Study Guide

A Guidebook for Participants and Their Study Partners

TRC-PAD study is short for the "Trial Ready Cohort for the Prevention of Alzheimer's Dementia." The purpose of the TRC-PAD study is to find several people (also called a "cohort") who are interested in participating in clinical trials aimed at discovering treatments that will reduce the risk of developing Alzheimer's dementia. TRC-PAD will help researchers enroll participants into these trials quickly to allow new treatments to be discovered as soon as possible.

About the TRC-PAD Study Partnership

The TRC-PAD study is funded by the National Institute on Aging/National Institutes of Health (NIA/NIH) and coordinated by the Alzheimer's Therapeutic Research Institute of the University of Southern California, in partnership with Brigham and Women's Hospital and the Cleveland Clinic.

Answers to Your Questions about the TRC-PAD Study and Alzheimer's Disease

Why have I been invited to an in-person visit for TRC-PAD?

The TRC-PAD study is for individuals, age 50 and older, who may be at increased risk for memory loss caused by Alzheimer's disease changes in the brain.

You are being asked to take part in this research study because you are currently a member of the Alzheimer Prevention Trials (APT) Webstudy. That study identified you as being eligible for an in-person TRC-PAD visit. If you are not enrolled in the APT Webstudy, you may have been invited to an in-person visit for TRC-PAD because other tests or procedures you have had suggest you might be eligible to participate.

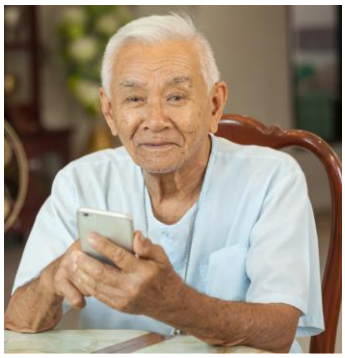
What is Alzheimer's disease?

Alzheimer's disease is a disease that affects the brain and it is the most common cause of dementia. The greatest risk factor for Alzheimer's disease is advancing age; however, Alzheimer's disease is not a normal part of aging.

"Dementia" is a term describing the progressive loss of thinking, memory, and other cognitive abilities that impair daily function. The most common symptom of dementia caused by Alzheimer's disease is a gradual loss of memory, but other thinking abilities are affected, such as not knowing the day of the week and difficulty solving problems.

How might the TRC-PAD Study help researchers learn more about Alzheimer's disease dementia?

Alzheimer's disease remains one of the most important medical conditions for which there is no treatment. Among the top ten causes of death, Alzheimer's disease is the only one that cannot be prevented, cured, or even slowed. To change this, researchers are conducting clinical trials to find new treatments for Alzheimer's disease.



These trials need to study large numbers of individuals and follow participants over long periods of time. The goal of TRC-PAD is to identify individuals for these trials. TRC-PAD will find a group of people who may be "at-risk" for developing Alzheimer's dementia in the future and are ask them to join clinical trials.

How was it decided that I am eligible for TRC-PAD?

A variety of factors are now being used to identify people being eligible for Alzheimer's disease prevention clinical trials. These and other factors are elements being used to decide who is eligible for TRC-PAD. A person's risk for developing Alzheimer's dementia is determined by a number of factors including family history, performance on memory tests,

and biological tests called biomarkers. Biomarkers are measurements in parts of the body - like blood tests or brain scans - to help assess the presence of, or potential to develop, a disease.

- Individuals who have a biological parent, brother or sister with Alzheimer's disease are at increased risk to develop Alzheimer's dementia. This does not mean every person with a family member who has Alzheimer's disease dementia will develop it.
- Individuals with certain genes are at increased risk of developing Alzheimer's disease. This does not mean every person with certain genes will develop it.
- Some studies indicate that physical inactivity, high cholesterol, diabetes, smoking and obesity, are associated with a higher risk of developing Alzheimer's disease and other dementias. This does not mean every person with cardiovascular disease risk factors will develop it.
- The results of recent research studies suggest that older individuals with abnormal levels of a protein called "amyloid" seen on their brain scans or in their spinal fluid may be at higher risk for memory loss. Again, this does not mean every person with elevated amyloid levels will develop Alzheimer's disease dementia.

If I decide to join TRC-PAD, what happens?

Individuals in the TRC-PAD study will be involved in several assessments. The following is a summary list of what you will need to do and, following the list, further details:

- Provide information on memory and thinking abilities, emotional and psychological status, and how well you perform everyday activities.
- List all of your medications, including non-prescription medicines, supplements, and herbal remedies.
- Provide general health information (for example, any illnesses or complaints).
- Have an electrocardiogram
- Provide blood and urine samples
- Undergo a brain scan or lumbar puncture
- Find a trusted friend or family member who can accompany you to some study visits or be available by phone. We call this person a "study partner." Your study partner will answer questions about your memory and daily life activities. The study partner should have regular contact with you – about once a week or so. This contact can be in-person, phone or electronic.

Memory and Think Tests

You will be given a variety of memory and thinking tests, most of which include remembering information, naming and drawing pictures, and similar tasks.

Questionnaires

You and your study partner will be asked about your daily functioning, mood and behavior, including feelings of depression.

Electrocardiogram (ECG)

The ECG procedure measures your heart's electrical activity.

Genetic Tests

At the beginning of the TRC-PAD study assessments, your blood will be drawn to allow us to check for genes that may be related to the development of Alzheimer's dementia. Because these are research tests, we will not share any of these test results with you, your family or your doctors; however, the information will be available to researchers trying to understand Alzheimer's and advance treatments. If you agree, your genetic samples will be stored for future research and may be provided to researchers at academic institutions, hospitals and pharmaceutical companies studying various diseases, including Alzheimer's disease. Information that can identify you will not be included with any shared research observations or genetic samples.

Blood and Urine Tests

Routine blood and urine tests will be collected to ensure there are no medical conditions that may interfere with your participation in the TRC-PAD study or that could be responsible for any changes in your well-being

throughout the study period. If any of the blood tests are abnormal, we will share the results with you so that you may discuss it with your doctor.

Brain Scan

An amyloid PET scan is a brain imaging test that uses a small amount of a radioactive dye to measure amyloid build-up in your brain.

The PET scan is similar to scans that are used routinely for other medical reasons, like x-rays or an MRI. The risk associated with the amount of radiation exposure an individual receives in this study is considered low and comparable to everyday risks. To minimize the risk, the lowest possible dose of radioactivity needed to get a good image is used.

Here are some other important things to know about an amyloid PET scan:

- The PET scan does not measure whether you have Alzheimer's dementia.
- The PET scan does not measure whether you will develop Alzheimer's dementia in the future.
- For the TRC-PAD Study, we are looking for people with a range of plaque build-up in their brain, including people with relatively low levels.
- You will not learn the level of plaque in your brain as part of TRC-PAD. You may, however, learn the result if you enroll in a clinical trial.

Lumbar Puncture for Cerebrospinal Fluid (CSF)

The lumbar puncture is an alternative to the PET scan, but instead of looking at a scan of your brain, researchers will analyze your cerebrospinal fluid (CSF) to measure the plaque-related protein. CSF is the fluid around your brain and spinal cord. Like the PET scan, CSF provides information on changes in the brain proteins related to Alzheimer's disease.

During a lumbar puncture, a small amount of CSF will be taken via a needle from your lower back and analyzed. In the TRC-PAD study, individuals having a lumbar puncture will not learn the level of plaque protein in their CSF.

Will I learn the results of my cognitive, genetic, or biomarker testing results?

You will not learn the results of your cognitive, genetic, or biomarker testing as part of TRC-PAD.

What will I learn?

You will be told that you are "eligible" or "not eligible" to participate in TRC-PAD.

How is it decided that I am eligible to enroll in TRC-PAD?

After the results from all of the screening activities described above have been reviewed, you will be told whether you are eligible or not eligible to join the TRC-PAD study. Your eligibility to participate in TRC-PAD will be based on the results of your brain scan or CSF measures and memory tests, combined with all of the information that we've collected about you in this study.

If you ARE eligible to enroll in TRC-PAD

You will not be told the specific results of any TRC-PAD tests. Eligibility does mean you may have an increased risk for developing Alzheimer's dementia in the future, compared to someone who is not eligible. It does not mean you will definitely experience cognitive impairment and does not mean you will definitely develop Alzheimer's dementia.

Being eligible for TRC-PAD also means you may be eligible to participate in an Alzheimer's disease clinical trial. Because not all future trials are known, whether you will be eligible to participate in one or more of these trials also is not yet known. It is possible you will not be enrolled in a trial or ever learn the results of your eligibility testing.

If, in the future, you do qualify for a trial, the study team will talk with you about what this means. If you are interested in participating in a trial, you will be asked to sign and date a separate consent form. If you are invited to join a clinical trial as a result of participating in TRC-PAD, you may learn, at that time, results of tests such as gene testing, blood tests, and brain scans. This means you may learn if you have specific risk factors related to Alzheimer's dementia.

You do not have to agree to participate in an Alzheimer's disease clinical trial to participate in the TRC-PAD study.

If you are NOT eligible to enroll in TRC-PAD

You will not be told the results of any testing in TRC-PAD. However, your testing indicates you are not eligible to participate in the TRC-PAD study at this time. Being "not eligible" does not mean you will never experience cognitive impairment and it does not mean you will never develop Alzheimer's dementia.

Although you may not be eligible now to participate in the TRC-PAD study, you could be eligible in the future. If you are already participating in the APT Webstudy, you are encouraged to continue doing so. If you have not yet participated in the APT Webstudy, you will be asked to join it. The APT Webstudy includes online memory and thinking tests aimed at identifying and tracking individuals who may be eligible for Alzheimer's clinical trials. It is funded and coordinated by the same group of partners as the TRC-PAD study and can be found at www.aptwebstudy.org.

How long will I be in the TRC-PAD Study?

Participation in the TRC-PAD study is entirely voluntary.

The TRC-PAD study requires a commitment of semi-annual (twice a year) in-person visits until you are enrolled in a trial. Regardless of whether you are eligible to participate in TRC-PAD, you will be asked to continue your quarterly, remote, web-based follow-up in the APT Webstudy. We anticipate continuing the APT Webstudy and TRC-PAD for many years.

What are the risks of participating in TRC-PAD?

Potential risks of joining the TRC-PAD study will be discussed with you in detail during the informed consent process. Your study information is not released to personal physicians without permission, and we protect the confidentiality of participants. Though it is unlikely, it is possible information about you could be entered into your medical record, particularly if you experience an adverse event from one of the study procedures requiring treatment.

You should also be aware that information about eligibility or participation in this study could influence the ability to obtain life, health, or long-term care insurance. It could affect your future employability. Some people may find that having a study partner knowing they are eligible changes the relationship with that person. Some people may find learning they are eligible and potentially at increased risk for Alzheimer's Dementia changes how they feel about their future and their memory and their abilities to perform day to day tasks. If these feelings are bothersome, please reach out for help to manage them, such as talking to your family, your study team or your physician.

Your Participation Matters

Thanks to individuals like you, researchers are learning more and more about Alzheimer's disease. By identifying a large group of individuals who may be eligible for Alzheimer's clinical trials, TRC-PAD seeks to accelerate the development of new treatments for those suffering from this disease. Whether you are eligible for TRC-PAD or the APT Webstudy, your participation brings us closer to understanding and treating Alzheimer's disease.