INFORMED CONSENT

For a research study entitled:

"Synbiotic Supplementation to Reduce Anxiety Symptoms in Female Breast Cancer Survivors"

A description of this clinical trial is available at https://clinicaltrials.gov/ct2/show/NCT04784182, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

This study is funded by the Auburn University College of Human Sciences and the University of Alabama at Birmingham Center for Clinical and Translational Science and is being conducted by Andrew D. Frugé, PhD, Auburn University Assistant Professor.

PURPOSE
The purpose of this study is to explore the beneficial effects of a combination prebiotic and probiotic (synbiotic) supplement on anxiety symptoms in females with a family history of or have survived a breast cancer diagnosis who are currently experiencing moderate to severe anxiety.

ELIGIBILITY
You were selected as a potential participant because you are a female breast cancer survivor who:
1) is 50 years of age or older;
2) has a family history of breast cancer OR have completed primary treatment for breast cancer;
3) are currently experiencing anxiety symptoms determined by the GAD-7 (total score >5 out of 21 possible points);
4) agree to not change dietary supplements over the course of the study;
5) are willing to comply with the daily supplement regimen over the course of the study;
6) are able to speak and read English.

Exclusion criteria:
1) changes in anxiety treatment (i.e., initiation of Cognitive Behavioral Therapy within the last 4 weeks)
2) changes in or initiation of anxiolytic medications within 6 months
3) Use of the following drugs within the last four weeks (unless indefinitely prescribed): systemic antibiotics, corticosteroids, immunosuppressive agents, or commercial probiotics, which can drastically affect the gut microbe composition.

Screening protocol and other details related to COVID-19
(Constructed to be in line with Auburn IRB COVID-19 Guidance March 27, 2020
(updated April 22, 2020, June 4, 2020, October 30, 2020, and July 21, 2021)
On your medical history form are questions related to COVID-19. We will ask you COVID-19 screening questions over the phone prior to any face-to-face visit, but ask that you answer these questions in writing as well.
Throughout the study, we will continue to ask as to whether or not any of those conditions apply to you. Also note that there are other precautions taking place to mitigate your exposure to COVID-19. These precautions will be highlighted throughout this document.

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If you have questions related to your risk of contracting the virus, please ask a staff member and they will be happy to answer questions.
Additionally, please visit https://cws.auburn.edu/ovpr/pm/irb-covid19-precautions for more details regarding safety precautions being taken by research staff throughout this study.

EXPLANATION OF PROCEDURES
This is a six-week study which involves two phases lasting 2-weeks and 4-weeks, respectively. All participants will participate in each of these phases; however, the allocation to either the synbiotic or placebo group will be random, like the flip of a coin. The entire study will require a time commitment of approximately 4 hours total over the six weeks.

In the first phase, 2-week run in period, you will be instructed to avoid fermented foods such as yogurt or sauerkraut while continuing your normal diet. In the second phase, you will receive 28-days worth of capsules containing either synbiotic compounds or placebo capsules containing starch.
You will be asked to come to the Auburn University campus a total of three (3) times throughout the study to provide the following:

1) At the first visit, you will be asked about your medical history and medications. At all visits you will be asked about your diet and physical activity and you will be asked to complete a short survey about anxiety symptoms.
2) Prior to each visit, you will be provided with a kit to collect a small fecal sample after a bowel movement. You will be instructed to freeze this sample and bring it with you to your next visit. We will analyze the fecal microbiome, which is the population of bacteria that live in your large intestine and whose composition may be associated with anxiety symptoms.
3) During each visit, a trained phlebotomist will draw 15mL (1 Tablespoon) of blood from your arm. Because of the blood tests that will be performed, you will be asked to "fast," that is, to not eat or drink anything except water for 12 hours before these appointments. We will analyze different proteins in your blood that may be associated with anxiety symptoms.
4) During each visit, we will measure your height, weight, waist, hips, and body composition using a handheld analyzer.

Details related to COVID-19
***Constructed to be in line with Auburn IRB COVID-19 Guidance March 27, 2020 (updated April 22, 2020, June 4, 2020, October 30, 2020, and July 21, 2021)
All visits will involve close interaction between you and staff due to testing procedures. We ask that you wear a cloth face covering during these visits (see the www.cdc.com for guidance on cloth face coverings for reference.)
Research Personnel that come within 6 feet of you will also be wearing a face covering, gloves, a face shield or goggles, and a surgical mask. We will be disinfecting testing equipment surfaces between participants with either 10% bleach or 0.5% hydrogen peroxide.
Finally, we will ensure that all Research Personnel do note present symptoms related to COVID-19 prior to their dealings with you as a research participant during these visits.

RISKS AND DISCOMFORTS
Participation in this study may involve some risks and discomforts that are included here for your information.

1) Blood draws will cause some pain when your arm is stuck with the needle. You could feel dizzy or faint. A bruise could be left temporarily at the spot where your arm is stuck. There is a slight

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chance of excessive bleeding, infection, inflammation of your vein, and/or blood clot formation; these are extremely rare.
2) You may feel some discomfort when disclosing personal information. When answering the questionnaires, you can skip any of the questions that you do not want to answer.
3) While we will protect your privacy and the information collected about you the very best we can, there always is a small chance of a breach in confidentiality.
4) It is possible that the synbiotic can cause gastrointestinal distress or discomfort

Risk & Precautions for COVID-19

Due to the need for your physical presence at the research site, there is a risk that you may be exposed to COVID-19 and the possibility that you may contract the virus. For most people, COVID-19 causes only mild or moderate symptoms. For some, especially older adults and people with existing health problems, it can cause more severe illness. Current information suggests that about 2% of people who are infected with COVID-19 might die as a result. You will need to review the Information on COVID-19 for Research Participants that is attached to this consent document. To minimize your risk of exposure we will describe precautions such as screening/rescreening of participant(s)/researcher(s), personal protection equipment for participant(s)/researcher(s), decontamination of surfaces, location configuration and distance between persons, etc. You will need to follow any precautions or procedures outlined by Auburn University and, when applicable, offsite locations.

BENEFITS

Participating in this study will involve consuming a supplement or placebo daily. While taking the supplement, you may experience reduced anxiety symptoms and improved bowel function. If you are in the placebo group, you will be provided with a four-week supply of the supplement at the conclusion of the study and receive the potential benefit at that time.

ALTERNATIVES

You are under no obligation to participate in this research, and foregoing this opportunity will in no way affect your insurance coverage or healthcare delivery.

CONFIDENTIALITY

The information gathered during this study will be kept confidential to the extent permitted by law. Therefore, all information collected will be stored in locked file cabinets in locked study offices, or in password protected computer files that are available only to trained study staff. Study ID numbers will be assigned to study participants to protect confidentiality.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed. You are free to withdraw from this research study at any time. Your choice to leave the study will not affect your relationship with this institution.

If you are an Auburn University student or employee, taking part in this research is not a part of your Auburn University class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at Auburn University. You will not be offered or receive any special consideration if you take part in this study.

COST OF PARTICIPATION

There will be no cost to you for participation in this research study. All study related examinations and education will be provided to you at no cost. In the unlikely event that you sustain an injury from participation in this study, the investigators have no current plans to provide funds for any medical expenses or other costs you may incur.

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PAYMENT FOR PARTICIPATION
If you are eligible, we will ask you to come to campus at the beginning of the study, and then twice more for your pre- and post-intervention visits. After each visit, you will receive $25, for a total of $75 over the 6-week period.

Should you have any questions about this research study, you can contact the study coordinator, Kristen Smith at 410-274-1784 or kss0034@auburn.edu, or Principal Investigator, Drew Frugé at 334-844-3271 or adf0003@auburn.edu. A copy of this document will be given to you to keep.

If you have any questions or concerns about your rights as a participant in this study, you can call the Auburn University Office of Research Compliance/IRB at 334-844-5966, or email at IRBadmin@auburn.edu.

SIGNATURES

HAVING READ THE INFORMATION PROVIDED, YOU MUST DECIDE WHETHER OR NOT YOU WISH TO PARTICIPATE IN THIS RESEARCH STUDY. YOUR SIGNATURE INDICATES YOUR WILLINGNESS TO PARTICIPATE.

_____	_____
Signature of Participant Date	Investigator obtaining consent Date
_____	_____
Printed Name of Participant	Printed name of investigator
	_____
	Coinvestigator Date
	_____
	Printed name of coinvestigator

The Auburn University Institutional Review Board has approved this Document for use from 04/10/2022 to 04/09/2023
Protocol # 21-110 MR 2104

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Information on COVID-19 For Research Participants (updated 05/27/2021)

Auburn University recognizes the essential role of research participants in the advancement of science and innovation for our university, community, state, nation, and beyond. Therefore, protection of those who volunteer to participate in Auburn University research is of utmost importance to our institution.

As you are likely aware, COVID-19 references the Coronavirus that is being spread around the world including in our country, state, and community. It is important that we provide you with basic information about COVID-19 and the risks associated with the virus so that you can determine if you wish to participate or continue your participation in human research.

How is COVID-19 spread? COVID-19 is a respiratory virus that is spread by respiratory droplets, mainly from person-to person. This can happen between people who are in close contact with one another. COVID-19 may also be spread by exposure to the virus in small droplets that can linger in the air. This kind of spread is referred to as airborne transmission. It is also possible that a person can get COVID-19 by touching a surface or object (such as a doorknob or counter surface) that has the virus on it, then touching their mouth, nose, or eyes.

Please visit the CDC's web page for more information on how COVID-19 spreads.

Can COVID-19 be prevented? Although there is no guarantee that infection from COVID-19 can be prevented, there are ways to minimize the risk of exposure to the virus. For instance, stay 6 feet apart from others who don't live with you; get a COVID-19 vaccine when it is available to you; avoid crowds and poorly ventilated indoor spaces; use effective barriers between persons; wear personal protective equipment like masks, gloves, etc.; wash hands with soap and water or use hand sanitizer after touching objects; disinfect objects touched by multiple individuals.

What are the risks of COVID-19? For most people, COVID-19 causes only mild or moderate symptoms, such as fever and cough. For some, especially older adults and people with existing health problems, it can cause more severe illness. While everyone is still learning about this virus, current information suggests that about 1-3% of people who are infected with COVID-19 might die as a result.

Who is most at risk? Individuals over age 65 and those with chronic conditions such as cancer, diabetes, heart or lung or liver disease, severe obesity, and conditions that cause a person to be immunocompromised have the highest rates of severe disease and serious complications from infection.

What precautions should be taken? Based on the proposed research, precautions for the risk of COVID-19 will be addressed on a project by project basis. You will be provided with information about precautions for the project in which you may participate. Any site where research activities will occur that are not a part of Auburn University (offsite location) are expected to have standard procedures for addressing the risk of COVID-19. It is important for participants to follow any precautions or procedures outlined by Auburn University and, when applicable, offsite locations. Further, participants will need to determine how best to address the risk of COVID-19 when traveling to and from research locations. The US Center for Disease Control and Prevention has issued recommendations on types of prevention measures you can use to reduce your risk of exposure and the spread of COVID-19.

Auburn University is continuing to monitor the latest information on COVID-19 to protect our students, employees, visitors, and community. Our research study teams will update participants as appropriate. *If you have specific questions or concerns about COVID-19 or your participation in research, please talk with your study team.* The name and contact information for the study team leader, along with contact information for the Auburn University Institutional Review Board for Protection of Human Research Participants, can be found in the consent document provided to you by the study team.

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