regarding participation in future studies? If you agree to being contacted in the future, we will keep your contact information. Please write your initials next to your preferred choice.

_____ YES _____ NO
