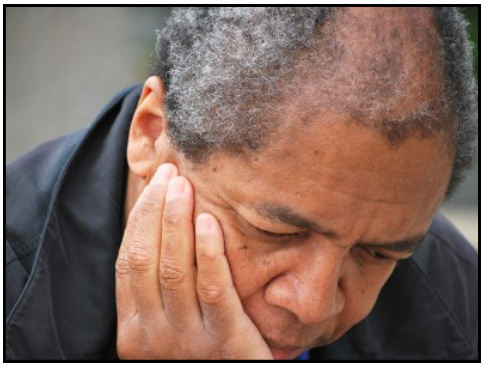
An Overview of Dementia: The Growing Crisis in West Virginia



WEST VIRGINIA Department of Health & Human Resources

Bureau for Public Health
Health Statistics Center
350 Capitol Street, Room 165
Charleston, WV 25301

Earl Ray Tomblin, Governor
Michael J. Lewis M.D, Cabinet Secretary

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Earl Ray Tomblin
Governor

Michael J. Lewis, M.D., Ph.D.
Cabinet Secretary
Department of Health and Human Resources

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Chris Curtis, MPH
Acting Commissioner

Nancye M. Bazzle, MPH
Deputy Commissioner

Catherine Slemp, MD, MPH
Acting State Health Officer

West Virginia Department of Health & Human Resources
Bureau for Public Health

Report Prepared By

Eugenia Thoenen, Consultant
Health Statistics Center

Statistics Center

Daniel Christy, MPA, Director
James C. Doria, Statistical Services Division Director
Thomas N. Leonard, MS, Programmer/Analyst
Tom Light, Programmer

The Growing Crisis of Dementia in West Virginia: Highlights

● It is estimated by the Alzheimer's Association that there are currently 44,000 people with Alzheimer's disease (AD) living in West Virginia. **By 2025, this number is expected to increase to over 50,000**. This will include approximately 3,000 to 4,000 people aged 65-74, 26,000 people aged 75-84, and 21,000 people aged 85 and older.

● The greatest risk factor for AD is age; it is estimated that 10% of people over the age of 65 have AD and nearly 50% of people over the age of 85 are at risk for developing the disease. According to the American Community Survey conducted by the U.S. Census Bureau, **in 2008 West Virginia had the 3rd highest median age in the nation**: 40.3 years, compared with a U.S. average of 36.7 years.

● Studies suggest that dementia caused solely by vascular abnormalities is rare, while AD is increasingly viewed as having a vascular basis and subject to the same risk factors as stroke and other cardiovascular illness, including smoking, high cholesterol, hypertension, physical inactivity, obesity, diets deficient in fruits and vegetables, and diabetes. **West Virginia adults traditionally have reported significantly higher prevalence of cardiovascular risk factors than adults nationwide.**

- **According to the Behavioral Risk Factor Surveillance System, West Virginia ranked first in the nation in 2008 in the prevalence of smoking and diabetes.** The state was 3rd in that year in the rate of obesity. In 2007, West Virginia ranked 1st among the 50 states and the District of Columbia in the prevalence of high cholesterol and 3rd in the rate of hypertension.

● In 2007, the rate of hospital discharges among state residents that had either a principal or secondary diagnosis of dementia was 33.9 discharges per every 10,000. **Between 1998 and 2007, the rate of hospital discharges with dementia as a principal diagnosis increased 29%, from 3.4 to 4.4 per 10,000 discharges.**

- Women who were hospitalized in 2007 were much more likely than men to have either a principal or secondary diagnosis of dementia. The rate among women was 44.5, compared with a rate of 22.8 among men. The rate of hospital discharges with a dementia diagnosis among patients aged 85 and older was 644.2 per every 10,000 discharges.

- In the decade from 1998 through 2007, estimated charges for hospitalizations of state residents with a principal diagnosis of dementia increased 184%, from $3,692,000 to $10,492,000.

- In 2007, the rate of hospital discharges with a principal or secondary diagnosis of AD was 29% higher in West Virginia than in the nation as a whole (24.4 per 10,000 discharges vs. 18.9).

● **Dementia was the 5th leading cause of death in West Virginia in 2007**. Approximately 5% of all deaths in the state in that year were due to AD or other dementia.

● Mortality rates for dementia as the underlying (or principal) cause of death have risen markedly in West Virginia over the past two decades due to several factors, including an enhanced awareness of AD and other dementias, earlier diagnosis of the illnesses, and an aging population. **From 1988 through 2007, the mortality rate for dementia increased from 8.2 deaths per 100,000 population to 49.9 deaths.** The increase was seen for both AD and other dementias and in 51 of the 55 counties in the state.

● When 2006 multiple-cause-of-death data were examined, the results showed that the state mortality rate for dementia as the underlying cause of death was similar to the national rate (48.6 deaths per 100,000 population vs. 50.8). **The state rate for mortality from dementia as an any-listed cause of death, however, was 11% higher than the national rate (99.4 deaths per 100,000 population vs. 89.9).**

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AN OVERVIEW OF DEMENTIA: THE GROWING CRISIS IN WEST VIRGINIA

Forgetting a name . . . misplacing the car keys . . . being unable to think of the right word. These used to be viewed as just a normal part of the aging process, having a "senior moment," and indeed that might be all that is occurring. In recent years, however, there has been an increased fear that such absentmindedness might instead be the beginning of a slow decline into dementia, or severe loss of mental function. Cases of dementia and, in particular, Alzheimer's disease (AD) have soared over the past few decades, to the point where most people now know of someone or have a family member with the illness. As the baby boomer generation ages, an avalanche of new cases is predicted, causing a catastrophic drain on the health care system and the families of dementia patients. It is imperative to meet the public health challenges this disease places on our society through research directed toward both treatment of existing disease and eventual primary prevention.

The current report is a revised and updated version of a report originally published by the West Virginia Department of Health and Human Resources, Bureau for Public Health in 2005. It seeks to present an overview of the causes and types of dementia, with an updated examination of research on prevalence, costs, risk factors, and prevention of dementia, as well as the most current statistics on dementia hospitalization and mortality in West Virginia. Since the publication of the original report, legislation creating a population-based Alzheimer's registry has been passed by the West Virginia Legislature, becoming law in 2006. The West Virginia Alzheimer's Registry, housed at the Blanchette Rockefeller Neurosciences Institute at West Virginia University, will collect and maintain data on the number of people in West Virginia with AD and related disorders. The Registry, only the third in the country, is scheduled to begin data collection in 2010.

AN OVERVIEW OF DEMENTIA

The adult brain weighs about three pounds, a scant 2% of the total weight of a 150-pound person. As insignificant as it is in size, this amazing organ allows us to carry out our everyday functions through the electrical and chemical processes that are constantly taking place among its 100 billion neurons, or nerve cells. These functions range from those that occur without our direction, such as breathing, heart rate, and digestion, to our sophisticated cognitive abilities, including thinking, learning, reasoning, remembering, making judgments, and speaking. **Dementia** results when the areas of the brain that are involved with cognitive functions are damaged, either through disease or trauma, to an extent that interferes with a person's ability to perform day-to-day activities.

The brain is made up of three main structures: the cerebrum, the cerebellum, and the brainstem. The **cerebrum**, with its left and right hemispheres, accounts for 85% of the brain's weight. Each of its two hemispheres consists of four lobes: frontal, parietal, occipital, and temporal. The hemispheres are connected by a thick bundle of nerves called the corpus callosum and are covered by the **cerebral cortex**, the outer layer comprising the "gray matter" of the brain. It is in the tightly packed neurons in the cerebral cortex that the regions of the brain involved in voluntary movement, sensory perceptions (e.g., seeing and hearing), memory, emotions, and speech reside. Conscious thought and mental activity are processed by the cortex.

Several essential parts of the brain lie deep within the cerebrum, in the "white matter" of the brain. These include the limbic system, which links the cerebral cortex to the brainstem. The limbic system

includes the hippocampus (important for short-term memory), the amygdala (controls autonomic, emotional, and sexual behavior), the thalamus (relays sensory information), and the hypothalamus (monitors body temperature and food intake, among other activities).

The **cerebellum**, located at the base of the brain, accounts for slightly more than 10% of the brain. Responsible for balance and coordination, it receives information from the inner ear, eyes, and muscles to provide control over our movements. The **brainstem** is the smallest portion of the brain. It sits at the base of the brain, connecting the spinal cord to the rest of the brain. The brainstem controls our body's automatic functions, such as heart rate, blood pressure, circulation, and breathing, as well as sleep and dreaming.

The brain has two principal kinds of cells, **neurons** and **glia cells**. Our cognitive functions are made possible through the connections that exist among the billions of neurons; glia cells, which outnumber neurons by at least threefold, support and nourish neurons.

Neurons are specialized cells that conduct and transmit electrical signals that, when assembled into circuits, pass sensory and motor signals to all areas of the body. Each neuron consists of many dendrites, short branches off the main body of the cell, and an axon, a long, thread-like extension of the cell that carries nerve impulses (electrical charges) to its end, where each electrical charge is transformed into a chemical messenger called a **neurotransmitter**. This messenger travels across a small gap, known as a **synapse**, to the receiving end of another cell's dendrites. Once attached to the new cell, it is changed back into an electrical charge. Billions of these signals are constantly traveling the pathways of our brain, allowing us to receive and process information and send instructions to the various parts of our bodies.

Dementia occurs when there is disruption of the communication among neurons, through cell death or isolation. There are many different types of dementia; the causes of some types are known, while research is still trying to understand the processes that cause others. Some dementias are reversible or partially reversible through treatment, such as those caused by drug abuse, certain medications, depression, or certain tumors; these, however, account for a smaller percentage of all dementia than originally believed (1,2). The majority of dementias are irreversible.

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>
> Alzheimer's Association

Dementia exacts a heavy burden on society; when people are no longer able to carry out their daily lives due to cognitive deficits, it falls to family members, social service agencies, and long-term care facilities to help meet their needs. In the later stages of dementia, patients are totally dependent on others for their care; life becomes a round-the-clock vigil for caregivers, many of whom are elderly and in poor health themselves. More than 40% of caregivers rate the stress of caregiving as high or very high; approximately one-third of caregivers suffer from depression (3). Many dementia patients live in long-term care. Approximately two-thirds of nursing home residents suffer from dementia; **in West Virginia in 2007, it was estimated that 64% of nursing home residents had some level of cognitive impairment** (3). This, however, represents the minority of persons living with dementia. At any one time approximately 70% of people with dementia are living at home (3), cared for by families until physical and emotional stress and financial hardship make home care too difficult.

TYPES OF DEMENTIA

Alzheimer's disease (AD) is by far the most frequently diagnosed form of irreversible dementia, accounting for 60% to 80% of all dementia cases, according to the Alzheimer's Association (3). Early-onset AD, which develops before the age of 65, is relatively rare, accounting for less than 10% of all AD patients. Late-onset AD, occurring after age 65, is the most common form. The symptoms of both types

of AD are the same; however, the progression of the disease is often more rapid among early-onset patients.

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The onset of AD is usually gradual, normally beginning with mild memory lapses and problems finding the right words. Symptoms worsen over a period of a few years until job performance is affected, activities such as bill paying become difficult, confusion about places leads to getting lost, and the individual loses initiative and spontaneity. This early stage of the disease usually lasts from two to four years and is when the patient normally is diagnosed.

The second, or middle, stage of AD is the longest and can last up to 10 years. This stage is marked by psychiatric and behavioral changes such as anxiety, paranoia, irritability, or depression. There is increasing memory loss; shortening of attention span; loss of impulse control; difficulty in reading, writing, understanding numbers, and thinking logically; and perceptual motor problems. It is during this stage that close friends and family members often are not recognized.

In the third, or terminal, stage of the disease, the patient has little or no capacity for self-care, loses the ability to communicate with words, suffers weight loss even with a good diet, and cannot control bodily functions. There may be difficulty in swallowing and seizures may occur. The last stage of AD usually lasts from one to three years.

The pathology of AD is characterized by hard, insoluble **plaques** between the nerve cells in the hippocampus and other areas of the cerebral cortex and neurofibrillary **tangles** within the cells. Plaques are made up of beta-amyloid. Amyloid is a term that refers to protein fragments that are produced naturally by the body and would be broken down and eliminated in a healthy brain. Beta-amyloid is a protein fragment that is snipped from a larger protein known as an amyloid precursor protein (APP), which is important to the survival of neurons by helping the cells repair themselves after injury. APP attaches to the cell membrane, positioning itself both inside and outside of the membrane. When AD is present, certain enzymes cut the APP into fragments; the beta-amyloid fragments then clump together outside of the cells, joining with non-nerve cells and other molecules to form plaques. The plaques interfere with the neurons' ability to communicate with each other, eventually destroying whole regions of the brain.

Neurofibrillary tangles are made up of insoluble twisted fibers that accumulate within the nerve cell. A healthy neuron has an internal support system made up of structures called microtubules that transport nutrients from one part of the cell to another. Part of the microtubule consists of a protein called tau. In AD, the tau protein is abnormal and begins to pair with other tau strands, becoming tangled. This causes the microtubule to collapse, destroying the neuron's transport system and eventually causing the death of the cell.

Vascular dementia is the second most frequently diagnosed type of dementia. It is estimated that it comprises from 10% to 20% of all dementia (4). The symptoms of vascular dementia and AD are often the same, but the onset is more abrupt in vascular dementia. While AD is marked by a gradual worsening of symptoms, vascular dementia usually follows an irregular, stepwise pattern, with long periods of stability before a sudden worsening. Gait problems frequently are noticed in the beginning stages of vascular dementia, unlike AD.

Strokes are the most common cause of vascular dementia, through the death of brain cells resulting from diminished or disrupted blood flow to the brain. Vascular dementia can develop from one large stroke or from a series of small strokes (transient ischemic attacks, or TIAs) that don't seem to cause permanent damage at the time. However, the buildup of

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damage from TIAs can cause what is termed **multi-infarct dementia** (MID). While strokes are the most common cause of vascular dementia, arteriosclerosis (hardening of the arteries) can also be at fault by extensively narrowing or blocking arteries and causing decreased blood flow. This normally occurs among older persons with high blood pressure or high cholesterol levels. **Binswanger's disease** is a rare form of vascular dementia that affects the white matter deep within the brain. Hypertension is the main predisposing factor to Binswanger's; its onset occurs around 50 years of age and symptoms include slowed thinking and reacting, walking difficulty, emotional swings, and loss of bladder control early in the disease.

Lewy Body disease has symptoms similar to AD and Parkinson's disease, including memory problems, confusion, hallucinations, and language problems. In this case, however, dementia is caused by tiny round protein deposits ("Lewy bodies") that form in the nerve cells and disrupt cerebral functioning. It has been suggested that Lewy Body disease may be the second most common form of dementia in elderly patients (5).

There are other, less common, types of irreversible dementia. In **frontotemporal dementia** (FTD), damage is localized in the front part of the brain, resulting in personality and behavioral changes and language deficits before memory loss. FTD has a strong genetic component. **Pick's disease,** a form of FTD, is marked by "Pick bodies," another form of abnormal structure found within nerve cells that causes them to swell and eventually fail to function. **Creutzfeldt-Jakob disease** is caused by an infectious organism and progresses rapidly with dementia, involuntary movements, blindness, and finally coma. **Parkinson's disease** can eventually result in dementia, beginning with slowed thinking and progressing to confusion. Dementia usually develops in the latter stages of **Huntington's disease**, an inherited, degenerative disease of the nervous system.

Mixed dementia occurs when both AD and vascular dementia are present, a condition now thought to become increasingly common among the elderly. Autopsies of the brain, the only definitive diagnosis of dementia, have shown that up to 45% of people suffering from dementia have both types of the disease (6). Mixed dementia is suspected when the patient has symptoms of AD but also has a diagnosis of cardiovascular disease. Evidence of Lewy Body disease and Parkinson's disease has also been found to be present in the brains of people with mixed dementia. A clinical-pathologic study by Schneider et al. of 141 elderly community-living people who died while participating in the Rush Memory and Aging Project in Chicago found that only 38% had pure AD; over 50% of participants had multiple dementias, i.e., AD, vascular dementia, and Parkinson disease/Lewy Body disease (7).

INCIDENCE AND PREVALENCE OF DEMENTIA

Someone in the United States develops Alzheimer's disease (AD) every 70 seconds (3). By 2050, someone will develop AD every 33 seconds. An estimated 5.3 million people of all ages currently have AD, 5.1 million aged 65 and older and 200,000 with younger-onset AD, according to *2009 Alzheimer's Disease Facts and Figures* (3). In 1998, Brookmeyer et al. estimated the annual number of new clinically diagnosed cases (incidence) of AD at 360,000 (8). Evans et al. estimated 411,000 new cases in 2000 and 454,000 new cases in 2010 (9). As the population ages, these numbers will continue to rise. Recent research suggests that both the incidence and prevalence of dementia continue to rise with age, even among the "oldest old" (10). Dementia incidence was previously thought to plateau or even decline among people in their 80s and 90s and beyond.

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Gender. Women are more likely to be diagnosed with AD and other dementias than are men. Results from the Aging, Demographics, and Memory Study (3) estimated that, in 2002, 14% of all people aged 71 and older had some form of dementia, 16% of women and 11% of men. This difference, however, is explained by the fact that women on average live longer than men (3).

Race. Research has produced mixed results on the rates of dementia among minorities when compared to those in whites. In studies presented at the 9th International Conference on Alzheimer's Disease and Related Disorders (ICAD), African Americans and Hispanics were found to have higher rates and earlier onset of AD and other dementias (11). However, other analyses cited in *2009 Alzheimer's Disease Facts and Figures* suggest that these differences are explained by factors other than race such as age, gender, years of education, and comorbid conditions. More research is needed to determine the effect of race, if any, on the development of dementia.

Predictions. Evans et al. presented research in 2002 at the 8th ICAD that made dire predictions about the future of AD in the United States (9), based on data from the Chicago Health and Aging Project, supported by the National Institutes of Health. They projected that by 2050 an estimated 13.2 million Americans will have AD if nothing is done to forestall or treat the disease. Table 1 below shows these projections, in millions, by age group:

Table 1. Projected Number (in Millions) of People with Alzheimer's Disease by Age Group United States, 2000-2050

Year	Ages 65-74	Ages 75-84	Ages 85+	Total
2000	0.3	2.4	1.8	**4.5**
2010	0.3	2.4	2.4	**5.1**
2020	0.3	2.6	2.8	**5.7**
2030	0.5	3.8	3.5	**7.7***
2040	0.4	5.0	5.6	**11.0**
2050	0.4	4.8	8.0	**13.2**

*Does not add to total due to rounding.

Dementia Prevalence in West Virginia. Evans et al. expanded their study to include state-specific projections of AD prevalence through 2025 and published their results in *Neurology* in 2004 (12). For West Virginia, their model produced an estimate of 40,000 affected individuals in 2000. **By 2025, West Virginia is expected to experience a 25% increase in number of persons with AD, to 50,000.** Table 2 shows the projections, in thousands, by age group for the state.

Table 2. Projected Number (in Thousands) of People with Alzheimer's Disease by Age Group West Virginia 2000-2025

Year	65-74	75-84	85+	Total	% Change (from 2000)
2000	2.7	21.0	16.0	**40.0**	
2010	2.5	22.0	19.0	**44.0**	10
2020	3.2	22.0	20.0	**46.0**	15
2025	3.5	26.0	21.0	**50.0**	25

COSTS OF DEMENTIA

The estimated economic costs of Alzheimer's disease (AD) in the United States total at least $148 billion annually according to 2005 data published by the Alzheimer's Association (3). This amount includes: (1) $91 billion in Medicare costs for beneficiaries with AD and other dementias; (2) $21 billion for state and federal Medicaid costs for nursing home care for people with AD and other dementias, and (3) $36.5 billion for indirect costs to businesses through the employment of caregivers of people with AD and

other dementias (including $10 billion due to absenteeism, $18 billion due to lost productivity, and $6 billion in worker replacement costs). It is estimated by a University of Pennsylvania study, *Alzheimer's Disease: The Costs to Businesses in 2002*, that the cost to businesses actually approaches $61 billion when health care for people with dementia ($24.6 billion) is included (13).

> In 2004, total health care costs from all sources for Medicare beneficiaries aged 65 and older with AD or other dementias averaged $33,007 per person, more than three times greater than the average per person cost of $10,603 for beneficiaries without AD or other dementias.
>
> Alzheimer's Association

Dementia patients have high rates of hospital visits, nursing home stays, and other long-term care services, placing a huge financial burden on families and government programs such as Medicare, Medicaid, and the Veterans Administration. As dementia, and AD in particular, is primarily an illness of the elderly, the costs to Medicare are tremendous. *2009 Alzheimer's Disease Facts and Figures* reports that Medicare costs for AD patients aged 65 and older are nearly three times higher than the average for all Medicare beneficiaries aged 65 and older. Medicare per person payments in 2004 for health care and long-term care services for beneficiaries with AD or other dementias totaled $15,145, compared with $5,272 for beneficiaries without AD or other dementias (3). The difference in per person Medicaid payments in 2004 was even greater: $6,605 in payments for Medicare patients aged 65 and older with AD or other dementias compared with $718 for those patients without dementia. The Geriatric Mental Health Foundation has estimated the per patient cost for nursing home care alone for patients with AD ranges from $42,000 to $70,000 a year; for a growing number of people with low incomes and few assets, this is paid by Medicaid (14).

Most people with AD or other dementias have at least one additional serious medical condition; having dementia creates complications in treating these other conditions, increasing the medical costs. According to *2009 Alzheimer's Disease Facts and Figures* (3), in 2004 Medicare beneficiaries aged 65 and older who had diabetes in addition to dementia had 64% more hospital stays than those beneficiaries having diabetes but no dementia. The average per person Medicare payment for patients with diabetes was $20,655 for those with dementia compared with $12,979 for those with no dementia. People with coronary heart disease and dementia had 42% more hospital stays than heart patients without dementia; their average Medicare payment was $20,780, compared with $14,640 for those without dementia (3).

The costs of treating AD increase with the severity of the disease. Researchers at Duke University estimated that direct medical costs for patients with advanced AD were 60% to 200% higher than for those with mild AD (15). The study found the highest costs to be incurred after a patient has had AD for 10 years. According to Henry Glick, the study's lead author, "In women, it's $30,000 a year among survivors if you survive 10 years and in men it's $20,000." The higher costs for women result from longer stays in nursing homes.

In 2005, the Institute for the Study of Aging found the costs of treating Medicare patients who had vascular dementia and were still living in the community were significantly higher than those for treating AD patients living in the community. The annual costs for patients with vascular dementia were estimated at $14,387, substantially higher than the $7,839 estimated for AD patients and the $5,494 for patients without dementia (16).

> "Unless a prevention or cure is found soon, Alzheimer's disease will overwhelm our already stretched health-care system and bankrupt Medicare and Medicaid."
>
> Alzheimer's Association

RISK FACTORS FOR DEMENTIA

The greatest risk factor for Alzheimer's disease (AD) is **age**. While about 10% of people in the United States over the age of 65 have AD, the Alzheimer's Association estimates that nearly 50% of those over age 85 are at risk for developing the disease (3). **Women** are more likely than men to develop AD; this may be age-related, as women live longer than men.

Research has shown that individuals with a **family history** of AD are more likely to have the disease themselves (3). The risk increases if more than one family member has developed AD. While there is not just one cause that can be pinpointed for AD, scientists know that there can be a genetic factor in the development of both the early-onset and late-onset types of the disease.

Genes are categorized as either deterministic genes (those that directly cause the disease) or risk-factor genes (those that increase the likelihood of the disease but do not cause it) (17). Deterministic genes are rare and are implicated in the development of some cases of early-onset AD; they are the result of gene mutations on chromosomes 21, 14, and 1 (18). This type of the disease is called familial Alzheimer's disease (FAD); it accounts for less than 5% of AD cases. FAD presents in people aged 30 to 60 and can affect many family members in multiple generations.

Most cases of AD are termed late-onset and occur in people over the age of 60. People who have a specific version of the apoE gene (i.e., apoE-e4), which is found on chromosome 19, have been found to be several times more likely to develop late-onset AD than those who have another version of that gene (17). Separate studies have found that chromosome 10 might also have genes that increase a person's chances of developing late-onset AD (19,20). Research suggests that a number of additional genes might be risk genes for AD (21), including one called SORL 1 located on chromosome 11, discovered in 2007 (22). Two European studies published in *Nature Genetics* in 2009 identified three new gene variants (CLU, CR1, and PICALM) involved with AD (23). Intensive research efforts are currently under way to identify and analyze the multiple genetic factors involved in AD development.

> The genetic component of AD is being intensely studied by scientists worldwide. In addition to the identified apoE-e4 gene on chromosome 19, a number of other genes might be risk genes for the disease. These genes may increase an individual's likelihood of developing AD.

Oxidative damage is being investigated as a possible contributor to AD. It has been suggested that damage from free radicals can accumulate in neurons, eventually resulting in a loss of function (24). The brain's high rate of metabolism and the longevity of its cells make it vulnerable to this type of damage over the course of a person's life span. **Inflammation** in the brain is another factor under study in the development of AD; inflammation has been linked to a number of age-related diseases, including heart disease. Part of the body's natural immune response, inflammation occurs when the body activates white blood cells and produces chemicals to fight infection and invading foreign substances. The types of cells and compounds normally involved in inflammation have been found in AD plaques, leading scientists to suggest that these aid in the development of the plaques that ultimately cause the neurons to die (25). Recent studies have suggested that anti-inflammatory drugs may protect against AD or reduce the characteristic AD lesions (26).

A study that analyzed the medical records of World War II veterans linked **head injury** in early adulthood to AD in later life (27). The authors speculated that brain trauma can trigger a degenerative process that eventually results in the development of AD. Researchers at the University of Pennsylvania have also documented a link between repetitive head injuries and the subsequent development of AD (28).

Coronary artery bypass surgery has also been linked to cognitive decline. Researchers at Duke University Medical Center reported in 2001 that among 261 patients who underwent bypass surgery 53%

showed cognitive decline at discharge, 24% at six months, and 42% at five years (29). Boston University School of Medicine (BUSM) researchers found an association between coronary bypass surgery and AD in a study of 5,216 people who underwent the surgery that was published in the *Journal of Alzheimer's Disease* in 2005 (30). BUSM researchers also found a link between angioplasty and development of AD.

The Alzheimer's Association reports that individuals with **Down's syndrome** (trisomy 21) have a higher incidence of developing AD in middle age; it is estimated that 36% of all people with Down's syndrome aged 50-59 have dementia, with the percentage increasing to 55% among those aged 60-69 (31). The prevalence of dementia in people with other **learning disabilities** is estimated to be approximately four times higher than that in the general population (31).

Research conducted at the Duke University Medical Center has supported evidence of a link between AD and exposure to certain **environmental toxins** (32). The study, presented at the 9th ICAD in 2009, examined the effects of occupational pesticides on the risk of AD and suggested that the pesticides may affect the release of acetylcholine, a chemical involved in memory. After adjusting for age, sex, education, and the apoE genotype, researchers found people with pesticide exposure were 53% more likely than those without exposure to develop AD. Researchers reporting in the *Journal of Neuroscience* in 2008 found evidence of an association between early life exposure to lead and the development of AD in later life (33); other research has found associations between occupational lead exposure and memory impairment in older adults (34,35). Research continues into the possible role of mercury in the development of AD (36).

Cerebral infarctions (strokes) are associated with vascular dementia, especially in the elderly, and impaired cognitive function. Two separate studies found a twofold increase in the risk of vascular dementia following a cerebral infarction, including silent brain infarcts (37,38). The risk increased with multiple, large, or clinically evident strokes.

A 2003 study by Honig et al. has linked stroke with an increased risk of AD as well (39). The relationship was found to be strongest when stroke was accompanied by known cardiovascular risk factors, i.e., hypertension, diabetes, and heart disease. The authors offer two possible explanations for the association: (1) poor vascular health in the brain may accelerate AD symptoms and (2) an underlying physiological cause may make some people more prone to both AD and stroke. Recent research published in *Neuron* in 2008 found evidence of an increase in the production of the toxic amyloid peptides thought to cause AD following a stroke (40).

Educational Attainment. Years of education and the development of dementia and AD have been addressed in numerous studies. Less education appears to be associated with a higher risk of developing dementia. Plassman et al. reported in *Neuroepidemiology* in 2007 that data from the Aging, Demographics, and Memory Study indicated that people with less than 12 years of education had a 15% greater risk of developing dementia compared with people with 12 to 15 years of education and a 35% greater risk than those with more than 15 years of education (41). However, Wilson et al reported in *Neurology* in 2009 that, while more education appears to reduce the risk of AD and dementia, it does not protect against how rapid the decline in memory occurs once it begins (42).

Modifiable Behavioral Risk Factors and AD/Vascular Dementia

The connection between AD and vascular dementia is of great interest to scientists as more is learned about each disorder. Autopsy results suggest that dementia caused solely by vascular abnormalities is rare, while AD is increasingly viewed as having a vascular basis and subject to the same risk factors as stroke and other cardiovascular illness, including **smoking, high cholesterol, hypertension, physical inactivity, obesity, diets deficient in fruits and vegetables, and diabetes**. The blood vessel damage caused by these and other risk factors may result in the production of the proteins that then kill the nerve cells and leave behind the characteristic plaques and tangles of AD. West Virginia adults report high rates of all of these risk factors, in some instances having the worst rates in the nation, as shown in Table 3 on the following page.

Table 3. Prevalence (%) of Selected Risk Factors Among All Adults and Adults Aged 65 and Older West Virginia Behavioral Risk Factor Surveillance System, 2008							
	Total		Male		Female		U.S. Ranking* (Total %)
	All Ages	Ages 65+	All Ages	Ages 65+	All Ages	Ages 65+	
Current Smoking	26.6	9.5	26.0	8.7	27.1	10.0	**1**
Hypertension**	33.3	60.1	35.0	57.6	31.6	61.9	**3**
High Cholesterol**	42.4	53.1	42.4	47.4	42.4	57.3	**1**
Diabetes	11.9	22.8	12.1	26.4	11.8	20.2	**1**
Physical Inactivity***	28.3	34.7	25.6	29.3	30.7	38.7	**12**
Poor Nutrition**	80.3	77.3	84.9	82.0	75.9	73.9	**9**
Obesity	31.9	23.5	32.3	22.3	31.6	24.3	**3**

*West Virginia ranking among 50 states and the District of Columbia. States are ranked worst (1) to best (51).
**2007 data
***2006 data

Smoking. A meta-analysis of 19 studies on smoking and dementia concluded that current cigarette smokers are more likely to develop dementia than former or never smokers (43). Current smokers were shown to have a higher risk of developing both AD and vascular dementia. Research presented at the American Academy of Neurology's Annual Meeting in 2008 supported these findings, with researchers from the Wien Center for Alzheimer's Disease reporting that heavy smokers, i.e., those who smoked one or more packs of cigarettes a day, developed AD 2.3 years earlier than people who were not heavy smokers (44). Heavy drinking and having the apoE-4 gene increased the risk even more. British researchers publishing in the *British Medical Journal* in 2009 extended the risk to secondhand smoke exposure in a study linking passive smoke to increased odds of cognitive impairment (45).

Smoking in West Virginia. West Virginia traditionally has reported high rates of cigarette smoking, a trend that continues to the present. In 2008, the state reported the highest prevalence of smoking in the nation among adults aged 18 and older. Over one-fourth (26.6%) of the state's adults reported being a current smoker, 26.0% of men and 27.1% of women (Table 3). More than one in nine state residents aged 65 and older (8.7% of men and 10.0% of women) reported being current smokers in 2008.

Hypertension. According to the American Heart Association, high blood pressure is the most important controllable risk factor for stroke, which in turn can result in vascular dementia. As researchers continue to study vascular factors in the development and progression of AD, there is also increasing evidence of an association between AD and hypertension. In a study conducted by Khachaturian et al of Johns Hopkins University School of Medicine, data from a three-year memory and aging study involving 3,300 participants aged 65 and older were analyzed to determine the relationship between blood pressure and the risk of AD. A lower Alzheimer's risk was found among users of hypertension medications, especially potassium-sparing diuretics (46). Findings from the Cache County Dementia Progression Study revealed a greater rate of decline among patients with AD and hypertension (47). Research presented at the Radiology Society of North America (RSNA) 93rd Scientific Assembly held in 2007 showed a significant decrease of cerebral blood flow in AD patients with high blood pressure, suggesting that they may be more vulnerable to the effects of the disease (48) and allowing the disease to progress more rapidly. As the lead researcher noted, "Hypertension may increase the vulnerability of the brain to Alzheimer's."

Hypertension in West Virginia. According to data from the BRFSS, West Virginia ranked 3rd among the 50 states and the District of Columbia in 2007 in the prevalence of adults aged 18 and older who reported having been told by a health professional that they had high blood pressure. The state prevalence of 33.3% was 20% higher than the national median of 27.8%. The rate of hypertension among adults in West Virginia has increased steadily since a rate of 25.5% was reported in1995, reflective in part of the state's aging population. As shown in Table 3, six out of 10 (60.1%) adults aged 65 and older reported being hypertensive, 57.6% of men and 61.9% of women.

High Cholesterol. Evidence is growing that monitoring cholesterol levels is just as important for a person's brain as for his or her heart. Harvard researchers involved in the ongoing Women's Health Study assessed more than 4,000 women aged 65 and older over several years and found that those women with the highest HDL, or "good," cholesterol were less likely to develop AD (49). Women whose HDL levels were in the 60 to 75 mg/dL range decreased their risk of dementia by almost 50%. A Kaiser Permanente study, published in *Dementia and Geriatric Cognitive Disorders* in 2009, conducted among nearly 10,000 people over four decades discovered links between high and borderline total cholesterol levels and the development of vascular dementia and AD (50). Even after controlling for weight, hypertension, and diabetes, the study participants with high cholesterol levels (240+) at the beginning of the study had a 66% greater risk of developing AD in later life, while those with borderline-high cholesterol (200-240) had a 25% greater risk. Recent findings from the British Whitehall II Study discovered a direct association between low HDL cholesterol levels and poor memory and decline in memory in middle-aged adults by age 60; total cholesterol and triglycerides were not found to have this association (51). The precise mechanism behind this requires future research but it has been proposed that HDL cholesterol may block the formation of beta-amyloid (the main component in AD protein plaques), maintain overall vascular health, and/or reduce inflammation and free radical damage.

High Cholesterol in West Virginia. In 2007, West Virginia ranked 1st in the nation in the rate of adults who had been told their cholesterol was high (Table 3). In that year, a total of 42.4% of all adults aged 18 and older in the state reported high cholesterol, compared with a national median of 37.6%. The overall prevalence of adults with high cholesterol has increased from 30.4% in 1995. Among adults aged 65 and older, over half (53.1%) reported that they had been told they had high cholesterol levels, 47.4% of men and 57.3% of women.

Physical Inactivity. The effect of physical inactivity on the development and progression of dementia and AD has been the focus of numerous studies. Research suggests that physical exercise can prompt the development of new brain cells while also triggering the release of a substance that can protect the cells (52). Scientists examining physical exercise at midlife and subsequent risk of dementia among members of the HARMONY study, using participants from the Swedish Twin Registry, followed twin pairs for an average of 31 years prior to dementia assessment, measuring levels of exercise. They found that light exercise such as walking and gardening was associated with lower odds of dementia compared with little or no exercise (53). Supporting these findings was a study conducted by researchers at the University of Washington, who followed 1,740 people aged 65 years and older over an average period of 6.2 years. Those who exercised at least three times a week were 38% less likely to have developed dementia than those who exercised less than three times a week (54). Participants aged 65 and over who participated in the Cardiovascular Health Cognition Study from 1992-2000 were also found to be significantly less likely to develop dementia at follow-up if they had engaged in moderate leisure-time physical activity than those who had engaged in little or no activity (55). The findings suggest that midlife physical activity may be associated with a reduced risk of AD or vascular dementia in later life.

Physical Inactivity in West Virginia. In 2006, the state ranked 12th among the 50 states and the District of Columbia in physical inactivity. In that year, the overall prevalence of physical inactivity among adults in West Virginia reported to the BRFSS was 28.2% (Table 3). Women were significantly more likely to report no leisure-time activity than men (30.7% vs. 25.6%, respectively). While decreasing significantly from a rate of 45.3% in 1994, the rate of physical inactivity has edged back up from a low of 24.5% reported in 2004. Among older adults aged 65 and over, the gap between men and women in 2007 was even more pronounced: Nearly four out of 10 (38.7%) older women reported no leisure-time physical activity, compared with 29.3% of older men.

Obesity. As reported in *The Journals of Gerontology Series A*, participants in the Swedish Twin Aging Study (56) were examined to determine if there existed a link between being overweight in midlife and the subsequent development of dementia. The findings showed a direct association between higher midlife body mass index (BMI) and lower general cognitive ability and significantly steeper progression of dementia in late life. In 2007, a review of eight studies on increased BMI as a risk factor for dementia was conducted; four of those studies found a significantly increased risk of dementia with elevated BMI after adjusting for factors including age, smoking, and comorbidities (57). There is what has been called an "obesity paradox," however. Researchers analyzing data from the Cardiovascular Health Study (58), for example, found a significantly increased risk of dementia for middle-aged participants who were obese (BMI 30+); this association was not found among the elderly, with the risk of dementia reduced among those who were obese and increased among those who were underweight (BMI <20).

Obesity in West Virginia. According to 2008 BRFSS data, West Virginia ranked 3rd in the nation in the rate of obesity (BMI 30+) among all adults aged 18 and older (Table 3). The state's rate of 31.9% was markedly higher than the U.S. median of 26.7%. Men and women had similar rates of being obese, 32.3% and 31.6%, respectively. The highest rates of obesity for both sexes were found in middle age (42.2% and 34.1% for men and women, respectively, for ages 45-54; 41.6% and 37.1% for men and women, respectively, for ages 55-64). When obesity and overweight are combined (BMI 25+), West Virginia ranked 1st in the U.S. in 2008, with 68.8% of the state's adult population at an unhealthy weight. More than eight out of every 10 men and nearly seven out of every 10 women in middle age (45-64) were either overweight or obese.

Poor Nutrition. Diets deficient in fruits and vegetables have been known to increase the risk for cardiovascular disease, and studies are now showing that inadequate consumption of fruits and vegetables may lead to an increased risk of dementia as well. A 1999-2000 French study of over 8,000 participants aged 65 and older revealed on re-examination after four years that frequent (daily) consumption of fruits and vegetables was associated with a decreased risk of all-cause dementia (59). Data from the Cache Country Study on Memory, Health and Aging supported these findings, showing that higher intakes of fruits and vegetables over the eight-year study period from 1995-2003 resulted in a decreased risk of dementia and AD. The participants who consumed five or more servings of fruits and vegetables daily scored the highest on cognitive function tests, compared with those who consumed fewer servings (60).

Poor Nutrition in West Virginia. The BRFSS includes self-reported data on fruit and vegetable consumption, reporting the prevalence of respondents who consume the recommended five or more servings per day. In 2007, eight out of 10 (80.3%) West Virginia adults reported eating fewer than five fruits and vegetables daily, 84.9% of men and 75.9% of women (Table 3), with the state ranked 9th overall among the 50 states and the District of Columbia. Among respondents aged 65 and older, 77.3% did not eat the recommended number of fruits and vegetables, 82.0% of men and 73.9% of women.

Diabetes. Research continues to support the association between Type 2 diabetes and the development of dementia in later life. Scientists analyzing data from the Swedish Twin Aging Study found a significantly greater risk of dementia, both vascular dementia and AD, among people who have diabetes, especially if the onset of diabetes occurs in middle age (61). The same researchers also found a link between borderline diabetes and increased risks of dementia and AD, even when controlling for the future development of diabetes (62). Their findings also suggested that the presence of borderline diabetes may interact with hypertension to multiply the risk for dementia. The Cache County Memory Study found a significant association between Type 2 diabetes and vascular dementia (63); an association between diabetes and AD without vascular dementia was found to be significant among men but not among women.

Diabetes in West Virginia. BRFSS data have shown an increasingly high rate of diabetes among West Virginia's adults, ranging from 4.7% in 1995 to a high of 12.1% in 2006. The overall state prevalence in 2008 was 11.9%, 12.1% among men and 11.8% among women (Table 3). West Virginia's 2008 rate was the highest among the 50 states and the District of Columbia and was 43% higher than the U.S. median of 8.3%. Older state residents reported a rate of 22.8%: 26.4% of men and 20.2% of women aged 65 and over reported having been told they had diabetes.

PREVENTION OF DEMENTIA

Although the causes of dementia are not yet defined and there is currently no cure, there is growing evidence that certain measures can be taken that will postpone the onset of the disease and/or slow its progression.

Cardiovascular Risk Factors. According to Marilyn Albert, a Johns Hopkins University researcher with the Alzheimer's Association, "All the things that we know are bad for your heart turn out to be bad for your brain" (64). Not only is it important to your cardiovascular health to maintain a healthful lifestyle, it is increasingly evident that it is important to your brain's health as well. In the preceding section of this report, the associations between modifiable health behaviors and the development or progression of Alzheimer's disease (AD) and other dementias were discussed. Studies are showing an increasingly high association between the components of metabolic syndrome, i.e., insulin resistance or diabetes, visceral obesity, hypertension, and high cholesterol levels, that are known cardiovascular risk factors and the development of AD or dementia. **Not smoking, maintaining a healthy weight, being physically active, achieving good HDL cholesterol and blood pressure levels, and controlling blood glucose levels all appear to provide some protection against dementia. Good nutrition is essential in addressing many of these risk factors.**

The Mediterranean diet, which includes a high consumption of fruits, vegetables, legumes, grains, fish, and mono- or polysaturated fats combined with a low consumption of red meat and saturated fats, has long been shown to lower risk for cardiovascular disease, as well as some cancers. Recent evidence shows that it is also a brain-healthy diet. Scarmeas et al published findings in 2006 indicating that a higher adherence to the Mediterranean diet resulted in a lower risk for AD (65). A follow-up study released in 2007 found that adherence to the diet influences not only risk for AD but also the subsequent disease course, with higher adherence associated with lower AD mortality (66). A study at Chicago's Rush-Presbyterian-St. Luke's Medical Center involving 815 elderly Chicago residents found that the study participants who ate large quantities of polyunsaturated fats (found in vegetables and nuts) experienced a 70% reduction in the risk of developing AD compared with those who ate small amounts (67). Those people who ate

You are what you eat: Studies have shown that the Mediterranean diet, with its emphasis on fruits, vegetables, grains, fish, and healthy fats, is associated with a lower risk for AD.

large quantities of saturated (animal-based) fats, on the other hand, had double the risk of AD compared with people who ate small amounts.

The association between the DASH (Dietary Approaches to Stop Hypertension) diet and dementia was studied by researchers in the Cache County Study on Memory, Health and Aging (68). The DASH diet also emphasizes the generous consumption of fruits, vegetables, low-fat or nonfat dairy products, whole grains, lean meats, and fish and poultry. The researchers found high adherence to the DASH diet lowered dementia risk, supporting the findings of the proponents of the Mediterranean diet.

Other scientists have determined that a diet high in the omega-3 fatty acid DHA (docosahexaenoic acid) that is found in cold water fish such as salmon, halibut, and tuna can help protect the brain against the cell damage caused by AD. A UCLA study used genetically modified mice that developed brain lesions similar to those found in advanced AD to study the effects of diet on the brain cells (69). Those mice fed a diet high in the omega-3 fatty acid DHA did not suffer the memory loss or cognitive damage evidenced by the mice whose diets did not include the supplement. According to Dr. Greg Cole, the study's senior author, "This is the first proof that our diets affect how our brain cells communicate with each other under the duress of Alzheimer's (70)." Researchers in the Chicago study noted above also found a positive association between eating fish at least once a week and a lowered risk of AD (67).

Data are more inconsistent on the effects of antioxidants such as beta carotene and vitamins C and E on the risk of dementia. Antioxidants combat free radicals, or charged particles, that are generated by normal metabolism but can over time damage cells, including neurons, and thus contribute to dementia. Scientists have been hopeful that taking antioxidant supplements or eating a diet rich in antioxidants could help prevent dementia. The results of studies to date, however, have been mixed. Scientists in the Netherlands conducted the Rotterdam Study, a population-based, prospective cohort study, following 5,395 participants aged 55 and older for 10 years, and examining their diets over the duration. The study's authors found that a high dietary intake of Vitamins C and E was associated with a lower risk of AD, a relationship most pronounced among smokers (71). Similarly, researchers at Chicago's Rush-Presbyterian-St. Luke's Medical Center found separate, positive relationships between dietary Vitamin E intake and dietary niacin and a lowered risk of AD (72). However, no association was found in the Chicago study between intake of Vitamin C, beta carotene, and Vitamin E from supplements and risk of AD.

Scientists analyzing data from the Cache County Study, a prospective study of 4,740 elderly (65 and older) participants in Cache County, Utah, found that use of Vitamin C and E supplements in combination was associated with reduced AD prevalence and incidence (73). They found no evidence, however, of reduced risk with Vitamin E or C supplements alone, with multivitamins alone, or with Vitamin B-complex supplements.

A report published in the *Journal of Geriatric Psychology and Neurology* in September 2009 confirms an association between Vitamin D and cognitive impairment, a precursor to dementia (74). The study, based on nearly 2,000 adults aged 65 and older, found that those participants with the lowest levels of Vitamin D were more than twice as likely to be cognitively impaired as those with optimum levels of the vitamin. Older people absorb less Vitamin D from sunlight, suggesting that supplements of the vitamin may play a role in decreasing the risk for dementia.

Researchers at the Children's Hospital and Research Center in California have published a 2004 study suggesting that iron deficiency may lead to the destruction of brain cells and progressive dementia (75). According to their research, when too little heme, a form of iron, is present in brain cells, the cells respond by overproducing the substance, which then reacts with oxygen to produce free radicals that cause the cell damage. The study's authors recommend sufficient iron as a way to slow down or delay the onset of dementia.

"Use It or Lose It." Research increasingly shows that engaging in intellectual activities may help keep a person mentally sharp in their senior years. The Nun Study, a longitudinal study of aging begun in 1986 and carried out by researchers at the University of Kentucky (and recently moved to the University of Minnesota), examined the autobiographies of nearly 100 nuns written as young women (76). Those women who evidenced low linguistic ability in early life were found to be more likely to develop AD in later years. The Einstein Aging Study conducted by Verghese et al studied the relationship between leisure activities and the risk of dementia in a prospective cohort of 469 subjects older than 75 years. Their findings, published in the *New England Journal of Medicine* in 2003 and *Neurology* in 2009 (77,78), showed that reading, playing cards or board games such as chess, checkers or Scrabble, and playing a musical instrument all correlated with a lower risk of developing dementia, both AD and vascular dementia. In addition, the more frequent the activity, the lower the risk. The later study found the association between delay of memory decline and frequent cognitive activity in old age to be valid even when controlling for past cognitive activity and early educational level.

Use it or lose it: Research shows that engaging in intellectual activities may help keep a person mentally sharp in their senior years. Scientists speculate that mentally engaged people build up a "brain reserve" that might delay the onset of dementia.

Scientists speculate that mentally engaged people build up a "brain reserve" that protects them from dementia (79,80). Intellectual activity causes the brain cells of these individuals to establish more complex connections that are more resistant to damage. They also suggest that mental stimulation may cause new brain cells to grow, delaying the onset of dementia's symptoms. Researchers at Case Western Reserve University School of Medicine studied the link between having a mentally demanding occupation and the later development of AD (81). They found that people in mentally challenging occupations in their thirties, forties, and fifties were less likely to develop AD.

NSAIDS. The possibility that inflammation in the brain plays a role in the development of AD has led scientists to study the effect of NSAIDs (nonsteroidal anti-inflammatory drugs) on the risk of dementia. While several studies have shown a positive association between the taking of NSAIDs and a reduced risk of dementia, there have been contradictory findings on which NSAIDs work best, if NSAIDs should be given in combination with antioxidant supplements, and the duration of use necessary to have a preventive effect (82,83,84). Because of the risks of long-term NSAID use, i.e., gastrointestinal bleeding and stomach ulcers, and the questions that remain on the overall benefit and timing of taking NSAIDs as a protective measure against dementia, most doctors advise against their use for this purpose at this time.

Statins. The growing evidence between cholesterol levels and the risk of dementia has resulted in numerous studies being conducted on the use of statins, cholesterol-lowering medications, in the prevention of dementia, with contradictory findings to date on their benefit. Researchers at the University of Kuopio in Finland followed 17,257 participants aged 60 and older over 12 years. Their findings, presented at the 2009 ICAD, indicated that the use of statins decreased the risk of developing dementia by more than half (85). The results of the Cardiovascular Health Study, a longitudinal study of nearly 6,000 people aged 65 and older, however, did not find an association between statin therapy and a decreased risk of dementia (86). A review of studies published in April 2009 found that the medications did not prevent dementia (87). Research is continuing into the potential of statins to prevent dementia if begun in middle age rather than in later life.

Insulin Therapy. As the relationship between metabolic syndrome and dementia is further investigated, many scientists are concentrating on the role of insulin resistance or diabetes in the development of the disease. It is known that insulin is vital in memory and learning, a necessary component of cell survival and memory formation. Research suggests that insulin resistance in the brain is associated with cognitive impairment and AD-type neurodegeneration (88). Some scientists have called AD "Type 3" diabetes because of the link between insulin resistance and the development of the characteristic tangles and toxic protein buildup found in the brains of people with AD. Insulin was shown in a Northwestern University study to reduce the damage to the brain's neurons by blocking the

attachment of these toxic proteins (89). The possible use of insulin as a preventive mechanism for AD is the subject of continued research.

Vaccine. Attempts to develop an immunization to prevent or delay AD are ongoing worldwide. Most research centers around using the body's own immune system to generate antibodies to attack and clear the beta-amyloid plaques found in the brains of AD patients. An experimental drug tested on 300 human subjects in 2000-2001 slowed memory decline, but clinical trials were halted when 18 participants developed brain inflammation. Another clinical trial of a potential AD vaccine, ACC-001, was halted in 2008 due to potential side effects, including skin lesions (90).

Research continues at many institutions, including the Ohio State University Medical Center, where scientists are studying the effects of an experimental drug called bapineuzumab on patients diagnosed with mild to moderate cognitive impairment (91) and the University of Rochester Medical Center, where animal studies have showed success with a drug designed to prevent the accumulation of amyloid plaques in the brain (92). A paper published in *The Lancet* in 2008 described the efforts of scientists at the University of Southampton, whose experimental vaccine stopped the buildup of plaque in the brains of study participants, who had moderate AD, but did not reverse their dementia (93). Scientists at the University of Zaragoza in Spain hope to begin human trials on a new vaccine therapy in 2010, focusing their investigation on healthy participants who have no sign of dementia at the start of the trial (94). Other experimental therapies are ongoing using both animal and human subjects. Even a modest delay of the onset of AD/dementia would save billions of dollars in health care related expenses as well as reducing the suffering of dementia patients and their families. Caregivers of dementia patients are likely to be elderly and in poor health themselves. The stress that accompanies caring for someone with dementia can result in poor mental, physical, and financial outcomes for family members as well as the patient.

DIAGNOSIS OF DEMENTIA

As treatments for Alzheimer's disease (AD) and vascular dementia can be different, early determination of the type of dementia from which a patient is suffering is vital. Similar symptoms often make diagnosis difficult, however, unless a patient has experienced recognizable strokes. Neuroimaging techniques, often utilizing more than one type of imaging, are emerging that allow the differentiation between AD and other dementia at earlier stages of the diseases. In a 2007 study, a position emission tomography (PET) scan that measured the uptake of sugar in the brain identified cases of frontotemporal dementia, often misdiagnosed as AD, in 90% of cases (95).

Special types of PET scans are also being studied to detect AD in its early stages. Early success in detecting the brain proteins associated with plaque formation of AD was shown in a Finnish study of a PET scanning technique using a PET tracer called PiB (Pittsburgh Compound B) (96). Researchers at the Mayo Clinic published results of a study in May 2009 in *Brain* that implicated complementary roles for PiB imaging and MRI in determining and following the progression of AD (97). The Blanchette Rockefeller Neurosciences Institute (BRNI) at West Virginia University is currently studying a biomarker of AD-related inflammation in skin cells called fibroblasts. The presence of the biomarker indicates the presence of the protein responsible for AD development. Early results show a 98% accuracy rate when patients who died during the study period were autopsied (98).

The early diagnosis of AD and vascular dementia through neuroimaging and other techniques such as the BRNI test could determine the proper treatment for these diseases, prolonging productive life and decreasing suffering for patients and their families. As new medications become available, neuroimaging will also allow researchers to monitor their efficacy in slowing the progression of, or even eventually reversing the damage done by, the diseases.

The majority of doctors currently rely on several evaluations to diagnose AD. These include:

- a patient's medical history
- a mental status evaluation that assesses memory, communication and cognitive skills, and the ability to perform simple math problems
- a physical examination to assess the patient's blood pressure, pulse, and nutritional status and evaluate the nervous system
- basic laboratory tests, i.e., blood and urine, to rule out other causes of dementia
- a psychiatric examination, also to rule out other causes

Using these evaluations, doctors can accurately diagnose AD in 90% of cases. A definitive diagnosis remains an examination of the brain tissue itself.

DRUG THERAPY FOR DEMENTIA

There are currently no cures for the types of dementia covered in this report. There are, however, a handful of medications that have been shown to slow progression and lessen symptoms of both Alzheimer's disease (AD) and vascular dementia. The majority of drugs being used currently to treat AD, which also appear to help people suffering from vascular dementia, fall under the classification of cholinesterase inhibitors, which prevent the breakdown of acetylcholine. Acetylcholine is a chemical messenger used by neurons in the hippocampus and the cerebral cortex, areas important in thinking and memory skills. Four cholinesterase inhibitors have been approved by the FDA to treat mild to moderate AD symptoms: donepezil (Aricept), rivastigmine (Exelon), galantamine (Razadyne), and tacrine (Cognex), which was the first cholinesterase inhibitor approved but currently is rarely prescribed because of serious side effects and safety concerns.

There are currently no cures for dementia. There are, however, a handful of medications that have been shown to slow progression and lessen symptoms of AD and vascular dementia.

Another class of drugs approved to treat AD and vascular dementia is that of NMDA receptor agonists, which regulate the activity of glutamate, another brain chemical involved in memory function. Only one drug in this class, memantine (Namenda), had been approved to treat AD by 2009, but others are in clinical trials. Memantine may delay loss of daily function in patients with moderate to severe AD.

Medications for the behavioral symptoms that accompany AD include anti-anxiety medications for agitation and aggression. Anti-psychotic medications are often used to treat feelings of suspicion and paranoia that an AD patient can suffer,

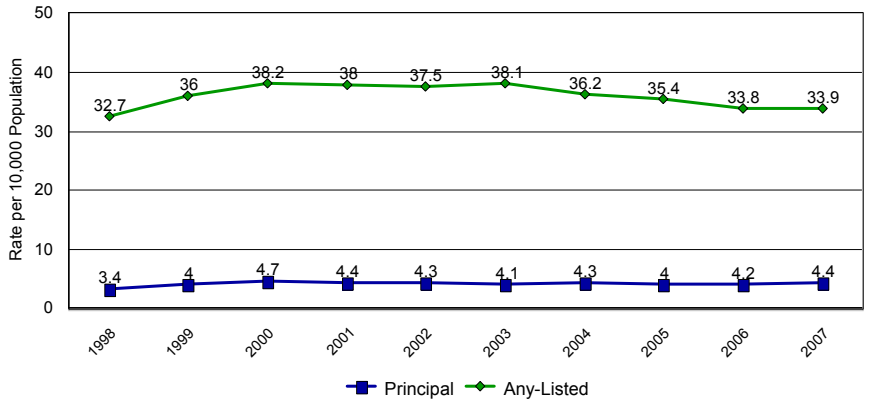
Additional recommended treatments for vascular dementia include those that treat the underlying causes of the condition, e.g., hypertension, diabetes, and high cholesterol. The primary goal of this treatment is to prevent further strokes or narrowing of the arteries. Hypertensive agents are often prescribed, as are medications to reduce cholesterol levels. Antiplatelet agents that lower blood viscosity are frequently prescribed. Antidepressant drugs may be used to treat the depression that often accompanies vascular dementia.

HOSPITAL DISCHARGE DATA ON DEMENTIA

Hospital discharge data provide an additional source of information on the prevalence of disease and the burden on the state. Data from the West Virginia Health Care Authority (WVHCA) were used to determine the rate of hospitalizations that included any diagnosis of dementia. The WVHCA collects inpatient data from all nonfederal licensed hospitals in the state and Medicare data on West Virginia residents hospitalized in out-of-state hospitals. Up to nine diagnoses (one principal and eight secondary) are recorded and coded according to the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM).

1998-2007 Hospitalizations. The overall rates of hospital discharges among state residents with either a principal or an any-listed (principal or secondary) diagnosis of dementia from 1998 through 2007 are presented in Figure 1. Rates of an any-listed dementia diagnosis ranged from a low of 32.7 per 10,000 discharges in 1998 to a high of 38.2 per 10,000 in 2000; in 2007, the rate of discharges with an any-listed diagnosis of dementia was 33.9. The rate of dementia as a principal diagnosis increased 29% between 1998 and 2007, from 3.4 to 4.4 per 10,000 discharges.

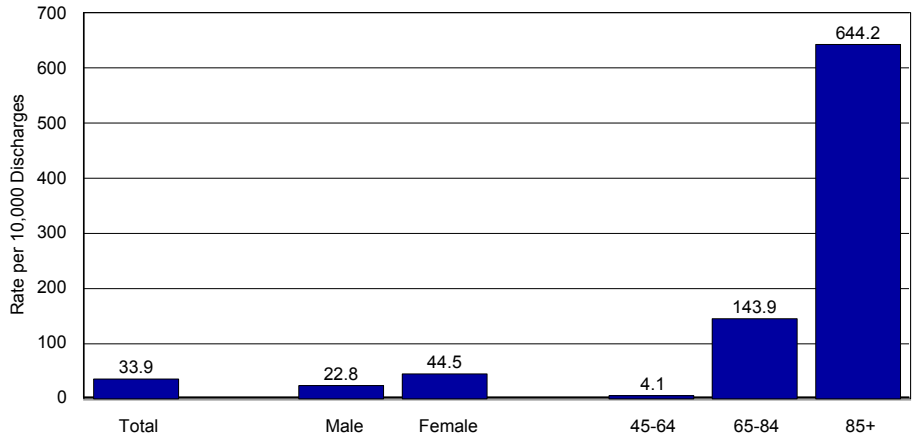
Figure 1. Hospital Discharge Rates for Principal or Any-Listed Diagnoses of Dementia (Alzheimer's Disease or Other Dementia) West Virginia Resident Hospitalizations, 1998-2007



NOTE: Alzheimer's Disease: ICD-9 331.0; Other dementia: ICD-9 290.0-290.4, 294.1
Source: WVHSC

2007 Hospitalizations by Gender and Age. Women were markedly more likely to have a hospital discharge diagnosis of Alzheimer's disease (AD) or other dementia than men in 2007 (Figure 2). The rate for women was 44.5 per every 10,000 discharges, compared with a rate of 22.8 for men. The rate for patients aged 65 through 84 was 143.9 discharges per 10,000; than for patients aged 85 and older was 644.2.

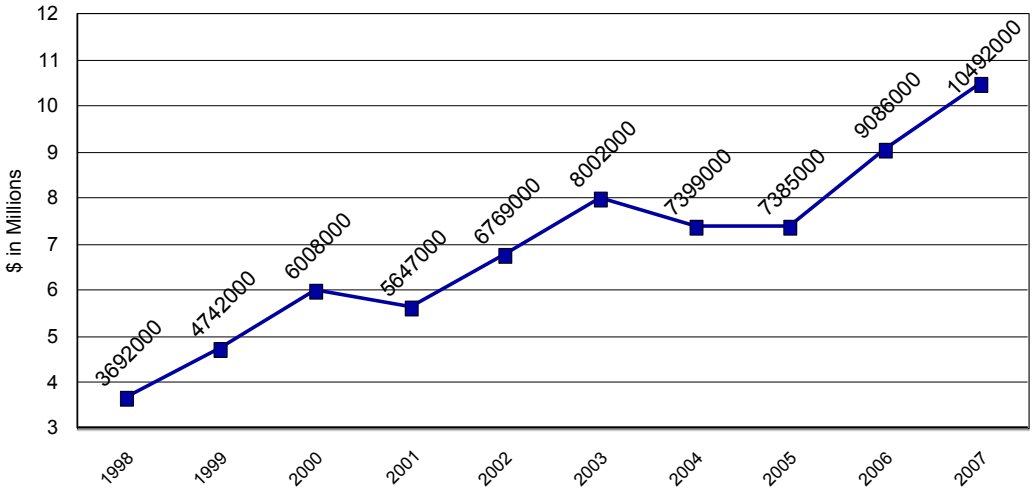
Figure 2. Hospital Discharge Rates for Any-Listed Dementia Diagnosis
(Alzheimer's Disease or Other Dementia) by Gender and Age
West Virginia Resident Hospitalizations, 2007



NOTE: Alzheimer's Disease: ICD-9 331.0; Other dementia: ICD-9 290.0-290.4, 294.1
Source: WVHSC

2007 Hospitalization Charges. The estimated total charges billed for hospitalizations with a principal diagnosis of dementia increased from $3,692,000 in 1998 to $10,492,000 in 2007 (Figure 3), an increase of 184%.

Figure 3. Estimated Charges for Hospital Discharges Having
A Principal Diagnosis of Dementia (Alzheimer's Disease or Other Dementia)
West Virginia Resident Hospitalizations, 1998-2007

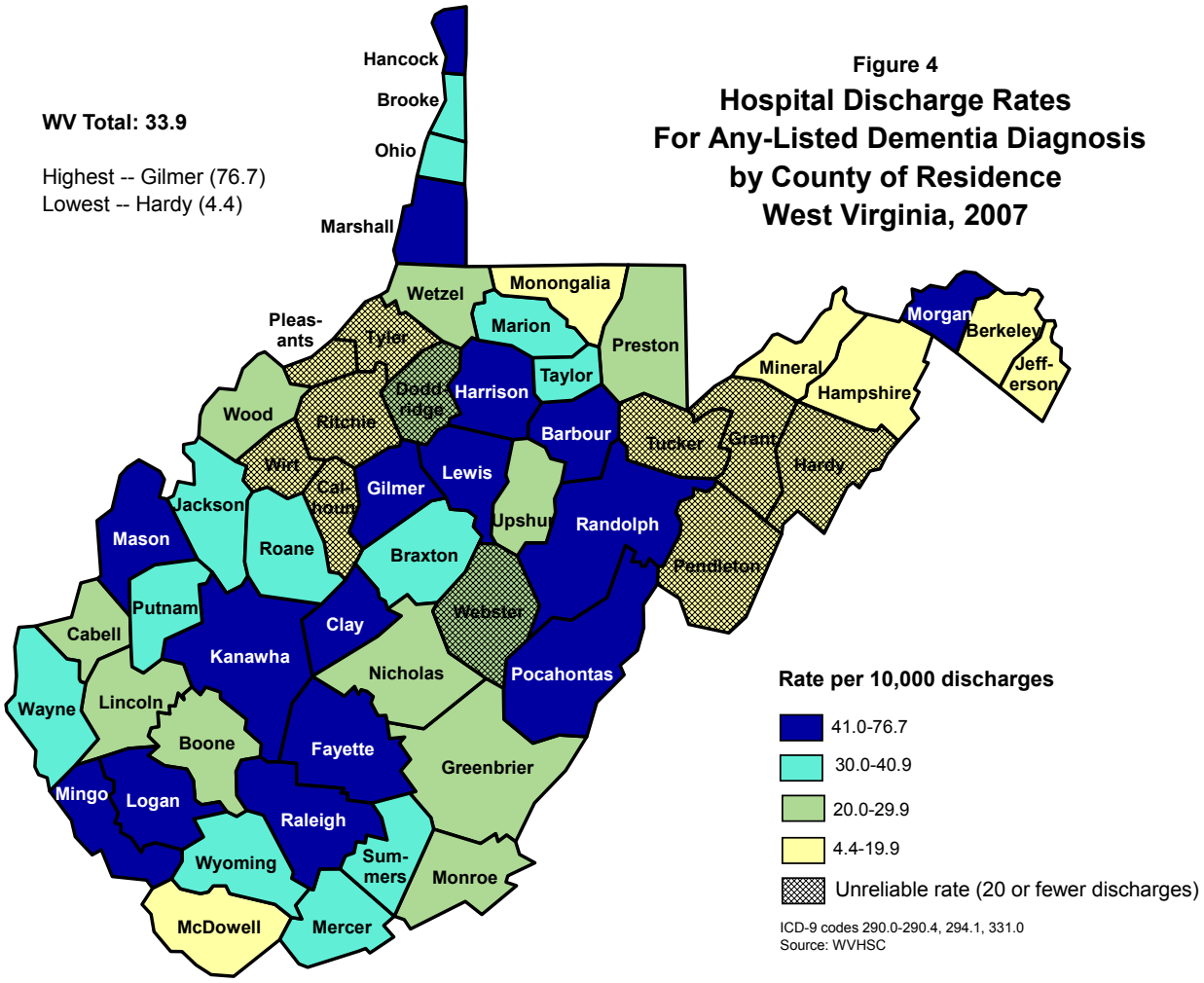


NOTE: Alzheimer's Disease: ICD-9 331.0; Other dementia: ICD-9 290.0-290.4, 294.1
Sources: WVHSC

Comparison of 2007 Hospitalization Rates for WV and US. Table 4 presents rates of hospital discharges with a dementia diagnosis for West Virginia and the United States. While overall rates for hospital discharges among patients with a diagnosis of AD were 29.1% higher in the state than in the nation (24.4 per 10,000 discharges vs. 18.9, respectively), similar rates were noted for total discharges with other dementia diagnoses. No marked differences in discharge rates were found among men; among women, however, state residents had higher hospital discharge rates for both AD and other dementia than did women nationwide. Higher rates were noted for state residents in all age groups for AD, with the reverse seen for other dementia diagnoses.

Table 4. Rate (per 10,000) of Resident Hospital Discharge Records Having an Any-Listed Diagnosis of Alzheimer's Disease or Other Dementia, By Gender and Age West Virginia and United States, 2007				
	West Virginia		United States	
	Alzheimer's	Other	Alzheimer's	Other
Total	24.4	27.2	18.9	26.2
Gender				
Male	15.5	18.7	13.7	20.5
Female	32.9	35.3	24.0	31.8
Age				
45-64	1.9	3.5	1.7	4.1
65-84	104.8	114.2	95.7	131.4
85+	472.7	518.6	447.7	596.0
NOTE: Alzheimer's Disease ICD-9 331.0; Other dementia ICD-9 290.0-290.4, 294.1				

2007 County-Specific Hospitalization Rates. The rate of hospital discharges having either a principal or secondary, i.e., any-listed, diagnosis of dementia in 2007 ranged from a high of 76.7 per 10,000 discharges in Gilmer County to a low of 4.4 in Hardy County (Figure 4). Individual county numbers and rates are listed in Appendix A.



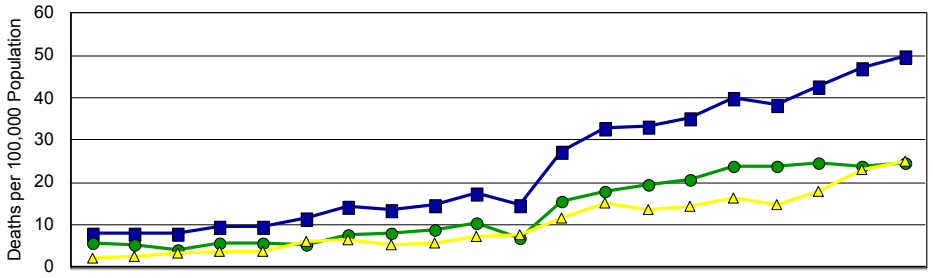
DEMENTIA MORTALITY

Most people who suffer from dementia do not die from the disease itself but rather from another cause such as pneumonia, heart disease, or complications from a fall. In recent years, however, the rate of deaths with Alzheimer's disease (AD) or other dementias as the underlying, or principal, cause of death has increased. AD first appeared in the 10 leading causes of death in West Virginia in 2000; nationally this occurred in 1999. By 2007, AD and other dementias combined (i.e., "dementia") represented the 5th leading cause of death in the state (separately, other dementias represented the 7th leading cause, while AD was the 8th leading cause). Total dementia accounted for 5.4% of all 2007 deaths among West Virginia residents (1,139 out of 21,067). In the United States in 2006 (the latest data available at the time of this report), AD was the 7th leading cause of death; other dementias were not included in the national top 10 causes.

> Dementia was the 5th leading cause of death in West Virginia in 2007, accounting for 5.4% of all deaths in that year.

Figure 5 shows the state trends in mortality from AD, other dementias, and total dementia from 1988 through 2007. A change in cause of death classification occurred between 1998 and 1999, which is reflected in the rates shown in the graph.[1] Although this shift in coding resulted in increased rates, the trends evidenced both before and after the coding change are apparent. Between 1988 and 1998, the rate of total dementia grew by 81.7%; between 1999 and 2007, the rate increased 82.8%. These increases are seen both in mortality from AD and mortality from other dementias. In addition to the coding change, the higher rates can be attributed to an enhanced awareness of AD and other dementias, earlier diagnosis of the illnesses, and an aging population.

Figure 5. Mortality Rates* for Alzheimer's Disease and Other Dementias
West Virginia Residents, 1988-2007



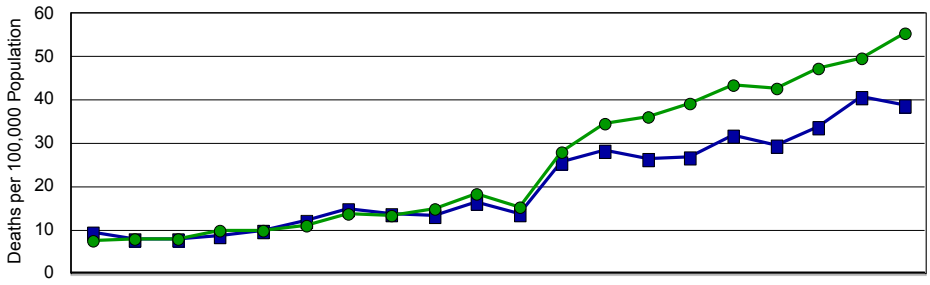
	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Total	8.2	8.1	7.9	9.5	9.7	11.6	14.3	13.5	14.7	17.6	14.9	27.3	32.9	33.2	35.2	40	38.4	42.7	47.2	49.9
AD	5.9	5.4	4.3	5.9	5.9	5.3	7.7	8.1	9	10.3	7.1	15.7	17.8	19.5	20.6	23.8	23.7	24.7	24	24.8
Other	2.3	2.6	3.5	3.6	3.8	6.3	6.6	5.4	5.7	7.3	7.7	11.7	15.1	13.6	14.5	16.2	14.7	18	23.2	25.1

*Rates are age adjusted to the 2000 U.S. standard million
NOTE: Alzheimer's (1988-1998: ICD-9 331.0; 1999-2007: ICD-10 G30-G31); Other Dementias (1988-1998: ICD-9 290.0, 290.4-294.1; 1999-2007: ICD-10 F01, F03)
Source: WVHSC

[1] A new cause-of-death classification, International Classification of Disease, Revision 10 (ICD-10), was introduced in 1999, superseding ICD, Revision 9 (ICD-9) codes that had been in use since 1979. The difference in coding is responsible for the large increase in rates seen between 1998 and 1999.

Figure 6 illustrates the upward trend in dementia mortality by gender over the same 20-year period. While the increase is apparent in both sexes, with similar rates until 1999, women have been more likely to die from dementia than men since 2000, with an increasing gap noted.

Figure 6. Mortality Rates* for Dementia (Alzheimer's Disease and Other Dementias)
By Gender, West Virginia Residents, 1988-2007

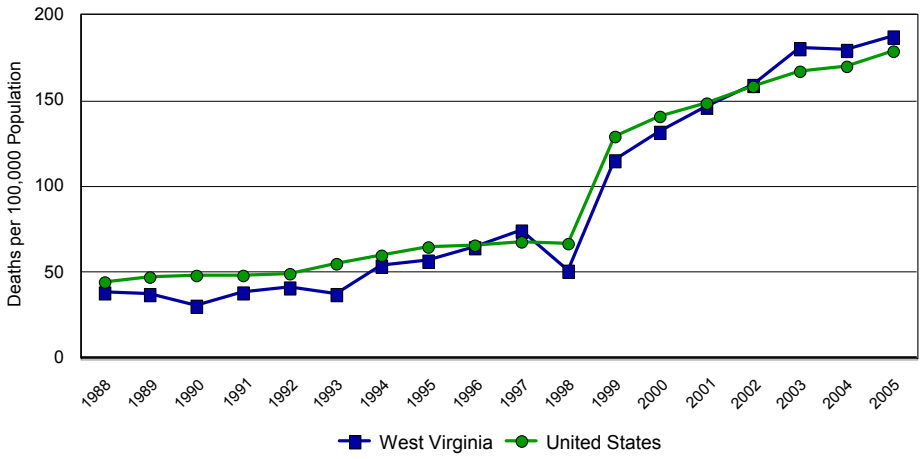


	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Males	9.3	8.1	8.1	8.6	9.7	12.2	14.8	13.8	13.4	16.3	13.9	25.6	28.5	26.6	26.9	32.1	29.5	33.8	40.7	38.9
Females	7.7	8	7.8	9.8	9.7	11.2	13.8	13.4	15	18.4	15.2	27.9	34.8	36.1	39.3	43.7	42.6	47.3	49.7	55.6

*Rates are age adjusted to the 2000 U.S. standard million
NOTE: Alzheimer's (1988-1998: ICD-9 331.0; 1999-2007: ICD-10 G30-G31); Other Dementias (1988-1998: ICD-9 290.0, 290.4-294.1; 1999-2007: ICD-10 F01, F03)
Source: WVHSC

At the time this report was prepared, the National Center for Health Statistics (NCHS) had published (on-line) mortality rates through 2005 for 113 selected causes, including AD (but not other dementias). The data presented in Figure 7 reflect AD death rates for persons aged 65 and older (both sexes and all races), comparing United States rates with West Virginia rates. Overall age-specific rates were similar in both the state and the nation over the time period examined.

Figure 7. Mortality Rates for Alzheimer's Disease among Persons Aged 65+
West Virginia and United States, 1988-2005



NOTE: Alzheimer's Disease 1988-1998: ICD-9 331.0; 1999-2007: ICD-10 G30
Sources: WVHSC; National Vital Statistics System

Data on dementia mortality were aggregated for the years 1998-2002 and 2003-2007 in order to examine death rates on the county level. Figures 8 and 9 illustrate the dramatic change in dementia mortality among West Virginia's 55 counties between the two time periods. In 1998-2002, only four counties had mortality rates for dementia of 46.0 deaths per 100,000 population or above; by 2003-2007, 19 counties had rates of 46.0 or greater. The overall state rate increased from 28.9 in 1998-2002 to 46.8 in 2003-2007, an increase of 61.9%. Individual county numbers and rates are listed in Appendix B.

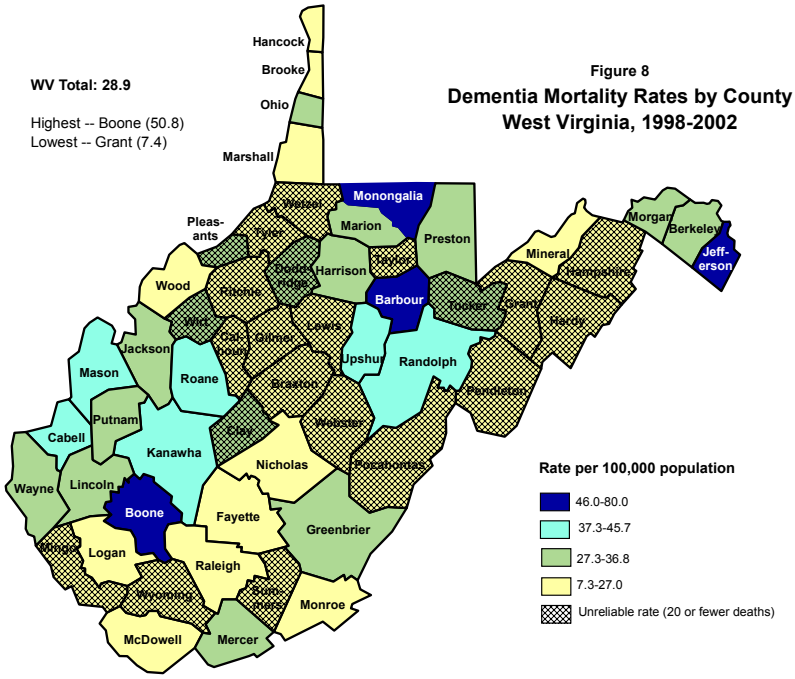


Figure 8
Dementia Mortality Rates by County
West Virginia, 1998-2002

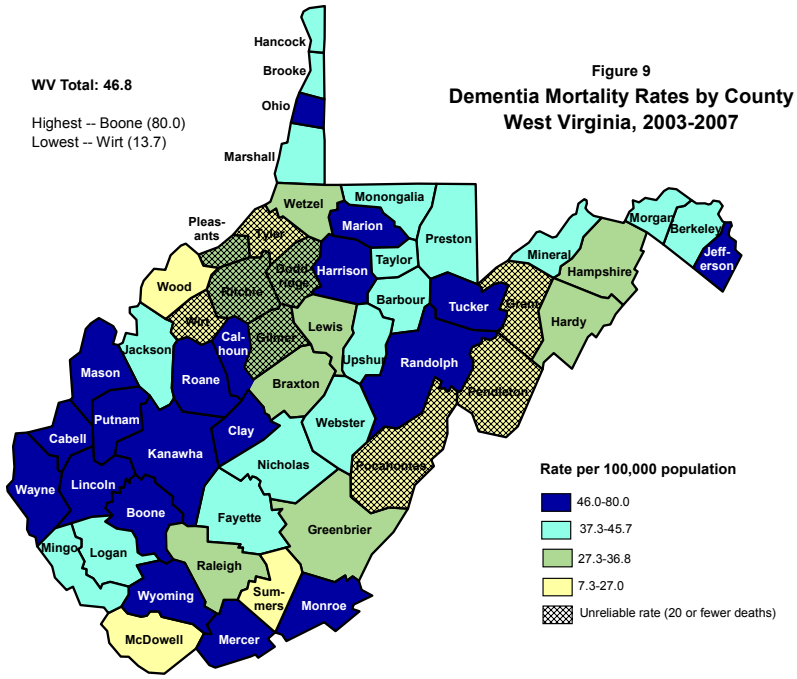
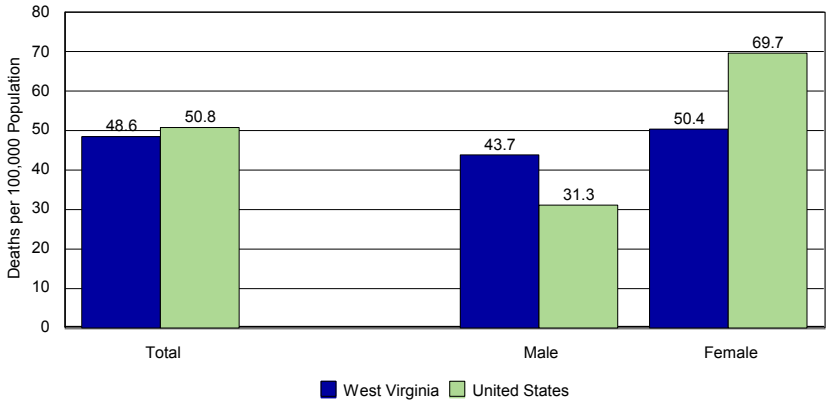


Figure 9
Dementia Mortality Rates by County
West Virginia, 2003-2007

The NCHS compiles and collects data on all deaths in the United States. This information is released on an annual basis and includes the following: decedent's age, sex, race, and state of residence; the underlying (principal) cause of death, and contributing (or any-listed) causes of death (up to 19 additional causes). The current analysis examines multiple-cause-of-death data related to dementia for West Virginia and the United States for 2006.

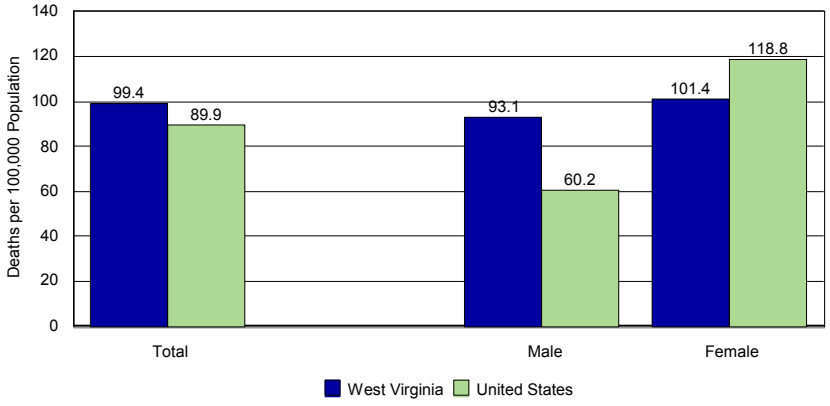
As shown in Figure 10, the overall mortality rate for dementia as the underlying cause of death was similar in the state and the nation (48.6 deaths per 100,000 population and 50.8, respectively). Distinct differences are seen in the rate by gender, however. The state rate among men was nearly 40% higher than that among men nationwide, while the state rate among women was approximately 28% lower than the national rate. The West Virginia overall mortality rate for dementia as an any-listed cause was over 10% higher than the United States rate (99.4 vs. 89.9) (Figure 11). The rate for dementia as an any-listed cause among men in the state was markedly higher than the national rate (93.1 vs. 60.2); the rate among women was lower in the state than in the nation (101.4 vs. 118.8). Table 5 presents mortality rates for underlying and any-listed causes of death by gender and age for West Virginia and the United States.

Figure 10. Mortality Rates* for Dementia as Underlying Cause of Death
West Virginia and United States, 2006



*Rates are age adjusted to the 2000 U.S. standard million.
NOTE: ICD-10 codes F01, F03, and G30-G31
Source: NCHS Multiple-Cause -of-Death tape, 2006

Figure 11. Mortality Rates* for Dementia as Any-Listed Cause of Death
West Virginia and United States, 2006



*Rates are age adjusted to the 2000 U.S. standard million.
NOTE: ICD-10 codes F01, F03, and G30-G31
Source: NCHS Multiple-Cause -of-Death tape, 2006

Table 5. Mortality Rates (per 100,000 Population) for Dementia* by Gender and Age West Virginia and United States, 2006 Multiple Cause of Death File				
	Underlying Cause		Any-Listed Cause	
	West Virginia	United States	West Virginia	United States
Male				
0-64	1.8**	0.9	3.0	1.6
65-74	48.3	45.3	111.6	88.2
75-84	393.1	326.2	829.1	644.0
85+	1400.2	1404.7	3001.7	2648.0
Total	**43.7**	**31.3**	**93.1**	**60.2**
Female				
0-64	0.5**	0.8	1.2**	1.4
65-74	43.8	41.3	99.1	73.4
75-84	383.7	361.3	811.5	637.5
85+	1936.7	2002.7	3722.3	3358.9
Total	**50.4**	**69.7**	**101.4**	**118.8**
Both Sexes				
0-64	1.2**	0.9	2.1	1.5
65-74	45.8	43.1	104.8	80.2
75-84	387.5	347.0	818.6	640.1
85+	35.2	1812.7	3504.0	3133.0
Total	**48.6**	**50.8**	**99.4**	**89.9**

*Dementia is classified as ICD-10 codes F01, F03, and G30-G31. Total rates for WV are age adjusted and were calculated using the 2006 population estimates and the U.S. 2000 standard million. Total rates for the U.S. are crude rates using the 2006 population estimates.

**Unreliable rate. Rate based on 20 or fewer deaths.

Source: NCHS Multiple-Cause-of-Death tape 2006

NOTE: The rates presented in Table 5 were calculated from an earlier version of the 2006 NCHS mortality file, one that did not contain all the deaths reported in the final mortality file for that year. This difference is reflected in the difference in the total rate for 2006 shown in Figure 5 on page 20.

DISCUSSION

Research on dementia treatment and prevention continues as the burden of dementia increases. This report has touched on just a few of the studies and findings to date in order to illustrate the extensive work that is being done. Mental health groups, universities, medical schools, the Blanchette Rockefeller Neurosciences Institute, the National Institutes of Health, the National Institute of Aging, numerous dementia and Alzheimer's organizations, and many other entities are working to discover ways to improve the lives of dementia patients and their families through treatment, behavioral management, and delayed onset or slower progression of disease. Study sites around the country are recruiting participants from minority populations including African-Americans, Latinos, Asian-Americans, and Native Americans to better understand the disease mechanism and burden on specific populations.

Current research has resulted in a growing number of pharmacological treatments, better diagnostic tests, and the hope of an eventual vaccine to prevent the disease or even reverse the damage in existing disease. Future clarification of the pathogenesis of the illness is occurring, resulting in a new generation of treatments. With the continued and successful refinement of gene therapy and neural transplantation techniques will come new breakthroughs. This cannot happen too soon. Alzheimer's disease and other dementias have the potential to overwhelm our health care systems if we do not significantly delay or prevent disease onset; this will most certainly happen in West Virginia, a state with the third oldest population in the nation. To quote Ed Duling, a West Virginia doctor who retired in 2004 after more than half a century in practice, "Senile dementia, Alzheimer's disease, is the big thing that's developed that we didn't have before. That's because people are living longer. Used to be, people died in their 50s. Now they live up into their 70s and 80s, and **they're outliving their brains**" (99). The challenge now is to find the key to keeping our brains healthy throughout our life spans.

Appendix A. Number and Rate of Inpatient Hospital Discharge Records Having an Any-Listed Diagnosis of Dementia By Patient's County of Residence West Virginia, 2007

	Estimated 2007 Population	Number	Rate*
Barbour	15,532	64	41.2
Berkeley	99,734	167	16.7
Boone	25,201	71	28.2
Braxton	14,639	58	39.6
Brooke	23,661	90	38.0
Cabell	94,435	269	28.5
Calhoun	7,201	7	9.7
Clay	10,120	49	48.4
Doddridge	7,262	17	23.4
Fayette	46,334	237	51.2
Gilmer	6,907	53	76.7
Grant	11,925	6	5.0
Greenbrier	34,586	100	28.9
Hampshire	22,577	42	18.6
Hancock	30,189	130	43.1
Hardy	13,661	6	4.4
Harrison	68,309	416	60.9
Jackson	28,223	112	39.7
Jefferson	50,832	84	16.5
Kanawha	191,306	862	45.1
Lewis	17,145	106	61.8
Lincoln	22,322	61	27.3
Logan	35,629	189	53.0
McDowell	22,991	44	19.1
Marion	56,728	226	39.8
Marshall	33,148	167	50.4
Mason	25,546	110	43.1
Mercer	61,350	226	36.8
Mineral	26,722	47	17.6
Mingo	26,755	110	41.1
Monongalia	87,516	168	19.2
Monroe	13,537	40	29.5
Morgan	16,351	70	42.8
Nicholas	26,160	78	29.8
Ohio	44,398	148	33.3
Pendleton	7,650	9	11.8
Pleasants	7,183	14	19.5
Pocahontas	8,571	43	50.2
Preston	30,254	73	24.1
Putnam	55,001	166	30.2
Raleigh	79,170	330	41.7
Randolph	28,292	116	41.0
Ritchie	10,371	19	18.3
Roane	15,295	47	30.7
Summers	13,202	40	30.3
Taylor	16,117	59	36.6
Tucker	6,868	6	8.7
Tyler	8,952	11	12.3
Upshur	23,508	62	26.4
Wayne	41,231	125	30.3
Webster	9,435	19	20.1
Wetzel	16,432	45	27.4
Wirt	5,809	11	18.9
Wood	86,088	235	27.3
Wyoming	23,674	86	36.3
WV Total	1,812,035	6,146	33.9

*Rate per 10,000 discharges. Use caution when interpreting and reporting rates based on fewer than 20 discharges.
Source: WVHSC

APPENDIX B. Dementia Deaths and Mortality Rates by County West Virginia Residents, 1998-2002 and 2003-2007									
County	**1998-2002**		**2003-2007**		**County**	**1998-2002**		**2003-2007**	
	#	**Rate***	**#**	**Rate***		**#**	**Rate***	**#**	**Rate***
Barbour	47	46.5	39	38.8	Monongalia	158	46.0	164	45.3
Berkeley	98	37.2	146	45.2	Monroe	21	26.4	38	52.4
Boone	63	50.8	100	80.0	Morgan	28	34.8	32	37.7
Braxton	18	18.3	36	36.8	Nicholas	28	19.4	62	43.4
Brooke	32	18.4	76	45.7	Ohio	110	30.3	165	48.2
Cabell	251	42.4	424	73.7	Pendleton	10	16.6	10	18.6
Calhoun	7	13.3	23	47.2	Pleasants	12	28.0	12	31.3
Clay	17	32.9	34	67.0	Pocahontas	6	8.7	16	25.8
Doddridge	12	30.7	14	35.9	Preston	47	28.6	65	39.1
Fayette	68	21.9	116	38.2	Putnam	60	29.6	129	60.2
Gilmer	9	18.9	13	28.6	Raleigh	78	16.9	160	35.1
Grant	5	7.4	15	21.6	Randolph	77	43.0	93	51.5
Greenbrier	75	30.8	84	34.0	Ritchie	9	14.5	20	31.9
Hampshire	16	15.3	30	27.3	Roane	32	37.3	60	71.3
Hancock	36	16.6	89	43.4	Summers	17	16.3	26	25.1
Hardy	14	21.1	22	32.0	Taylor	20	19.8	40	39.8
Harrison	139	29.6	225	48.4	Tucker	17	32.3	25	50.1
Jackson	42	27.9	58	38.3	Tyler	5	8.4	8	14.3
Jefferson	76	47.6	104	57.0	Upshur	59	39.4	58	38.4
Kanawha	487	38.2	790	64.5	Wayne	69	33.1	114	56.1
Lewis	19	16.9	31	27.3	Webster	6	10.3	23	40.1
Lincoln	30	29.6	55	54.0	Wetzel	11	9.9	32	30.5
Logan	35	19.0	73	43.5	Wirt	8	28.3	4	13.7
McDowell	29	17.1	38	26.1	Wood	85	15.8	116	21.9
Marion	129	30.5	234	55.7	Wyoming	20	18.6	52	50.2
Marshall	57	27.0	85	43.4	**WV Total**	3,034	28.9	4,854	46.8
Mason	58	42.7	74	55.8					
Mercer	133	31.4	200	48.6					
Mineral	24	15.6	59	39.1					
Mingo	15	12.1	43	41.5					

*Rates are per 100,000 population and are age adjusted to the 2000 standard million. The 1998-2002 rates are adjusted from the 2000 U.S. Census and the 2003-2007 rates are adjusted from the 2005 U.S. Census population estimates. Use caution when interpreting and reporting rates based on fewer than 20 deaths.
Source: WVHSC

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