Informed Consent

Study Title: INtervention for Cognitive Reserve Enhancement in Delaying the Onset of Alzheimer's Symptomatic Expression: The INCREASE Study

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	11/20/2019
NCT Number:	NCT02849639
IRB Number	16-0375-F2L
Coversheet created:	11/8/2021

Combined Consent and Authorization to Participate in a Research Study

INtervention for **C**ognitive **R**eserve **E**nhancement in delaying the onset of **A**lzheimer's **S**ymptomatic **E**xpression: The **INCREASE** study

WHY ARE YOU BEING INVITED TO TAKE PART IN THIS RESEARCH?

You are being invited to take part in a research study to see the effects of changing your medications on the onset of memory and thinking problems caused by Alzheimer's disease or other disorders of aging. You are being invited to take part in this research study because you are a normal elderly person that is taking medications that have been identified as potentially not appropriate for someone your age. If you volunteer to take part in this study, you will be one of about 90 people to do so at the University of Kentucky.

WHO IS DOING THE STUDY?

The person in charge of this study is Daniela Moga, M.D., Ph.D. of University of Kentucky, Department of Pharmacy Practice and Science, and Department of Epidemiology. Gregory A. Jicha, M.D., Ph.D. will also be assisting with the study and will serve as the study physician. There may be other people on the research team assisting at different times during the study.

WHAT IS THE PURPOSE OF THIS STUDY?

By doing this study, we hope to learn the effects of changing any potentially inappropriate medications you currently take, on Alzheimer's disease or other disorders of aging.

The purpose of this research is to gather information on how safe and effective reducing your use of inappropriate medications is. We will use a scopolamine patch (like those commonly used to treat or prevent motion sickness) to help us understand the effect of potentially inappropriate medications on your memory and thinking. The results of this study may be shared with federal agencies.

ARE THERE REASONS WHY YOU SHOULD NOT TAKE PART IN THIS STUDY?

You should not participate in this study if you do not wish to consider changing your current medicines, or if you have an allergy or other known intolerance to scopolamine patches that are commonly used to treat or prevent motion sickness.

Other reasons why you should not participate include narrow-angle glaucoma, difficulty swallowing, stomach or bowel problems (e.g., blockage, muscle weakness, ulcerative colitis), bleeding, myasthenia gravis, seizures, or a blockage of the urinary tract which could be worsened by use of the scopolamine patch that is part of the study.

WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST?

The research procedures will be conducted at the Sanders Brown Center on Aging, 1030 South Broadway, Suite #5, Lexington, KY and the UK Department of Radiology PET scan facilities on campus. You will need to come to the Sanders Brown Center on Aging, 1030 South Broadway, Suite #5, Lexington, KY, 6 times during the study. Each of those visits will take about 2 to 5 hours. The total amount of time you will be asked to volunteer for this study is about 40 hours over the next 62 weeks.

WHAT WILL YOU BE ASKED TO DO?

The study will involve assessing your medication use and identifying any medicines that may be inappropriate for someone your age. This will be done by a team including both a study doctor and a pharmacist with expertise in medication use for the elderly.

The following is a table of the study procedures you will undergo as part of your study participation if you decide to enroll in the study:

Procedure	Screening	Baseline scopolamine		Month 3	Month 6	Month 9	EOS scopolamine	
		Challenged	Non-challenged				Challenged	Non-challenged
Study week	-5 ± 2 weeks	-4 ± 1 week	0 ± 1 week	13 ± 1 week	26 ± 1 week	39 ± 1 week	52 ± 1 week	56 ± 1 week
Demographics	X							
Health History	X	X	X	X	X	X	X	X
Medication Review	X	X	X	X	X	X	X	X
Vital Signs	X	X	X		X		X	X
NART	X							
MoCA		X	X				X	X
CVLT		X	X				X	X
TMTB		X	X				X	X
SF-36	X							X
Gait & Balance Test	X	X			X		X	X
Lifestyle Factor Q.	X							X
Baseline Q.	X							
EOS Q.								X
ECG	X							
Physical exam	X							X
Neurological exam	X							X
Aβ-PET imaging	X							
Scopolamine Patch		X					X	
MTM Intervention			X		X		X	
Telephone check				X		X		

As part of the study (at the beginning and end) you will be asked to put on a scopolamine patch behind your ear as many people your age do when traveling by air or on a cruise ship to prevent motion sickness. This patch is not being used to prevent motion sickness in this study, but instead is being used to challenge your memory and thinking abilities. On the two days you are asked to wear the patch, you will need to find someone to drive you to and from your research appointment.

You will also be asked to undergo an amyloid-PET scan which will tell the study investigators if you have early amyloid plaques in your brain that could increase your risk of Alzheimer's disease in the near future. The study staff will not tell you if you have amyloid plaques or not if you choose to participate in the study, as there are no approved treatments or interventions for amyloid plaques in persons with normal memory and thinking currently available. The amyloid-PET scan will take about 20 minutes, but you will first need an IV placed and have a dose of tracer that contains radioactivity injected into your veins. The amount of radioactivity is low and will quickly wash out of your system. You will have only one PET scan at enrollment in the study as part of this research project. This procedure will take about 1-2 hours in total and you will be in the scanner for about 20 minutes or so as part of this procedure.

Part of the study includes collecting information on your memory and thinking abilities. This will include both questionnaires as well as memory and thinking tests. This will be performed 4 times during your study visits over the entire study period. These tests will take less than one hour every time they are performed.

You will also be asked to undergo tests of your gait and balance. The tests will involve walking on an electronic pressure-sensitive walkway and completing various physical tasks while wearing six watch-sized sensors. Should you agree, these gait and balance tests will be video recorded to help the study doctors better understand your test results. The video recordings will not capture your face; only your body from your shoulders down will be in frame. These tests will occur five times throughout the study, and they will take less than thirty minutes each time they are performed.

Do you give the study team permission to video record your gait and balance test sessions?

☐ **Yes** ☐ **No** _____**Initials** ☐ **Yes** ☐ **No** _____ **LAR Initials**

A study doctor will review your medical history with you, and then perform a routine medical (physical and neurologic) examination. This will be done twice during the study, once at the beginning and again at the end.

An ECG (heart tracing) will also be done at the beginning of the study to see the potential effects your medicines on your heart rhythm and to ensure that medication changes are safe for you.

Vital signs will be obtained at all on-site study visits.
Two of the study visits will be conducted by phone to check up on you and your health conditions.

At the beginning, middle, and end of the study, you may meet with a doctor and pharmacist to review and make any changes to your medicines that are needed to eliminate medicines on your list that are not recommended for the elderly. These visits are referred to as the Medication Therapy Management (MTM) visits below.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Memory and thinking testing: These study procedures could cause anxiety, fatigue or boredom.

ECG: The ECG (electrocardiogram) is a picture of the electrical activity of the heart. During this procedure you will need to lie still for a few minutes while electrodes are attached to your chest. The electrodes may cause some discomfort when they are put on and taken off your skin. If you are a male and have any chest hair, it may need to be shaved off in the areas where the electrodes will be placed.

Risks of PET Scans: Being in the PET scanner may cause you to experience discomfort or musculoskeletal pain, such as back or neck pain. Some people do not like the small space (claustrophobia) and might feel confined or bothered by being in the PET scan machine for a long period of time.

Risks of Radiation Exposure: This research study involves exposure to radiation from positron emission tomography (PET) scans. Please note that this radiation exposure is not necessary for your medical care and is for research purposes only. The total amount of radiation you will receive during the 1 PET scan sessions in this study is from 1 injection of 18F-Florbetapir. Although each organ will receive a different dose, the amount of radiation exposure you will receive from this study is equal to a uniform whole-body exposure of up to 1.52 rem, which is the equivalent of approximately 5 years of exposure from natural environmental sources. This value is known as the "effective dose equivalent" and is used to relate the dose received by each organ to a single value. This amount of radiation exposure is below the annual limit of 5-rem set by the federal government for research subjects.

The effects of radiation exposure on humans have been studied for over 60 years. In fact, these studies are the most extensive ever done of any potentially harmful agent that could affect humans. In all these studies, no harmful effect to humans has been observed from the levels of radiation you will receive by

taking part in this research study. However, scientists disagree on whether radiation doses at these levels are harmful. Even though no effects have been observed, some scientists believe that radiation can be harmful and may cause cancer at any dose- even low doses such as those received during this research.

Please tell your study doctor or other study personnel if you have taken part in other research studies that used radiation. This way we can make sure that you will not receive too much radiation. You should consider x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body. Before you take part in any future studies that use radiation, you should also tell those study doctors about your participation in this study.
If you are pregnant, breast-feeding, or of childbearing potential you may not participate in this research study.

Risks of 18F-Florbetapir: The most common side effect in completed studies with florbetapir was headache, which was reported in less than 2% of subjects. Additional uncommon (reported by 0.1% to 1.0% of subjects) side effects reported were: musculoskeletal (muscle and bone) pain, increased blood pressure/hypertension, nausea, fatigue, injection site reaction (bleeding, irritation, pain), anxiety, back pain, claustrophobia (fear of being in closed or narrow spaces), dizziness, feeling cold/chills, insomnia (inability to sleep), neck pain, infusion site rash, dysgeusia (bad taste in the mouth), pruritus (itching), urticaria (hives), and flushing.

Risks of gait and balance testing: The risks of completing gait and balance testing five times during the study are no greater than your risks while walking in daily life. It is possible that you may trip or lose your balance during the test session. All gait and balance tests will be performed only by trained study personnel who are equipped to prevent falls

Risk of scopolamine patch: The risks of using a scopolamine patch twice during the study for a day each is low. This patch is used commonly in the elderly for the prevention and or treatment of motion sickness associated with travel by land, sea, or air. The scopolamine patch can however cause some temporary adverse side effects that are detailed below. In this study we are using the patch to provoke memory and thinking problems. In the elderly this can be a common side effect of this medicine.

	Transderm Scōp® (N=461)		Placebo (N=457)	
	n	%	n	%
Adverse Drug Reactions	303	65.7	259	56.7
Dry mouth	133	28.9	72	15.8
Dizziness	57	12.4	33	7.2
Somnolence	36	7.8	16	3.5
Urinary Retention	33	7.2	30	6.6
Agitation	28	6.1	20	4.4
Visual Impairment	23	5.0	12	2.6
Confusion	18	3.9	14	3.1
Mydriasis	16	3.5	2	0.4
Pharyngitis	15	3.3	10	2.2

*The FDA-approved package insert will be provided to all research participants enrolled in the study for review prior to consent.

Risk of intervention vs. placebo: If you are assigned to the placebo group, you are at no increased risk over standard clinical care which you are already receiving. If you have concerns about the appropriateness of your medicines, you are free to discuss with your doctor or pharmacist. The risks of

being assigned to the interventional arm include the possibility of being recommended a change in your current medications in line with current medical recommendations. Changing your medications could result in worsening or improvement of your medical symptoms for which your current medications are being prescribed. If you experience side effects or worsening of your medical conditions, the study team will work with your primary care doctor to find suitable alternatives or recommend that you return to your previous medicine that was managing your symptoms when you enrolled in the study. Change of medications indicated by the study team will follow standard of care practices and should lead to no more risk of harm than that associated with regular doctor visits and medication changes.

There is always a chance that any medical treatment can harm you, and the investigational treatment in this study is no different. In addition to the risks listed above, you may experience a previously unknown risk or side effect.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

There is no guarantee that you will get any benefit from taking part in this study. However, some people have experienced improved memory and thinking when inappropriate medications are replaced with more appropriate alternatives. Your willingness to take part, however, may also, in the future, help doctors better understand and/or treat others who are at risk for memory and thinking problems as they age.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any benefits or rights you would normally have if you choose not to volunteer. You can stop at any time during the study and still keep the benefits and rights you had before volunteering. If you decide not to take part in this study, your decision will have no effect on the quality of medical care you receive.

IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

If you do not want to take part in the study, there are other choices such as discussing the appropriateness of your medications with your doctor and pharmacist. You may be able to work with them to reduce your use of inappropriate medicines without study participation.

WHAT WILL IT COST YOU TO PARTICIPATE?

You and/or your insurance company, Medicare or Medicaid will be responsible for the costs of all care and treatment you receive during this study that you would normally receive for your condition. These are costs that are considered medically reasonable and necessary and will be part of the care you receive if you do not take part in this study.

No study procedures will be billed to you or your insurance.

However in this study, the study doctors and pharmacists may recommend changes to you medications that could potentially result in higher costs to you (deductible or other out-of-pocket expenses). The study team will work with you to find the lowest cost alternatives and if financial issues cannot be resolved, the study team is OK with you continuing with your current medications rather than accepting potentially higher cost changes. If you choose to accept a higher cost medication as part of the recommended medication changes, this cost will be will be your responsibility.

You should know that such costs may be paid by your insurer if you are insured by a health insurance company (you should ask your insurer if you have any questions regarding your insurer's willingness to pay these costs), or may be paid by Medicare or Medicaid if you are covered by Medicare, or Medicaid, (if you have any questions regarding Medicare/Medicaid coverage you should contact Medicare by calling

1-800-Medicare (1-800-633-4227) or Medicaid at 1-800-635-2570.
A co-payment/deductible from you may be required by your insurer or Medicare/Medicaid even if your insurer or Medicare/Medicaid has agreed to pay the costs. The amount of this co-payment/deductible may be substantial and is your responsibility to pay.

WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?

If you believe you are hurt or if you get sick because of something that is done during the study, you should call Dr. Gregory Jicha at (859) 323-5550 immediately. If you are unable to reach Dr. Jicha at this number, you should call (859) 559-7429.

It is important for you to understand that the University of Kentucky does not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study.

The medical costs related to your care and treatment because of research related harm will be your responsibility or may be paid by your insurer if you are insured by a health insurance company (you should ask your insurer if you have any questions regarding your insurer's willingness to pay under these circumstances); and may be paid by Medicare or Medicaid if you are covered by Medicare, or Medicaid (if you have any questions regarding Medicare/Medicaid coverage you should contact Medicare by calling 1-800-Medicare (1-800-633-4227) or Medicaid 1-800-635-2570.

A co-payment/deductible from you may be required by your insurer or Medicare/Medicaid even if your insurer or Medicare/Medicaid has agreed to pay the costs). The amount of this co-payment/deductible may be substantial.

You do not give up your legal rights by signing this form.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

We will make every effort to keep confidential all research records that identify you to the extent allowed by law.

Your information will be combined with information from other people taking part in the study. When we write about the study to share it with other researchers, we will write about the combined information we have gathered. You will not be personally identified in these written materials. We may publish the results of this study; however, we will keep your name and other identifying information private.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. Your paper records will be kept under double lock-and-key at the Sanders-Brown Center on Aging Clinic, 1030 South Broadway Suite #5 or in the College of Pharmacy, 789 S Limestone. After your name and identifying information is removed, your research data will be uploaded through a secure web-link to an electronic database (REDCAP) that prevents others from accessing this information.

You should know, however, that there are some circumstances in which we may have to show your information to other people. For example, the law may require us to show your information to a court or to tell authorities if you report information about a child or vulnerable adult being abused or if you pose a danger to yourself or someone else.

Officials of the Food and Drug Administration, the National Institutes of Health, the Center for Clinical and Translational Science, and the University of Kentucky may look at or copy pertinent portions of records that identify you.

CAN YOUR TAKING PART IN THE STUDY END EARLY?

If you decide to take part in the study you still have the right to decide at any time that you no longer want to continue. You will not be treated differently if you decide to stop taking part in the study. If you choose to withdraw from the study early, the data collected until that point will remain in the study database and may not be removed.

The individuals conducting the study may need to withdraw you from the study and the study intervention, medication will no longer be provided by the investigator and may not be accessible commercially. This may occur if you are not able to follow the directions they give you, if they find that your being in the study is more risk than benefit to you, or if the agency funding the study decides to stop the study early for a variety of scientific reasons.

ARE YOU PARTICIPATING OR CAN YOU PARTICIPATE IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?

You may take part in this study if you are currently involved in another research study. It is important to let the investigator/your doctor know if you are in another research study. You should also discuss with the investigator before you agree to participate in another research study while you are enrolled in this study.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?

You will be compensated $200.00 for taking part in this study. You will receive $100 for each scopolamine challenge visit, to allow for transportation or lost wages costs for study partners that provide such service. You will receive at $100.00 Visa Card upon completion of each scopolamine challenge visit.
If you earn $600.00 or more by participating in research, it is potentially reportable for tax potentially for tax purposes.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS, CONCERNS, OR COMPLAINTS?

Before you decide whether to accept this invitation to take part in the study, please ask any questions that might come to mind now. Later, if you have questions, suggestions, concerns, or complaints about the study, you can contact the investigator, Dr. Daniela Moga at (859) 323-9682. If you have any questions about your rights as a volunteer in this research, contact the staff in the Office of Research Integrity at the University of Kentucky between the business hours of 8am and 5pm EST, Mon-Fri at 859-257-9428 or toll free at 1-866-400-9428. We will give you a signed copy of this consent form to take with you.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?

If the researcher learns of new information in regards to this study, and it might change your willingness to stay in this study, the information will be provided to you. You may be asked to sign a new informed consent form if the information is provided to you after you have joined the study.

Contacting Research Subjects for Future Studies

Do you give your permission to be contacted in the future by Drs. Moga or Jicha regarding your willingness to participate in future research studies about how to prevent, detect, or treat memory and aging problems that are associated with aging?

☐ **Yes** ☐ **No**_____**Initials** ☐ **Yes** ☐ **No** _____ **LAR Initials**

WHAT ELSE DO YOU NEED TO KNOW?

There is a possibility that the clinical and imaging data collected from you may be shared with other investigators in the future. If that is the case the clinical and imaging data will not contain information that can identify you unless you give your consent/authorization or the UK Institutional Review Board (IRB) approves the research. The IRB is a committee that reviews ethical issues, according to federal, state and local regulations on research with human subjects, to make sure the study complies with these before approval of a research study is issued.

The National Institutes of Health (NIH) is providing financial support and/or material for this study.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov 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.

AUTHORIZATION TO USE OR DISCLOSE YOUR IDENTIFIABLE HEALTH INFORMATION

The privacy law, HIPAA (Health Insurance Portability and Accountability Act), requires researchers to protect your health information. The following sections of the form describe how researchers may use your health information.

Your health information that may be accessed, used and/or released includes:

- Demographic information (name, initials, age, gender, race, study number, mailing address, email address, and home/work/cell phone numbers.)
- Results of physical exams
- Amyloid PET scan results
- Medical and medication history as it relates to the study
- Results from questionnaires
- Study visits

The Researchers may use and share your health information with:

- The University of Kentucky's Institutional Review Board/Office of Research Integrity.
- Law enforcement agencies when required by law.
- University of Kentucky representatives.
- National Institutes of Health (NIH)
- UK Investigational Drug Service (IDS)
- The Sanders-Brown Center on Aging Biostatistics core at the University of Kentucky
- Members of the Data Safety Monitoring Board
- Your primary physician will be contacted if we, in the course of the research, learn of a medical condition that needs immediate attention.

The researchers agree to only share your health information with the people listed in this document. Should your health information be released to anyone that is not regulated by the privacy law, your health information may be shared with others without your permission; however, the use of your health information would still be regulated by applicable federal and state laws.
You may not be allowed to participate in the research study if you do not sign this form. If you decide not to sign the form, it will not affect your:

- **Current or future healthcare at the University of Kentucky**
- **Current or future payments to the University of Kentucky**
- **Ability to enroll in any health plans (if applicable)**
- **Eligibility for benefits (if applicable)**

After signing the form, you can change your mind and NOT let the researcher(s) collect or release your health information (revoke the Authorization). If you revoke the authorization:

- You will send a written letter to: Daniela Moga, MD Ph.D., Pharmacy Practice and Science, College of Pharmacy, 789 S Limestone Room 241, Lexington, KY 40536 to inform her of your decision.
- Researchers may use and release your health information **already** collected for this research study.
- Your protected health information may still be used and released should you have a bad reaction (adverse event).

You understand that you will not be allowed to review the information collected for this research study until after the study is completed. When the study is over, you will have the right to access the information.

The use and sharing of your information has no time limit.

If you have not already received a copy of the Privacy Notice, you may request one. If you have any questions about your privacy rights, you should contact the University of Kentucky's Privacy Officer between the business hours of 8am and 5pm EST, Mon-Fri at: (859) 323-1184.

You are the subject or are authorized to act on behalf of the subject. You have read this information, and you will receive a copy of this form after it is signed.

_____ _____
Signature of research subject Date

_____
Printed name of research subject

_____ _____
Signature of Subject Legally Authorized Representative Date

_____ _____
Name of [authorized] person obtaining informed consent/HIPAA authorization Date

_____
Signature of Principal Investigator or Sub/Co-Investigator