



































# Risk Factors for Dementia

The following risk factors can increase a person's chance of developing one or more kinds of dementia. Some of these factors can be modified, while others cannot.

- **Age.** The risk goes up with advanced age.
- **Alcohol use.** Most studies suggest that drinking large amounts of alcohol increases the risk of dementia, while drinking a moderate amount may be protective.
- **Atherosclerosis.** The accumulation of fats and cholesterol in the lining of arteries, coupled with an inflammatory process that leads to a thickening of the vessel walls (known as atherosclerosis), can hinder blood from getting to the brain, which can lead to stroke or another brain injury. For example, high levels of low-density lipoprotein (LDL, or “bad” cholesterol) can raise the risk for vascular dementia. High LDL levels also have been linked to AD.
- **Diabetes.** People with diabetes appear to have a higher risk for dementia, although the evidence for this association is modest. Poorly controlled diabetes, however, is a well-proven risk factor for stroke and cardiovascular disease-related events, which in turn increase the risk for vascular dementia.
- **Down syndrome.** Many people with Down syndrome develop early-onset AD, with signs of dementia by the time they reach middle age.
- **Genetics.** One's likelihood of developing a genetically linked form of dementia increases when more than one family member has the disorder. But in some cases, such as with CADASIL, having just



one parent who carries a mutation increases the risk of inheriting the condition. In other instances, genetic mutations may underlie dementias in specific populations. For example, a mutation of the gene TREM2 has been found to be common among people with a form of very early onset frontotemporal dementia that runs in Turkish families.

- **Hypertension.** High blood pressure has been linked to cognitive decline, stroke, and types of dementia that affect the white matter regions of the brain.
- **Mental illness.** Depression has been associated with mild mental impairment and cognitive function decline.
- **Smoking.** Smokers are prone to diseases that slow or stop blood from getting to the brain.



## Diagnosis

Doctors first assess whether the individual has an underlying treatable condition such as depression, abnormal thyroid function, drug-induced encephalopathy, normal pressure hydrocephalus, or vitamin B<sub>12</sub> deficiency. Early diagnosis is important, as some causes for symptoms can be



treated. In many cases, the specific type of dementia that a person has may not be confirmed until after the person has died and the brain is examined.

An assessment generally includes:

- **Patient history.** Typical questions about a person's medical and family history might include asking about whether dementia runs in the family, how and when symptoms began, and if the person is taking certain medications that might cause or exacerbate symptoms.
- **Physical exam.** Measuring blood pressure and other vital signs may help physicians detect conditions that might cause or occur with dementia. Such conditions may be treatable.
- **Neurological evaluations.** Assessing balance, sensory function, reflexes, vision, eye movements, and other functions helps identify signs of conditions that may affect the diagnosis or are treatable with drugs. Doctors also might use an electroencephalogram, a test that records patterns of electrical activity in the brain, to check for abnormal electrical brain activity.

The following procedures also may be used when diagnosing dementia:

- **Brain scans.** These tests can identify strokes, tumors, and other problems that can cause dementia. Scans also identify changes in the

brain's structure and function. The most common scans are computed tomographic (CT) scans and magnetic resonance imaging (MRI). CT scans use X-rays to produce images of the brain and other organs. MRI scans use a computer, magnetic fields, and radio waves to produce detailed images of body structures, including tissues, organs, bones, and nerves.

Other types of scans let doctors watch the brain as it functions. Two of these tests are single photon-emission computed tomography, which can be used to measure blood flow to the brain, and positron emission tomography (PET), which uses radioactive isotopes to provide pictures of brain activity. These scans are used to look for patterns of altered brain activity that are common in dementia. Researchers also use PET imaging with compounds that bind to beta-amyloid to detect levels of the protein, a hallmark of AD, in the living brain.

- **Cognitive and neuropsychological tests.** These tests measure memory, language skills, math skills, and other abilities related to mental functioning. For example, people with AD often show impairment in problem-solving, memory, and the ability to perform once-automatic tasks.
- **Laboratory tests.** Many tests help rule out other conditions. They include measuring levels of sodium and other electrolytes in the blood, a complete blood count, a blood sugar test, urine analysis, a check of vitamin B<sub>12</sub> levels, cerebrospinal fluid analysis, drug and alcohol tests, and an analysis of thyroid function.
- **Presymptomatic tests.** Some dementias are associated with a known gene defect. In these cases, a genetic test could help people know if they are at risk for dementia. People should talk with family members, their primary health care professional, and a genetic counselor before getting tested.
- **Psychiatric evaluation.** This will help determine if depression or another mental health condition is causing or contributing to a person's symptoms.

## Treatment

Some dementias are treatable. However, therapies to stop or slow common neurodegenerative diseases such as AD have largely been unsuccessful, though some drugs are available to manage certain symptoms.

Most drugs for dementia are used to treat symptoms in AD. One class of drugs, called cholinesterase inhibitors, includes donepezil, rivastigmine, and galantamine. These drugs can temporarily improve or stabilize memory and thinking skills in some people by increasing the activity of the cholinergic brain network. The drug memantine is in another class of medications called NMDA receptor agonists, which prevents declines in learning and memory. NMDA receptor agonists work by regulating the activity of the neurotransmitter glutamate. When glutamate activity levels are excessive, neurons may die. Memantine may be combined with a cholinesterase inhibitor for added benefits. These drugs are sometimes used to treat other dementias as well. None of these drugs can stop or reverse the course of the disease.



- **Creutzfeldt-Jakob disease.** There are no treatments to cure or control CJD. Management focuses on reducing symptoms and making people comfortable.
- **Dementia with Lewy bodies.** Drugs available for managing DLB are aimed at relieving symptoms such as stiffness, hallucinations, and delusions. However, many of the agents for treating the physical symptoms, particularly antipsychotics, can make the mental health symptoms worse. Conversely, drugs used to treat mental health

symptoms can exacerbate physical symptoms. Studies suggest that AD drugs may benefit people with DLB.

- **Frontotemporal disorders.** There are no medications approved to treat or prevent FTD and most other types of progressive dementia. Sedatives, antidepressants, and other drugs used to treat Parkinson's and Alzheimer's symptoms may help manage certain symptoms and behavioral problems associated with the disorders.
- **Parkinson's disease dementia.** Some studies suggest that the cholinesterase inhibitors used in people with AD might improve cognitive, behavioral, and psychotic symptoms in people with Parkinson's disease dementia. The U.S. Food and Drug Administration has approved one Alzheimer's drug, rivastigmine, to treat cognitive symptoms in PDD.
- **Vascular dementia.** This type of dementia is often managed with drugs to prevent strokes. The aim is to reduce the risk of additional brain damage. Some studies suggest that drugs that improve memory in AD might benefit people with early vascular dementia. Most of the modifiable risk factors that influence development of vascular dementia and VCI are the same risk factors for cerebrovascular disease, such as hypertension, atrial fibrillation, diabetes, and high cholesterol. Interventions that address these risk factors may be incorporated into the management of vascular dementia.



## Current Research

In 2012, the President announced the National Plan to Address Alzheimer's Disease, a national effort to expand research in Alzheimer's and related dementias prevention and treatment and to move the most promising drugs from discovery into clinical trials. The Plan aims to prevent and effectively treat Alzheimer's and related dementias by 2025. Its foundation is the 2011



National Alzheimer's Project Act (NAPA), which was developed to create and maintain a national strategy to overcome the disease. The National Plan calls for increased federal funding for AD research, support for those affected by AD and their families, increased public awareness about AD, and improved data collection and analysis to better understand the impact of AD on people with the disease, families, and the health and long-term care systems. These goals also apply to AD-related dementias, including dementia with Lewy bodies as well as frontotemporal, mixed (characteristics of more than one type of dementia occur simultaneously), and vascular dementias. For more information, see <http://aspe.hhs.gov/daltcp/napa/NatlPlan.pdf>.

The National Institute of Neurological Disorders and Stroke (NINDS), a component of NIH, is the leading federal funder of research on nervous system disorders. Another NIH Institute, the National Institute on Aging (NIA), is the leading federal funder of research on AD. Together, these Institutes are world leaders in supporting research on the dementias, including Lewy body dementia, frontotemporal disorders, and vascular dementia.

Although scientists have some understanding of these dementias and the mechanisms involved, ongoing research may lead to new ways to diagnose,

treat, or perhaps prevent or block disease development. Current areas of research include:

**Clinical studies.** Clinical studies offer an opportunity to help researchers find better ways to safely detect, treat, or prevent dementias. Various NIH Institutes support clinical studies on AD and related dementias at the NIH research campus in Bethesda, MD, and at medical research centers throughout the U.S. For information about participating in clinical studies for AD, related dementias, and other disorders, visit “NIH Clinical Research Trials and You” at [www.nih.gov/health/clinicaltrials](http://www.nih.gov/health/clinicaltrials). For a list of AD clinical trials and studies, see [www.nia.nih.gov/alzheimers/clinical-trials](http://www.nia.nih.gov/alzheimers/clinical-trials). For a comprehensive list of all trials, go to [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

**Drugs.** A number of agents that might slow the progression of AD and other dementias are in various stages of testing.

The NIA-supported Alzheimer’s Disease Cooperative Study (ADCS) ([www.adcs.org](http://www.adcs.org)) is a consortium of academic medical centers and clinics set up by NIH in 1991 to collaborate on the development of promising Alzheimer’s treatments and diagnostic tools.

In the latest round of studies, the ADCS will test drug and exercise interventions in people in the early stages of the disease, examine a medication to reduce agitation in people with Alzheimer’s dementia, and test a cutting-edge approach to speed testing of drugs in clinical trials. Because Alzheimer’s-related brain changes begin years before symptoms appear, the A4 (Anti-amyloid Treatment in Asymptomatic Alzheimer’s Disease) trial is testing a promising therapy in the early stages of the disorder. This secondary prevention trial will test an amyloid-clearing drug in the symptom-free stage of the disease in 1,000 cognitively healthy older volunteers whose brain scans show abnormal levels of amyloid accumulation. Another of the newly funded ADCS drug trials is the

Prazosin for Treating Agitation trial, which will test the use of the generic drug prazosin as a treatment for agitation that may also be well-tolerated in frail and elderly people.

**Exercise.** Researchers are assessing the effectiveness of a supervised aerobic exercise program to enhance general cognition in adults with age-related cognitive decline. They predict that greater cognitive gains will be made by individuals with more fitness gains. Another study will determine if exercise prevents memory loss from getting worse, and if it improves daily functioning and attitudes of those with probable AD. Researchers also hope to gain a better understanding of the effects of exercise and cognitive training on improving brain function in healthy older adults who may be at risk for developing AD.



**Genetics.** Several genes—most notably ApoE and the gene for tau (MAPT)—have been implicated in AD and other forms of dementia. Many dementia-related disorders share genetic and other characteristics of AD. Some families share a particular genetic mutation that causes dementia. Researchers are using samples of a person's genetic material, or genome, to identify genes that may be responsible for the development of dementia and AD. For example, NIH-funded researchers recently examined ApoE's role in the development of late-onset AD and found that one of the three forms of the ApoE gene triggers an inflammatory reaction and damages the blood vessels that feed the brain. Other researchers have identified a gene variant of TREM2 that is involved with a form of frontotemporal dementia that runs in families. Additional research may identify novel genes involved with FTD and other neurodegenerative diseases, perhaps leading to therapeutic approaches where delivery of normal genes would improve or restore normal brain function.

**Imaging.** Clinical imaging may help researchers better understand changes in the brains of people with dementia, as well as help diagnose these disorders. Magnetic resonance imaging may reveal structural and functional differences in the brains of individuals with Parkinson's disease dementia and AD and identify small vessel disease. PET scanning uses ligands—radioactive molecules that bind to proteins to show chemical functions of tissues and organs in the body—to help produce images of brain activity. Scientists funded by NIA are testing new PET ligands that bind to beta-amyloid for early detection of Alzheimer's-type pathology and cognitive decline. Studies of PET ligands that bind to aggregates of tau are ongoing in people with very early-stage AD.



**International efforts.** The International Alzheimer's Disease Research Portfolio (IADRP) helps individuals learn about AD research at public and private organizations in the U.S. and abroad. It also helps organizations leverage resources and avoid duplication of effort. The Common Alzheimer's Disease Research Ontology—a classification system that allows organizations to integrate and compare research portfolios—was developed by NIA, NIH, and the Alzheimer's Association. For more information about IADRP, see <http://iadrp.nia.nih.gov/cadro-web/about>.

**Proteins.** One feature that several major dementias have in common is an excess in the brain of certain proteins or protein fragments that have taken abnormal forms thought to be toxic to brain cells. NIH-funded research projects are aimed at better understanding the toxic effects of protein buildup and how it is related to the development of AD and related dementias. Some of these protein abnormalities can be detected in cerebrospinal fluid.

For example, an abnormally high accumulation of beta-amyloid protein in the brain is a hallmark of AD. NINDS-funded researchers are determining which neural pathways are affected by beta-amyloid and contribute to the development of Alzheimer's pathology and symptoms. NINDS funding also led to a genetically engineered rat model of AD that has the full array of brain changes associated with the human disease and may be used to better define causes and effects of AD related to beta-amyloid accumulation. Funding also was provided by NIA, the National Institute of Mental Health (also part of NIH), and other organizations.

In FTD, AD, and other neurodegenerative diseases, the protein tau collects in abnormal tangled masses of filaments that disrupt nerve signaling, cause cell death, and impair cognition. NINDS-funded researchers are determining whether specific forms of tau interfere with nerve cell signaling and decrease memory function. Others are studying how tau pathology spreads from cell to cell. Tau-related investigations are aimed at identifying common mechanisms of FTD, as well as biomarkers (signs that may indicate disease risk and progression, and improve diagnosis) that will speed the development of novel therapeutics for PDD and other forms of dementia.

Similarly, the abnormal accumulation of the protein alpha-synuclein is a hallmark of Parkinson's disease and Lewy body dementia. Scientists hope to identify what causes alpha-synuclein to form abnormal aggregates and become toxic to nerve cells, and to understand why the aggregation is an age-related phenomenon in Parkinson's disease and other synuclein-related disorders.

**Sleep.** The sleep and wakefulness cycle plays an integral, but not well understood, role in many dementias, including dementia with Lewy bodies, AD, prion dementias, and PDD. Sleep studies in individuals during periods of excessive daytime sleepiness and nocturnal sleep can help determine if fluctuations in mental status among people with

DLB are related to excessive daytime sleepiness. Sleep studies also can assess whether declining cognition is predicted by sleep-related and neurobehavioral markers in parkinsonism.

**Stem cells.** Scientists are exploring various types of cells, including stem cells, to discover nerve cell mechanisms that lead to the initiation and progression of AD and other forms of dementia. Significant research efforts have focused on induced pluripotent stem cells (iPSC), which can be “reprogrammed” from skin cells into any cell type in the body, including nerve cells. NINDS funds three research consortia to develop well-characterized iPSC for amyotrophic lateral sclerosis (ALS), Huntington’s disease, and Parkinson’s disease. These cells can then be used by the research community to study the effects of mutant genes and misfolded proteins on nerve cell function and health, as well as to test potential drugs and therapies for AD and related dementias.



## Conclusion

Currently, there are no cures for the common dementias caused by progressive neurodegeneration, including AD, frontotemporal disorders, and Lewy body dementia. However, some forms of dementia are treatable. A better understanding of dementia disorders, as well as their diagnosis and treatment, will make it possible for affected individuals and their caretakers to live their lives more fully and meet daily challenges. NIH, primarily through research activities funded by NINDS and NIA, continues to make discoveries in the lab, design therapeutic approaches to dementias, and create tools and resources to help speed the development of treatments that can be used in practice. These discoveries may eventually lead to ways to slow disease progression or even cure and prevent the dementias.



## Glossary

**Alpha-synuclein**—a protein that is implicated in abnormal clumps called Lewy bodies, which are seen in the brains of people with Parkinson's disease and some dementias. Disorders in which alpha-synuclein accumulates inside nerve cells are called synucleinopathies.

**Alzheimer's disease**—the most common cause of dementia in people age 65 and older. Nearly all brain functions, including memory, movement, language, judgment, and behavior, are eventually affected.

**Amyloid**—a protein found in the characteristic clumps of tissue (called plaques) that appear in the brains of people with Alzheimer's disease.

**Chronic traumatic encephalopathy**—a form of dementia caused by repeated traumatic brain injury.

**Corticobasal degeneration**—a progressive disorder characterized by nerve cell loss and atrophy in multiple areas of the brain.

**Dementia**—a term for a collection of symptoms that significantly impair thinking and normal activities and relationships.

**Dementia with Lewy bodies**—a type of Lewy body dementia that is a common form of progressive dementia.

**Frontotemporal disorders**—a group of dementias characterized by degeneration of nerve cells, especially those in the frontal and temporal lobes of the brain.

**HIV-associated dementia**—a dementia that results from infection with the human immunodeficiency virus that causes AIDS.

**Lewy body dementia**—one of the most common types of progressive dementia, characterized by the presence of abnormal structures called Lewy bodies in the brain.

**Mixed dementia**—dementia in which one form of dementia and another condition or dementia cause damage to the brain, for example, Alzheimer's disease and small vessel disease or vascular dementia.

**Multi-infarct dementia**—a type of vascular dementia caused by numerous small strokes in the brain.

**Neurofibrillary tangles**—bundles of twisted filaments found in nerve cells in the brains of people with Alzheimer's disease. These tangles are largely made up of a protein called tau.

**Parkinson's disease dementia**—a secondary dementia that sometimes occurs in people with advanced Parkinson's disease. Many people with Parkinson's have the amyloid plaques and neurofibrillary tangles found in Alzheimer's disease, but it is not clear if the diseases are linked.

**Tau**—a protein that helps the functioning of microtubules, which are part of the cell's structural support and help deliver substances throughout the cell. In Alzheimer's disease, tau twists into filaments that become tangles. Disorders associated with an accumulation of tau, such as frontotemporal dementia, are called tauopathies.

**Vascular dementia**—a type of dementia caused by brain damage from cerebrovascular or cardiovascular problems, usually strokes.

## Resources

For more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information Network (BRAIN) at:

### BRAIN

P.O. Box 5801

Bethesda, MD 20824

1-800-352-9424 (toll-free)

*[www.ninds.nih.gov](http://www.ninds.nih.gov)*

Information on dementia is also available from the following organizations:

### Alzheimer's Disease Education and Referral (ADEAR) Center National Institute on Aging

P.O. Box 8250

Silver Spring, MD 20907-8250

1-800-438-4380 (toll-free)

*[www.nia.nih.gov/alzheimers](http://www.nia.nih.gov/alzheimers)*

### Alzheimer's Association

225 North Michigan Avenue, Floor 17

Chicago, IL 60601-7633

1-800-272-3900 (toll-free, 24-hour helpline)

1-312-335-5886 (TDD)

*[www.alz.org](http://www.alz.org)*

### Alzheimer's Foundation of America

322 Eighth Avenue, 7th Floor

New York, NY 10001

1-866-232-8484 (toll-free)

*[www.alzfdn.org](http://www.alzfdn.org)*



### Alzheimer's Drug Discovery Foundation

57 West 57th Street, Suite 904

New York, NY 10019

1-212-901-8000

*[www.alzdiscovery.org](http://www.alzdiscovery.org)*



### Association for Frontotemporal Degeneration

Radnor Station Building #2, Suite 320

290 King of Prussia Road

Radnor, PA 19087

1-866-507-7222 (toll-free)

*[www.theaftd.org](http://www.theaftd.org)*



### BrightFocus Foundation

22512 Gateway Center Drive

Clarksburg, MD 20871

1-800-437-2423 (toll-free)

*[www.brightfocus.org/alzheimers](http://www.brightfocus.org/alzheimers)*



### John Douglas French Alzheimer's Foundation

11620 Wilshire Boulevard, Suite 270

Los Angeles, CA 90025

1-310-445-4650

*[www.jdfaf.org](http://www.jdfaf.org)*



### Lewy Body Dementia Association

912 Killian Hill Road, S.W.

Lilburn, GA 30047

1-404-935-6444

1-800-539-9767 (toll-free LBD Caregiver Link)

*[www.lbda.org](http://www.lbda.org)*

CheapNursingCEUs.com



**National Institute of Mental Health**

6001 Executive Boulevard, Room 8184

Bethesda, MD 20892-9663

1-866-415-8051 (toll-free)

1-301-443-8431 (TTY)

*[www.nimh.nih.gov](http://www.nimh.nih.gov)*



**National Organization for Rare Disorders**

55 Kenosia Avenue

Danbury, CT 06810

1-800-999-NORD (1-800-999-6673) (toll-free)

*[www.rarediseases.org](http://www.rarediseases.org)*





"This course was developed from the public domain document: The Dementias: Hope Through Research – National Institute of Health, National Institute of Neurological Disorders and Stroke, National Institute on Aging."