When Margaret was diagnosed with early-stage Alzheimer’s disease at age 68, she wanted to do everything possible to combat the disease. She talked with her doctor about experimental treatments and clinical trials she had heard about in the news and worked with the doctor to find a trial that was right for her. Margaret appreciated being able to talk to experts about Alzheimer’s and felt she was doing something that might also help her children and grandchildren avoid the disease.

This is an exciting time for Alzheimer’s disease clinical research. Thanks to advances in our understanding of this disease and powerful new tools for “seeing” and diagnosing it in people, scientists are making great strides in identifying potential new interventions to help diagnose, slow, treat, and someday prevent the disease entirely.

But Alzheimer’s research can move forward only if people are willing to volunteer for clinical trials and studies. Before any drug or therapy can be used in clinical practice, it must be rigorously tested to find out whether it is safe and effective in humans. Today, at least 50,000 volunteers, both with and without Alzheimer’s, are urgently needed to participate in more than 175 actively enrolling clinical trials and studies in the United States. To reach that goal, researchers will need to screen at least half a million potential volunteers.

This fact sheet describes Alzheimer’s disease clinical trials and studies, explains their scientific design, and offers key facts and questions to consider about volunteering for clinical research.

Comparing Alzheimer’s Disease Clinical Trials and Studies

Clinical research is medical research involving people. It includes clinical studies, which use long-term observation and analysis in large groups to determine how a disease or condition may occur and progress, and clinical trials, which test possible interventions to diagnose, prevent, treat, and someday cure a disease.
Clinical studies observe people in normal settings, with less direct intervention than in clinical trials. Researchers gather baseline information, group volunteers according to broad characteristics, and compare changes over time. Studies of Alzheimer’s disease may help identify new possibilities for clinical trials. The National Institute on Aging (NIA), part of the National Institutes of Health (NIH), sponsors several major ongoing studies, such as:

- **Alzheimer’s Disease Neuroimaging Initiative** investigators study brain images and biomarkers in people with normal cognitive aging, mild cognitive impairment (MCI)—a disorder that may precede Alzheimer’s disease, and early-stage Alzheimer’s to develop better indicators of the disease and its progression. For example, they have found that certain changes in biomarkers, like proteins or enzymes in blood or cerebrospinal fluid, may signal early Alzheimer’s and have established a method and standard for testing these biomarkers.

- **Alzheimer’s Disease Genetics Studies** researchers analyze DNA from persons with and without the disease to identify genes that may be Alzheimer’s risk factors.

Clinical trials test interventions such as drugs or devices, as well as prevention methods and changes in diet or lifestyle. (See examples below.) Drug testing is the focus of many clinical trials. Currently, more than 90 drugs are in clinical trials for Alzheimer’s disease, and more are in the pipeline awaiting U.S. Food and Drug Administration (FDA) approval to enter human testing.

FDA-approved clinical trials are always preceded by laboratory analyses in test tubes and in tissue culture, followed by studies in laboratory animals to test for safety and efficacy. If these show favorable results, the FDA gives approval for the treatment or intervention to be tested in humans.

Clinical trials advance through four well-defined phases to test the treatment, find appropriate dosage, and monitor side effects in increasing numbers of people. If investigators find an intervention safe and effective after undergoing the first three phases, the FDA decides whether to approve it for clinical use. In Phase IV, the FDA continues to monitor the effects of a new drug after its approval for marketing and clinical use. If problems occur, approval may be withdrawn and the drug recalled. After the efficacy of a drug for one health condition is established, Phase IV studies can evaluate the activity of the drug in other conditions.

**Clinical Trials Seek Answers Through Rigorous Testing**

Scientists conducting Alzheimer’s disease research test a theory by using the classic scientific method. They first identify a valid question related to Alzheimer’s. The question is posed as a hypothesis that is either proven or disproven by the clinical trial.
For example, research has linked high blood cholesterol with Alzheimer’s disease. Scientists asked: Will medications that lower cholesterol also have an effect on Alzheimer’s disease? They formed a hypothesis: IF reducing blood cholesterol has a beneficial effect on Alzheimer’s disease, THEN statins (drugs to reduce cholesterol) will slow the progression of Alzheimer’s disease. To test that hypothesis, NIA has funded a number of clinical trials, which are ongoing.

**Benefits of Volunteering**
- Help others, including future family generations, who may be at risk for Alzheimer’s disease
- Receive regular monitoring by Alzheimer’s professionals
- Learn more about the disease from experts
- Get information about support groups and resources

Comparing results indicates whether changes in the test group result from the treatment. In many trials, no one—not even the research team—knows who gets the treatment, the placebo, or another intervention. When the participant, family members, and staff all are “blind” to the treatment, the study is called a double-blind, placebo-controlled clinical trial.

Placebo and test groups are equally important, as shown in the results of numerous clinical trials. For example, early research suggested that ginkgo biloba, an herbal supplement, might be effective in delaying dementia. To find out, NIA sponsored a 6-year, Phase III clinical trial with more than 3,000 participants age 75 and older. In 2008, scientists reported no significant differences in effect on dementia in adults who received ginkgo biloba or placebo.

This result was disappointing, but scientists gained a wealth of information to inform future research. For example, researchers learned more about subgroups of participants who may be at greater risk for developing dementia, and ginkgo’s possible effects on cardiovascular disease, cancer, depression, and other age-related conditions. They also gained insights on issues related to the design and conduct of large dementia prevention trials in older adults, such as the number of participants needed to provide clinically significant measures on outcomes like occurrence of dementia.

**Why Placebos Are Important**
The “gold standard” for testing interventions in people is the randomized, placebo-controlled clinical trial, because it is designed to reduce error or bias. Volunteers are randomly assigned—that is, selected by chance—to either a test group receiving the experimental intervention or a control group receiving a placebo, an inactive substance resembling the drug tested.
**Participating in a Trial or Study**

**How Can People Find Out About Alzheimer’s Disease Trials and Studies?**

Information about Alzheimer’s disease clinical trials and studies is available through a number of sources. First, talk to your doctor, who may know about local or specific research studies that may be right for you. NIA-supported Alzheimer’s Disease Centers or specialized memory or neurological clinics in your community may also be conducting trials. You might also learn of clinical trials through newspapers or other media.

To search more widely for trials or studies, you can also visit websites like ClinicalTrials.gov or the NIA Alzheimer’s Disease Education and Referral (ADEAR) Center clinical trials database. See the “For More Information” section at the end of this fact sheet for resources and contact information.

**What Happens When a Person Joins a Clinical Trial?**

First, it is important to learn as much as you can about the trial. Staff members at the research center are trained to explain the trial in detail and describe possible risks and benefits. They clarify participants’ rights. Participants and their families can have this information repeated until they are sure they understand it.

After questions are answered, participants sign an *informed consent form*, which contains key facts about the trial. Next, they are screened

<table>
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<tr>
<th>Steps in Clinical Trial Participation</th>
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<tr>
<td>1. After initial phone screening, interested persons go to the study site.</td>
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<td>2. Staff members explain the trial and gather more information.</td>
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<td>3. The participant or proxy signs an informed consent.</td>
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<td>4. The participant undergoes a screening process that indicates whether he or she qualifies for the trial.</td>
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<td>5. A first visit (called the “baseline” visit) is scheduled, in which cognitive and/or physical tests may be administered.</td>
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<td>6. Selected participants are randomly assigned to distinct treatment groups.</td>
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<td>7. Participants and family members follow the trial protocol and report any issues or concerns to researchers.</td>
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<td>8. They may visit the research site for new cognitive, physical, or other evaluations and for discussions with staff.</td>
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<tr>
<td>9. Investigators collect information on effects of the intervention, disease progression, and the safety and well-being of the participant and caregiver.</td>
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<tr>
<td>10. The participant continues to see his or her regular physician for usual health care.</td>
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by clinical staff to see whether they meet criteria to participate in the trial. Screening examines the characteristics people must have to participate in a particular trial, as well as characteristics that may exclude them. The screening may involve cognitive and physical tests that provide baseline information to compare with future changes. If participants meet all criteria, they are enrolled in the trial.

Informed Consent
Each participant must sign an informed consent agreement, affirming that he or she understands the trial and is willing to participate. Laws and regulations regarding informed consent differ across States and institutions, but they are all meant to ensure participant safety and protection, and to prevent unethical experimentation on vulnerable populations.

Researchers conducting clinical Alzheimer’s research must consider the declining memory and cognitive abilities of people with this disease or another dementia and must evaluate their ability to understand and consent to participate in research. If the person with Alzheimer’s is deemed unable to provide informed consent because of problems with memory and confusion, an authorized legal representative, or proxy (usually a family member), may be able to give permission for the person to participate, particularly if it is included in the patient’s durable power of attorney.

A durable power of attorney is a legal agreement designating who will handle the patient’s affairs when he or she no longer can. NIA’s Legal and Financial Planning for People with Alzheimer’s Disease Fact Sheet (available at www.nia.nih.gov/Alzheimers/Publications/legaltips.htm) provides more information.

Inclusion and Exclusion Criteria
In the experimental protocol (written research plan), researchers define the inclusion criteria volunteers must meet to participate, such as age range, stage of dementia, racial and/or ethnic group, gender, genetic profile, and family history. The protocol also defines exclusion criteria, such as health conditions or medications that prevent volunteers from joining a trial. Many volunteers are needed for screening to find enough people for a study. Generally, volunteers can participate in only one trial or study at a time. It is important to realize that different trials have different inclusion and exclusion criteria, so being excluded from one trial does not necessarily mean exclusion from another.

What Happens During a Trial?
Usually, participants are randomly assigned to one of the trial groups. People in each group represent selected combinations of characteristics (such as age, sex, education, or cognitive ability). The test group receives the experimental drug or intervention. Other groups receive a different drug, a placebo, or another intervention.
Participants and family members follow strict instructions and keep detailed records. Every so often, they visit the research site to receive more physical and cognitive exams and talk with staff. Investigators collect information on the effects of the test drug or treatment, evaluate disease progression, and see how the participant and caregiver are doing.

**What Volunteers Need To Know**

The following issues are some of the key concerns potential participants should consider before deciding whether joining a trial or study is right for them.

**Expectations and motivations.** Single clinical trials and studies generally do not have miraculous results, and participants may not directly benefit.

**Uncertainty.** Some people have problems because they are not permitted to know whether they are getting experimental treatment or a placebo, or may not know results. Can you live with these sorts of uncertainties?

**Finding the right clinical trial or study.** Volunteers must meet the inclusion and exclusion criteria listed by researchers. Even if a participant is not eligible for one trial or study, another may be just right.

**Time commitment and location.** Clinical trials and studies last days to years and may require multiple visits to study sites, such as private research facilities, teaching hospitals, Alzheimer’s research centers, or doctors’ offices. How much time and travel are you willing and able to undertake?

**Risk.** Researchers make every effort to ensure the safety of participants, but all clinical trials have some risk. What level of risk are you comfortable with?

**Rights of Volunteers**

Clinical trial volunteers have important rights, including the rights to receive clear, complete information and to withdraw from a trial anytime.

**Right to Clear Information**

Understanding what is involved in a clinical trial or study can relieve anxiety. Potential volunteers have the right to a thorough explanation and answers to all of their questions. Participants and family members can have information repeated and explained until they understand it.

**Right To Withdraw**

Volunteers can withdraw from a trial or study anytime they or their physician feels it is in their best interests. For example, a new health condition in a volunteer may require medications that are risky if combined with experimental treatments.

**Clinical Trials and Studies Need All Kinds of People**

Clinical trials and studies are a partnership between researchers and volunteer participants, who work together to answer questions about humans we can answer in no other way. Ensuring that those answers are correct requires including volunteers of all kinds: men and women, African Americans, Latinos,
Native Americans, Asian Americans, whites, people with Alzheimer’s or a family history of the disease, people with conditions that may lead to Alzheimer’s, and those without the disease (controls).

An intervention may work differently in one group than in another. Without adequate representation of a particular group, questions about safety and effectiveness of a treatment in that group may remain unanswered. In addition to diversity, the number of people included in research can affect results. Changes or effects seen in smaller groups may or may not show up significantly in larger groups.

For More Information
To find out more, talk with your healthcare provider or contact NIA’s ADEAR Center at 1-800-438-4380. Or, visit the ADEAR Center clinical trials database at www.nia.nih.gov/Alzheimers/ResearchInformation/ClinicalTrials. You can sign up for e-mail alerts that identify new clinical trials added to the database. More information about clinical trials is available at www.ClinicalTrials.gov.

Alzheimer’s Disease Trials and Studies

Alzheimer’s Disease Education and Referral (ADEAR) Center
P.O. Box 8250
Silver Spring, MD 20907-8250
1-800-438-4380 (toll-free)
www.nia.nih.gov/Alzheimers

The National Institute on Aging’s ADEAR Center offers information and publications for families.
caregivers, and professionals on Alzheimer’s disease research, diagnosis, treatment, patient care, caregiver needs, long-term care, and education and training. Staff members answer telephone, e-mail, and written requests and make referrals to local and national resources, including clinical trials and studies. The ADEAR website offers a searchable database of Alzheimer’s clinical trials and studies (www.nia.nih.gov/Alzheimers/ ResearchInformation/ClinicalTrials), as well as free, online publications in English and Spanish; e-mail alert and online newsletter subscriptions; the Alzheimer’s Disease Library (AD Lib) database; and more.

Alzheimer’s Association
225 North Michigan Avenue, Floor 17 Chicago, IL 60601-7633
1-800-272-3900 (toll-free)
www.alz.org

The Alzheimer’s Association is a national, nonprofit organization with a network of local chapters that provide education, support, and referrals to local resources and services for people diagnosed with Alzheimer’s disease, their families, and caregivers. The Association also funds Alzheimer’s research.

Alzheimer’s Disease Cooperative Study (ADCS)
www.adcs.org

The ADCS, funded by the National Institute on Aging, is a consortium of medical research centers and clinics working to develop and test drugs to treat Alzheimer’s disease.

General Information About Research Participation
ClinicalTrials.gov
www.ClinicalTrials.gov

ClinicalTrials.gov is a comprehensive, searchable online registry of federally and privately funded clinical trials and studies.

U.S. Food and Drug Administration (FDA)
www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/ParticipatinginClinicalTrials/

The FDA regulates all U.S. clinical trials of drugs and devices and offers information and resources for clinical trials participants and professionals.

Center for Information and Study on Clinical Research Participation (CISCRP)
www.ciscrp.org
www.smartparticipant.org

CISCRP is an independent, national nonprofit organization working to promote greater understanding and awareness of clinical research participation and the role it plays in public health.

Project IMPACT (Increase Minority Participation and Awareness of Clinical Trials)
www.impact.nmanet.org

Project IMPACT, an initiative of the National Medical Association, seeks to increase awareness and participation of African Americans and other minorities in clinical trials and research.